Attentional Effects on Conditioned Inhibition of Discrete and Contextual Stimuli

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Dissertation submitted in partial fulfillment of
the requirements for the degree of
Doctor of Philosophy in the Department of
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ABSTRACT

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Abstract

In the present study, we examined the predictions of an attentional-associative model (Schmajuk, Lam, & Gray Journal of Experimental Psychology: Animal Behavior Processes, 22, 321–349, 1996) regarding the effect of attentional manipulations on both discrete and contextual conditioned inhibitors.

The SLG model assumes that non-reinforced presentations of an inhibitory conditioned stimulus (CS) do not decrease its inhibitory associations. However, the model predicts that extended presentations will decrease attention to the inhibitor, thereby, decreasing both the expression of its inhibitory power in a summation test and the rate of acquisition in a retardation test. The model also predicts that subsequent presentations of the inhibitory CS with a novel CS will increase both its inhibitory power in a summation test and the rate of acquisition in a retardation test. Using a predictive learning design in humans, Experiment 1 examined the predictions involving the summation tests, whereas Experiments 2 and 3 examined the predictions involving the retardation tests. Experimental results were in agreement with the predictions of the model.

The SLG model also predicts that a salient extinction context (CX) becomes inhibitory and prevents extinction of the excitatory CS-unconditioned stimulus (US) association. Although some data seem to contradict that prediction (e.g., Bouton and

King, 1983, Bouton and Swartzentruber, 1986, 1989), Larrauri and Schmajuk (2008) indicated that the CX might not appear inhibitory in a summation test because attention to the CX decreases with many but not few extinction trials. In a human predictive learning experiment, we confirmed the model's predictions that the inhibitory power of the extinction CX can be detected after a few extinction trials when attention to the CX is still high, but not after many extinction trials once attention to the CX has decreased (Experiment 4), and even after many extinction trials by presenting novel CSs to increase attention to the unattended CX (Experiment 5). Furthermore, using an eye-tracker, we confirmed the model's explanation of Experiment 4 results by showing decreased overt attention to the CX after many but not after few extinction trials (Experiment 6).

Importantly, the view that the extinction CX becomes inhibitory allows the model to explain spontaneous recovery (because attention to the excitatory CS increases before attention to the inhibitory CX), renewal (because the inhibition provided by the extinction CX disappears), and reinstatement (the inhibitory CX becomes neutral or excitatory), as well as a very large number of other experimental results related to extinction. Based on the prediction of the SLG, model the implications of our results for the treatments of anxiety disorders were discussed.

Dedication

I dedicate this dissertation to my wife, Banu. Without your help, support, and endurance this work would not be possible. I love you.

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I would like to express my deepest appreciation to my advisor Dr. Nestor Schmajuk. I have worked with Dr. Schmajuk for almost 5 years and learned so much from him and improved as a researcher thanks to his exceptional guidance. This dissertation is a product of our very fruitful collaboration.

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1. Introduction

In this dissertation, it is aimed to discuss the effects of attentional manipulations on the inhibitory power of conditioned stimuli. Chapter 1 of this dissertation describes the basic concepts and introduces a background for conditioned inhibition, extinction and extinction of conditioned inhibition. In Chapter 2, four associative models, the Rescorla-Wagner (1972), Wagner's (1981) SOP, Miller and Matzel's (1988) Comparator Hypothesis, and the Schmajuk-Lam-Gray (SLG, 1996) model, these models' explanations of extinction and conditioned inhibition and their predictions regarding extinction of conditioned inhibition are introduced. Chapter 3 focuses on the clinical aspects of the above mentioned phenomena. First, the parallels between Classical Conditioning and Behavioral Therapy are presented. Then, the chapter explains how extinction and conditioned inhibition can help clinical psychologists to treat anxiety disorders. Lastly, potential problems with this approach is described. In chapters 4 and 5, our experiments testing the predictions of the SLG model regarding the effects of attentional manipulations on the inhibitory power of discrete and contextual cues are described and the results are discussed. Finally, Chapter 6 summarizes the results of our experiments and discusses the implication of these results to develop more effective anxiety disorders. Neurobiology of extinction and inhibitory learning is also discussed in this chapter.

1.1 Conditioned Inhibition of Discrete Stimuli

As many other conditioning phenomena, conditioned inhibition, first described by Pavlov (1927), still remains a subject of careful scrutiny. Pavlov (1927) defined "internal inhibition" as an inhibitory relationship between a stimulus (e.g. tone) and a conditioned response (e.g. salivation, CR, see Table 1 for basic classical conditioning concepts, examples, and abbreviations). Later Spence (1936) and Hull (1943) renamed the phenomenon as "conditioned inhibition" as opposed to "unconditioned inhibition" (also known as external inhibition) in which the CR to a conditioned stimulus (CS) is reduced when a novel CS is introduced (Savastano, Cole, Barnet, & Miller,1999). Conditioned inhibition has been demonstrated in several different species and

Table 1. Basic Classical conditioning concepts, abbreviations, and real world.

Classical Conditioning Concept	Abbreviation	Real World Example
Conditioned Stimulus	CS	Tone, Light, and Noise
Unconditioned Stimulus	US	Shock, Food, and Drugs
Conditioned Response	CR	Freezing, Salivation, and Eye Blink
Context	CX	Test or Home Cages

paradigms including fear conditioning (e.g. Zimmer-Hart & Rescorla, 1974), appetitive conditioning (e.g. Bower & Grusec, 1964), and drug self-administration (e.g. Kearns, Weiss, Schindler, & Panlilio, 2005) in rats, nictitating membrane response in rabbits (e.g. Marchant, Mis, & Moore, 1972), autoshaping in pigeons (e.g. Brown & Jenkins, 1967), fear conditioning (e.g. Neumann, Lipp, & Siddle, 1997; Grillon & Ameli, 2001) and causal learning (e.g. Chapman, 1991) in humans.

There are at least 4 ways to produce true inhibition (see Figure 1). One way is to pair a CS (e.g. tone), A, consistently with the unconditioned stimulus (US, e.g. foot shock) while presenting another CS (e.g. light), X, consistently in the absence of the US. This method is called "differential inhibition" where consequently, X becomes a conditioned inhibitor. Another method is to present X "explicitly unpaired" with the US. That means the presentations of X and the US are set to be negatively correlated in time where the CS and US presentations never coincide. A third, method known as "inhibition of delay" is to use a long CS where the US occurs at the end of the presentation of that CS. Usually animals learn not to show CR during the earlier parts of the CS. Finally, the most common method is the "conditioned inhibition" method where A is presented with the US (A+ trials) and the US presentation is omitted when A is paired with X in compound (AX- trials). Consequently, animals learn to respond during A presentations but not during AX compound presentations.

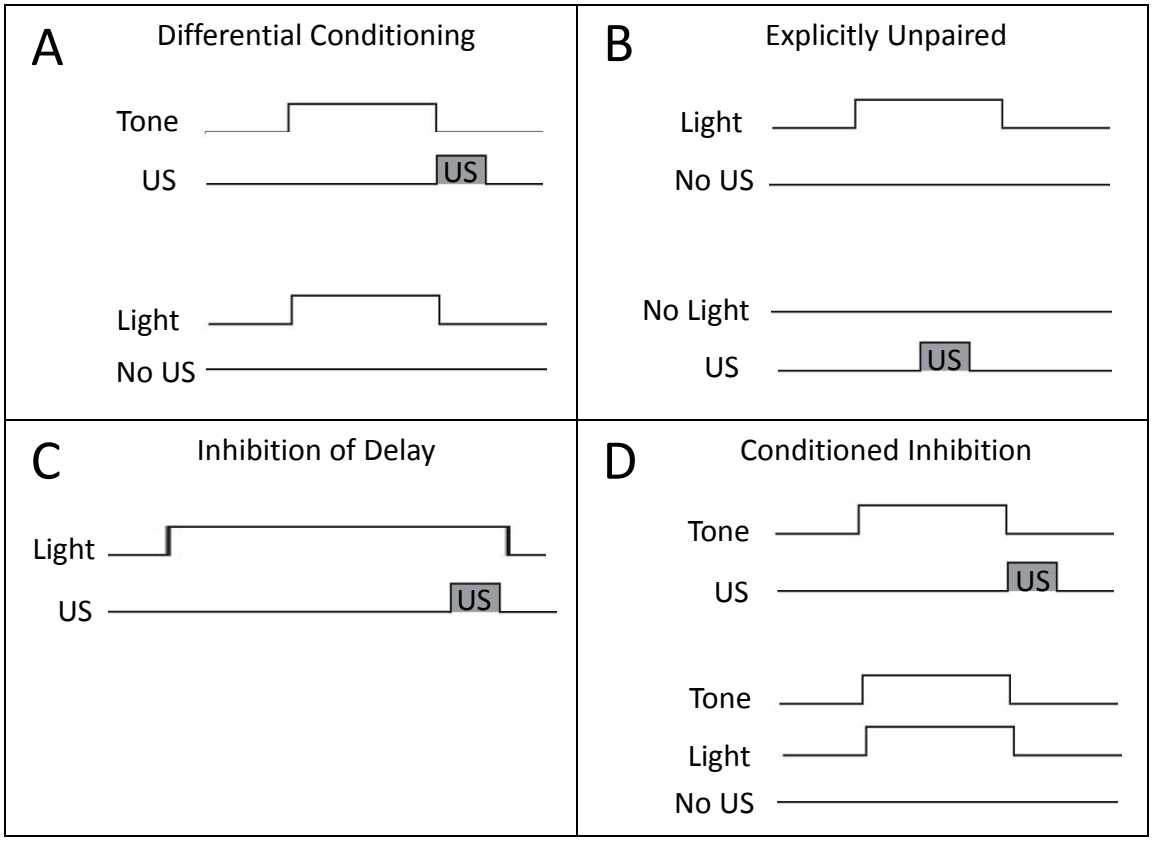

Figure 1. Four methods to produce true inhibition. A: Differential Conditioning (A+/X-). B: Explicitly Unpaired procedure (X-/+). C: Inhibition of Delay (X+ with a short CS-US overlap). D: Conditioned Inhibition (A+/AX-).

There are also two ways to test conditioned inhibitors (see Table 2). Pavlov (1927) proposed that in order to decide whether a CS had become inhibitory, the conditioned inhibitor (X) should pass a summation test. A summation test consists of presenting the putative inhibitor, X with a conditioned excitor with the expectation that the inhibitory CS would decrease the strength of the CR to the excitatory CS in comparison of the CR

only to the excitor. Passage of the summation test excludes the possibility of a configural interpretation which suggests only the configuration of the inhibitory CS and original excitatory CS yields reduced CR because the inhibitor also decreases responding to another excitor. In some summation tests, instead of presenting the excitor alone, the excitor is paired with a novel CS in order to control for external inhibition (Papini and Bitterman, 1993).

Table 2. Summation (A) and Retardation (B) tests.

A	Summation Test		B	Retardation Test	
CI	Transfer Excitor + Conditioned Inhibitor	Weak CR	Conditioned Inhibitor + US	Slow Conditioning (Retardation)
EI	Transfer Excitor + Novel CS	Relatively Strong CR	Novel CS + US	Relatively Fast Conditioning

In addition to the summation test, Rescorla (1969) suggested that a retardation test is also necessary to decide the inhibitory power of a CS. He claimed that if the conditioned inhibitor subtracts excitation from the excitatory CS, then it should be

harder to convert the conditioned inhibitor into an excitatory CS. In line with this idea, a retardation test consists of conditioning trials of the conditioned inhibitor with the expectation that the inhibitory CS takes longer to become excitatory than a neutral CS. In sum, it is generally accepted that passing both the summation and the retardation tests would confirm the inhibitory power of a given CS (Cole, Barnet, & Miller, 1997; Papini and Bitterman, 1993).

1.2 Extinction as Conditioned Inhibition of Contextual Stimuli

Extinction is a phenomenon where subsequent to the CS-US pairings, CS is presented alone in the absence of the US in order to decrease or eliminate the CR elicited by that CS. There are two basic hypotheses on the underlying mechanism of extinction. Some associative models such as Mackintosh (1975) and Rescorla-Wagner (1972) assumed that the association between the CS and the US is unlearned. Against this "unlearning hypothesis" other models such as Konorski (1948) and Pearce-Hall (1980) proposed that the initially established excitatory CS-US associations are counteracted by a new inhibitory association.

Supporting the "inhibitory learning hypothesis" the experimental evidence such as spontaneous recovery, recovery of the extinguished fear elicited by the previously extinguished CS as a result of passage of time, shows that extinction does not eliminate

the CS-US association but inhibits the expression of these associations (e.g. Pavlov, 1927; Myers & Davis, 2007). Bouton suggested that spontaneous recovery is a result of a change in the temporal context (e.g., Bouton, 1988, 1993). According to the temporal context idea, the memory of CX-CS associations become inactive as the temporal context (the time of testing) is different from the temporal extinction context (the time of extinction). Therefore, when the extinguished CS is tested in the same CX after a delay, the extinction memory cannot be retrieved completely which results in the recovery of the CR (see Chapter 2 for alternative explanations of spontaneous recovery and other recovery effects). In line with this interpretation, a retrieval cue that reminds the extinction context reduces the amount of recovery (Brooks and Bouton, 1993, 1994; Brooks, 2000; see Chapter 3 for further discussion on extinction reminders).

Another phenomenon showing that CS-US associations may be masked by the inhibition of the extinction context (CX) is renewal. To obtain a renewal effect, rats first receive CS-US pairings in CXA and CS alone trials in CXB. Finally, subjects are tested with the same CS back in the acquisition context, CXA. Results show that the extinguished CR is recovered as a result of returning to the acquisition CX (e.g. Bouton and King, 1983). This version of renewal is also known as ABA renewal. In the ABC version of this effect, the CS is extinguished in CXB and tested in a novel CX, CXC. As in the ABA version, the CR to the extinguished CS returns when it is tested in a novel CX

(e.g., Bouton and Bolles, 1979; Bouton and Brooks, 1993; Harris, Jones, Bailey, & Westbrook, 2000; Duvarci and Nader, 2004). Finally, in the AAB version of renewal, the CS is extinguished in the acquisition CX and tested in a novel CX, CXB. In this case, the CR to the extinguished CS is recovered (e.g., Bouton and Ricker, 1994; Tamai and Nakajima, 2000). There is some evidence suggesting that the amount of recovery is greater in the ABA and ABC renewal designs than the AAB renewal design (e.g. Rescorla, 2008; Tamai & Nakajima, 2000; Thomas, Larsen, & Ayres, 2003; Ungor & Lachnit, 2008). Overall, renewal effect suggests that extinction is specific to the CX in which CS presented in the absence of the US, and the CR is assumed to be extinguished during extinction returns in a context different than the extinction CX.

Finally, reinstatement, recovery of the extinguished CR as a result of isolated presentations of the US, shows that making the extinction CX neutral or excitatory eliminates the inhibition exerted by the CX and therefore, the CR for the extinguished CS is recovered (e.g., Pavlov,1927; Rescorla and Heth, 1975). Interestingly, if the reinstating US presentations take place in a different CX, the CR is not recovered when the CS is tested in the extinction CX (e.g., Bouton and Bolles, 1979; Bouton and King, 1983; Bouton, 1984; Baker, Steinwald, & Bouton, 1991; Wilson, Brooks, & Bouton, 1995; Frohardt, Guarraci, & Bouton, 2000).

Taken together, during extinction CS-US associations are not unlearned but masked by alternative direct or indirect inhibitory associations of the CX. In the absence of these associations, excitatory CS-US associations are expressed and the CR is recovered. In line these results, extinction can also be considered as "Conditioned Inhibition of the Context".

1.3 Extinction of Conditioned Inhibition

According to the Rescorla and Wagner model (1972), it is possible to extinguish inhibitory CS-US associations through non-reinforced presentations of the conditioned inhibitor (see 2.1 The Rescorla-Wagner (1972) Model section for details). This prediction has been initially tested by Zimmer-Hart and Rescorla (1974). In this study, subjects were first given a conditioned inhibition training of A+/AX- and then they received non-reinforced presentations of the conditioned inhibitor X (X- trials). Finally, X was paired with another excitor in the summation test and compared to a control group which was given context only exposure trials instead of X- trials. The results of the study suggest that X- trials did not affect the inhibitory properties of X. Since Zimmer-Hart and Rescorla's study, there have been numerous attempts to show extinction of conditioned inhibition using both animals and humans as subjects. While some researchers demonstrated the effect (e.g. Detke, 1991; Holland, 1985; Holland & Gory, 1986; Robbins,

1990, Melchers, Wolff, & Lachnit, 2006, Baetu & Baker, 2010) most studies failed to do so (e.g. DeVito & Fowler, 1986, 1987; Hallam, Grahame, Harris, & Miller, 1992; Lysle & Fowler, 1985; Miller & Schachtman, 1985; Pearce, Nicholas, & Dickinson, 1982; Rescorla, 1982; Williams, 1986; Williams & Overmier, 1988; Williams, Travis, & Overmier, 1986; Witcher & Ayres, 1984). For example, using a summation test, Williams, Travis, and Overmier's (1986) Experiment 4 showed that non-reinforced presentations of the inhibitor might increase the inhibition produced by that inhibitory CS when compared to the inhibition produced by another untreated inhibitor. Consequently, it is widely accepted that it is not possible to extinguish inhibitory associations or decrease the effectiveness of a conditioned inhibitor through non-reinforced manipulations of the conditioned inhibitor. Nevertheless, using a human causal learning paradigm, Melchers et al. (2006, also Lotz & Lachnit, 2009) found that extinction of conditioned inhibition through non-reinforced trials is possible under certain circumstances where the outcome could take negative values. Recently, Baetu and Baker (2010) demonstrated this effect more directly in humans. These results are partially supported by Pearce, Nicholas, and Dickinson (1982) study which found that while the summation test performance is not affected by the non-reinforced presentations of the conditioned inhibitor; conditioning becomes more retarded when the conditioned inhibitor is reinforced in a retardation test. Pearce et al. (1982) suggested that this effect might be a result of latent-inhibition, an

effect where non-reinforced preexposure to a CS retards acquisition compared to a novel CS as a result of decreased attention (Lubow & Moore, 1959).

The following chapters of this dissertation aim to address the theoretical aspects (Chapter 2) and clinical relevance (Chapter 3) of conditioned inhibition, extinction, and extinction of conditioned inhibition, and experimental tests of Schmajuk-Lam-Gray (1996) model's predictions regarding these phenomena (Chapters 4 and 5).

2. Theoretical Aspects of Conditioned Inhibition and Extinction

Starting with the Rescorla-Wagner model (1972), the discussion on conditioned inhibition, extinction and extinction of conditioned inhibition has been mostly theory driven. There are several theoretical accounts, which can describe and explain these associative learning phenomena. In this section we will introduce 4 mathematical models, the Rescorla-Wagner (1972) model, Wagner's SOP model (1981), Miller & Matzel's (1988) Comparator Hypothesis and the Schmajuk-Lam-Gray (1996) model, and describe how these models explain conditioned inhibition and extinction. Finally, we

Table 3. Summary of the predictions and definitions of the Rescorla & Wagner (1972) model, Wagner's (1981) SOP model, Miller & Matzel's (1988) Comparator Hypothesis (CH), and Schmauk, Lam, Gray's (1996) SLG model.

Model	Conditioned Inhibition	Extinction	Extinction of CI	Reactivation of CI
Rescorla & Wagner (1972)	Negative Association	Unlearning	Through Associative Change	Not Predicted
Wagner's (1981) SOP	Negative Association	Inhibitory Learning	Through Attentional Change	Not Predicted
Miller & Matzel's (1988) CH	Competition	Unlearning	Through Associative Change	Not Predicted
Schmajuk, Lam, & Gray's (1996) SLG	Negative Association	Inhibitory Learning	Through Attentional Change	Through Attentional Change

will introduce the predictions of these models regarding extinction of conditioned inhibition (see Table 3 for the summary).

2.1 The Rescorla-Wagner (1972) Model

2.1.1 Description of the Model

The Rescorla-Wagner (1972) model is one of the most influential associative learning models. By modifying Bush and Mosteller's (1955) ΔV equation Rescorla and Wagner were able to explain Kamin's (1969) blocking effect and conditioned inhibition in mathematical terms for the first time. Since then Rescorla and Wagner's common error term has been implemented in almost every influential associative learning accounts. According to the model changes in the associative strength ΔV_X is computed as:

$$\Delta V_X = \alpha_X \beta (\lambda - \sum V) \qquad [\ 1.1\ ]$$

where α_X refers to the salience of the CS, β is the learning parameter, λ refers to the asymptotic value that the US can support which takes the value of 1 when the US is present and 0 when it is absent, and finally $\sum V$ is the total associative value of the CSs that are present in a given trial. The common error term $(\lambda - \sum V)$ takes a positive value when the US is present and the total associative value of the CSs is smaller than 1.

2.1.2 Conditioned Inhibition, Extinction, and Recovery Effects

The model describes conditioned inhibition following A+/AX- training as the association of X and the US becomes negative because the associative value of A is subtracted from 0 as the US is absent and the error term becomes negative.

$\Delta V_X = \alpha_X \beta (0-0.5)$ [1.2]

The model assumes that in a summation test the associative strength of the conditioned inhibitor would be subtracted from the associative strength of the transfer excitor. The model also assumes that in a retardation test, due to its negative associative value, the conditioned inhibitor will take more trials to condition compared to a CS with neutral associative value. As mentioned above, although the acquisition of conditioned inhibition has been elegantly described by the Rescorla-Wagner (1972) model at a theoretical level, it was soon discovered that the theory wrongly predicted that repeated presentations of the inhibitor would lead to the elimination of its inhibitory power (Zimmer-Hart & Rescorla, 1974). According to the Rescorla-Wagner model, X- trials following A+/AX- training result in elimination of inhibition because the error term becomes positive when negative associative value of X is subtracted from 0.

$\Delta V_X = \alpha_X \beta (0- (-0.5)$ [1.3a]

$\Delta V_X = \alpha_X \beta (0+ 0.5)$ [1.3b]

Originally, the Rescorla-Wagner (1972) model suggested that extinction is an unlearning process as ΔV becomes negative and the CS loses its excitatory associations until ΔV becomes zero during non-reinforced trials. However, it is also possible to assume that the CX serves as another CS and it becomes a conditioned inhibitor during extinction. By doing so, the excitor will stop losing associations when the values of the excitatory and inhibitory associations become equal and ΔV becomes 0. This phenomenon is known as protection from extinction and demonstrated by several studies (Chorazyna, 1962; Soltysik, 1985; Rescorla, 2003). Protection from extinction also helps the model to explain renewal. According to the model, renewal is explained as the CS, which is still excitatory, yields CR in the absence of the inhibitory extinction CX. Similarly, reinstatement is explained because the CX becomes neutral during the US presentations in the extinction CX. However, the model cannot explain spontaneous recovery.

2.2 Wagner's (1981) SOP Model

2.2.1 Description of the Model

"Sometimes Opponent Process", also known as "Standard Operating Processes" or SOP (Wagner, 1981; Brandon, Vogel, & Wagner, 2003), is a model, which assumes

different nodes for CS and US and different activation levels for these nodes. According to the model, when a CS or a US is presented they first become activated at level A1 which is a high level activation equivalent to a high level of attention (focal attention). After some time the activation level automatically decreases to A2, which is equivalent to a low level of attention (peripheral attention). Eventually, the activation level of CS turns back to an inactive state as a result of repeated presentations. The model assumes that a CS in A2 level must go back to the inactive state before it can turn back to A1 level activation. The momentary activation changes are given by:

$$\Delta PA1 = P1(PI) - Pd1\,(PA1) \qquad [2.1]$$

$$\Delta PA2 = Pd1(PA1) - Pd2\,(PA2) \qquad [2.2]$$

$$\Delta PI = Pd2(PA2) \qquad [2.3]$$

where PI, PA1, and PA2 represent Inactive, A1, and A2 levels respectively, P1 is the parameter representing the salience of the CS; and Pd1 and Pd2 refer to decay parameters.

According to these equations, a CS with a strong salience will stay active longer in level A1. The associative activation of a US by all CSs at a time, $P2,US/\sum CS$, is given by the multiplication of the associative value and the A1-A2 activation levels of the CS:

$$P2,US/\sum CS = \sum i\,[VCSiUS\,(r1PA1,CSi + r2PA2,CSi)] \qquad [2.4]$$

where p2 take positive or negative values, VCSiUS is the associative strength of CS-US, and (r1PA1,CSi + r2PA2,CSi) refers to the proportion of the CS elements in A1 and A2 states. The model assumes that r1>r2 which ensures more A1 contribution than A2 contribution to the US activity. The model assumes that the level of responding (RJ) is proportional to the current activation levels of the CS and US in A1 and A2 and this is computed as:

$$RJ = fJ\ (w_{1,j\ PA1,US} + w_{2,j\ PA2,US}) \qquad [2.5]$$

where W1 is a multiplicative weight which is equal to or larger than 0, and w2 is a free parameter determined by the type of response measure. Since a CS will cause the US to be activated only in A2 in its absence, this level of US activity is assumed to reflect the Conditioned Response (CR). Furthermore, the model assumes that associations are formed between two CSs or a CS and a US only when both stimuli are in A1 level. Also, activation of the first CS causes an activation of the second CS or the US in A2 level through the CS-CS or CS-US associations. The learning rule for the excitatory CS-US associations (Vi) is computed as:

$$\Delta Vi+ = L+ \sum t\ (PA1,CSi\ \ PA1,USj) \qquad [2.6]$$

This equation where L+ represents the excitatory learning parameter and ensures that proportion of A1 elements of the CS and US determines excitatory associations, PA1,CSi and PA1,USj, respectively. In line with this idea the proportion of A1 to A2 elements gives the inhibitory associations:

$$\Delta Vi- = L- \sum t\ (PA1,CSi\ \ PA2,USj) \qquad [2.7]$$

Finally, the net associative strength is the difference between excitatory and inhibitory associations:

$$\Delta Vi- = \Delta Vi+ - \Delta Vi- \qquad [2.8]$$

2.2.2 Conditioned Inhibition, Extinction, and Recovery Effects

As Equation 2.7 suggests, the SOP model assumes that inhibition is the result of the target CS acquiring inhibitory associations when presented with the excitatory CS in the absence of the US because the CSs are presented in A1 while the absent but predicted US is active in A2 (see equation 2.7). According to the SOP model, extinction of the inhibitory CS increases the CX-CS association thereby decreasing A1 activity of the inhibitory CS but its inhibitory associative value does not change. As a result, when the conditioned inhibitor is tested in a summation test it will be activated more in the A2

state and therefore, lose its inhibitory power. Also, for the same reason, conditioning of the inhibitory CS will be more retarded after extinction trials.

According to the SOP model during acquisition Vi decreases in the CS-only portion of the trial, whereas Vi increases when the US is presented. During extinction, Vi only becomes inhibitory as the US is activated in A2 state which will decrease CS-US associations. Similar to the Rescorla-Wagner model, if we assume that the CX is also present during extinction, it will be activated in A1 state and acquire inhibition. Thus, the model can also explain renewal and reinstatement in the same terms with the Rescorla-Wagner model. Similarly, the model cannot explain spontaneous recovery unless it assumes that inhibition fades faster than excitation during the delay between extinction and test (Miller & Escobar, 2001).

2.3 Miller & Matzel's (1988) Comparator Hypothesis

2.3.1 Description of the Model

According to Miller and Matzel's (1988) Comparator Hypothesis, there are two connections determining the strength of CR, a) direct CS-US associations and b) indirect CS-Comparator, Comparator-US associations. The comparator is thought to be another CS or Context (CX) in the absence of a second CS. The model assumes that the strength of the CR is determined by comparing direct and indirect associations. Conversely,

when the indirect association is stronger than the direct association the inhibitory responding is elicited. Sometimes-Competing Retrieval (SOCR, Stout & Miller, 2007; Witnauer & Miller, 2010) model is a formalization of the Comparator Hypothesis. According to this model, changes in the strength of the association between a CS, X, and the Comparator, C, $\Delta V_{X,C}$, is computed as:

$$\Delta V_{X,C} = \alpha_X \beta_C (\lambda - V_{X,C}) \qquad [3.1]$$

where αX and βC refer to the associability of X and C respectively, λ represents the asymptotic level of associative strength the X and C can support, and finally VX,C represents the strength of the association of X and C. The associative strength of X is updated by:

$$V_X{}^{n+1} = \Delta V_X{}^{n} + V_X{}^{n} \qquad [3.2]$$

where n represents the trial number. In the absence of the Comparator CS, C, the decrease in the X-C association is given by:

$$\Delta V_{X,C} = \alpha_X (-k1 \; V_{X,C}) \qquad [3.3]$$

k1 is an extinction parameter between $0 < k1 < 1$. Responding to X, RX, is computed as:

$$RX = V_{X,US} - k2 \left(\sum Op_{X\text{-}C\text{-}US} \; rV_{X\text{-}C} \; rV_{C\text{-}US}\right) \qquad [3.4]$$

k2 is a free parameter valued between $0 < k1 < 1$ determining the weight of comparison. $\sum$OpX-i-US is the operator switch which determines the degree of discrimination between direct and indirect CS-US associations, finally rVx-c and rVc-US represent the prediction of the C by X and the prediction of the US by C respectively. This equation ensures that the response to X is not the absolute value of X-US associations but rather its relative value to C-US associations. In line with this idea when there is more than one comparator $rV_{X\text{-}C}$ is updated as:

$$rV_{X\text{-}C} = V_{X,C} - k2\ (\sum Op_{X\text{-}C\text{-}C2}\ rV_{C\text{-}C2}\ \ rV_{C2\text{-}US}) \qquad [\ 3.5\ ]$$

Finally, changes in the operator switch, ΔOpX-C-US, is given by:

$$\Delta Op_{X\text{-}C\text{-}US} = k3\ \alpha_X\ V_{X\text{-}C}\ V_{C\text{-}US}\ (1 - Op_{X\text{-}C\text{-}US}) \qquad [\ 3.6]$$

2.3.2 Conditioned Inhibition, Extinction, and Recovery Effects

The CH suggests that inhibition is the result of the target CS having a lower expectation of the US than its comparator cues. That is given by Equation 3.3 where ($rV_{X\text{-}C}$ $rV_{C\text{-}US}$) term being stronger than direct $V_{X,US}$ associations and the subtraction yields a negative result. Notice that, the CH model assumes that all associations have positive values and conditioned inhibition arises from competition between the comparator and target CSs. In line with this idea, the model predicts extinction of the inhibitory CS

should decrease its inhibitory value by decreasing its association with its excitatory comparator (see Equation 3.5).

According to the model, during extinction CX-Target CS associations are formed and therefore, the CX becomes a comparator and decreases responding to the target CS while the target CS loses some of its associative strength. However, the model cannot explain renewal, reinstatement or spontaneous recovery because it does not include a mechanism where summation between the testing CX and the target CS is allowed and CS-US associations are unlearned during extinction (Laborda, McConnell, & Miller, 2011).

2.4 The SLG attentional-associative model

Schmajuk, Lam, and Gray (SLG, 1996) proposed a real time, attentional-associative model of conditioning that incorporates a mechanism to store not only CS-US but also CS-CS associations based on a modified Rescorla-Wagner type error correction rule and an attentional system that assumes attention to all the present and predicted CSs increases when novelty detected in the environment is high (Figure 2). In the next sections the mathematical descriptions of these mechanisms will be described.

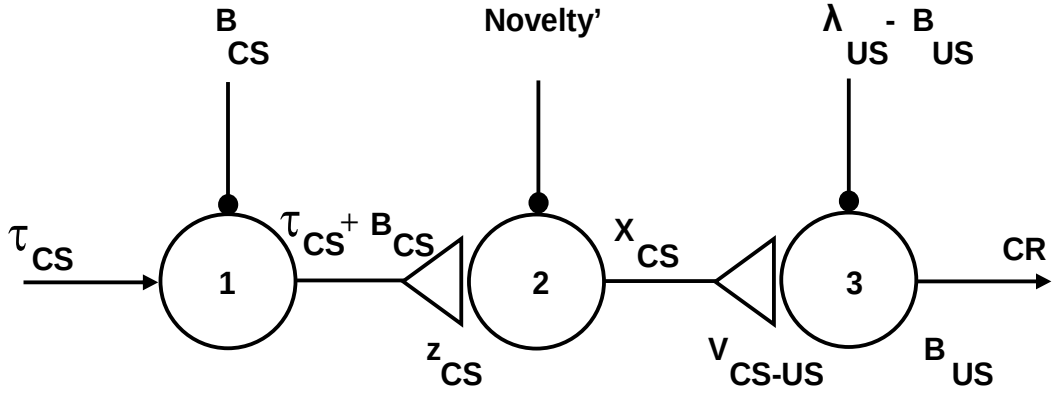

Figure 2. A simplified diagram of the SLG model. CS: conditioned stimulus; λ_{CS}: strength of the unconditioned stimulus; τ_{CS}: trace of the CS; z_{CS}: attention to the CS; X_{CS}: internal representation of the CS; $V_{CS\text{-}US}$: CS-US association; B_{US}; prediction of the US; CR: conditioned response. Triangles: variable connections (associations) between nodes that modulate the activation of the node. Arrows: inputs that control the output of the node. Solid circles: inputs that modify connections z_{CS} and $V_{CS\text{-}US}$ without affecting outputs X_{CS} and CR.

2.4.1 Short-term memory and feedback

Node 1 in Figure 2 is activated by a short-term memory trace of the CS, τ_{CS}, of the CS and changes in τ_{CS} are given by

$$d\,\tau_{CS}/dt = K_1\,(\lambda_{CS} - \tau_{CS}), \qquad [\,4.1\,]$$

where K_1 is a constant for the rate of increase and decay of τ_{CS} and λ_{CS} is the salience of the CS. Based on this equation τ_{CS} increases when the CS is present and decays to zero when it is absent. The output of Node 1 is given by $(\tau_{CS} + K_3\,B_{CS})$, where K_3 is a feedback constant and B_{CS} is the prediction of the CS by itself, and by other CSs, through CS-CS associations, and the context, through CX-CS associations.

2.4.2 Attention

Attention to a CS, z_{CS}, reflects the association between ($\tau_{CS} + K_3 B_{CS}$) and Novelty'. Changes in z_{CS} are given by

$$d z_{CS}/dt = (\tau_{CS} + K_3 B_{CS}) (K_5 \text{ Novelty}' (1- z_{CS}) - K_6 (1 + z_{CS})), \qquad [4.2]$$

where K_5 is a constant for the increase of z_{CS}, K_6 is a constant for the rate of decay of z_{CS}, and Novelty' is given by Equation 4.8. The value of z_{CS}, can vary between 1 and –1 while the initial value of z_{CS} is zero. Notice that z_{CS} value is based on the amount of novelty detected in the environment or Novelty'. In other words, when Novelty' is relatively large, z_{CS} gradually increases; when Novelty' is relatively small, z_{CS} gradually decreases and therefore, there is always a temporal gap between the increase in z_{CS} and the increase in Novelty'. Notice that Novelty' affects z_{CS} when the CS is present (when τ_{CS} is a positive value) or when the CS is predicted by other CSs or the CX (when B_{CS} is a positive value). Therefore, novelty detected in the environment can increase attention to the CS (or the internal representation of that CS) even when the CS is absent but predicted.

The attention-modulated representation of the CS, X_{CS} is the output of Node 2. Importantly, X_{CS} only takes values between 0 and 1 while it decreases to zero with negative values of z_{CS} it increases to 1 with positive values of z_{CS}. Hence, after Lubow

(1989), Schmajuk, Lam, and Gray (1996) interpreted the positive z_{CS} values as attention to a CS and negative values of z_{CS} as inattention to a CS. Negative z_{CS} values can also be interpreted as "beyond zero habituation", an experimental phenomenon which suggests repeated presentation of a stimulus can lead to more habituation and therefore, a delayed spontaneous recovery even after the response level reaches to zero or an asymptotic level (Rankin, et al., 2009). Therefore, this suggests although the decrement in attention is not observed it is possible to decrease attention to a negative value.

Internal representation of a CS, X_{CS}, is given by

$$X_{CS} = K_2 (\tau_{CS} + K_3 B_{CS}) (K_4 + z_{CS}). \qquad [4.3]$$

2.4.3 Novelty

The novelty of event k (a CS, CX or the US) is computed as the absolute value of the difference between the average observed value of that event ($\bar{\lambda}_k$), and the average of the aggregate predictions of that event by all active CSs and CXs ($\bar{B}_k$):

$$\text{Novelty}_k = | \bar{\lambda}_k - \bar{B}_k |, \qquad [4.4]$$

The average observed value of event k is given by

$$d\bar{\lambda}/dt = (1 - \bar{\lambda}_k) \lambda_k - K8 \ \bar{\lambda}_k, \qquad [4.5]$$

where K_8 is a constant for the rate of decay of $\bar{\lambda}k$.

The average aggregate prediction of event k is given by

$$d\overline{B}/dt = (1-\overline{B}_k)B_k - K_8\overline{B}_k, \quad [4.6]$$

Total novelty in the environment or Novelty is calculated as aggregate difference between the actual occurrence and prediction of all the events.

$$\text{Novelty} = \Sigma_k \left| \overline{\lambda}_k - \overline{B}_k \right|, \quad [4.7]$$

where event k includes all stimuli predicted and present. According to this equation, Novelty increases when there is a mismatch between the actual occurrence and prediction of the events and decreases otherwise .Then the model normalizes the value of Novelty, by calculating Novelty' which is given by

$$\text{Novelty}' = \text{Novelty}^2 / (K_9^2 + \text{Novelty}^2). \quad [4.8]$$

As discussed above, Novelty' is used by the attentional system to calculate the value of z_{CS} (Equation 4.2). Importantly, the model assumes that Novelty' and attention to a CS increase and decrease based on the prediction of the CS by itself and by other CSs. Therefore, the model assumes that attention to a CS increases when (a) that CS is not well predicted by itself, other CSs or the CX (like in Wagner's, 1981, SOP model); (b) that CS does not predict well the US (like Pearce and Hall's, 1980, model), or (c) that CS does not predict well other CSs or the CX (unlike any other model).

2.4.4 Changes in CS-US associations

As shown in Figure 2 Node 3, is responsible for forming associations and it receives X_{CS} as a signal from Node 2, as well as the error signal ($\lambda_{US} - B_{US}$). The $V_{CS\text{-}US}$

value is the strength of the inhibitory or excitatory associations between a CS and a US and the changes in the strength of these associations are given by

$$dV_{CS\text{-}US}/dt = K_7 X_{CS} (\lambda_{US} - B_{US}) (1 - |V_{CS\text{-}US}|), \quad [4.9]$$

where X_{CS} is the internal representation of the CS, λ_{US} is the intensity of the US, and B_{US} is the aggregate prediction of the US by all CSs present at that time (See Equation 4.10). Notice that $V_{CS\text{-}US}$ is given by a common error term as proposed by Rescorla and Wagner (1972) which is the difference between the prediction of the US and the actual US value. Also, the model incorporates an individual term to make changes in the associative strength slower when $V_{CS\text{-}US}$ value is closer to +1 or -1 (Schmajuk, 2010, pg. 29-30). The SLG model also forms CX-US associations following Baker, Mercier, Gabel, and Baker's (1981) study, which demonstrated that the CX elicits CR as a result of US exposures in that CX.

2.4.5 Changes in CS-CS associations

As well as associations between a CS and a US the model assumes that there are associations formed between multiple CSs, and between a CS and a CX. These assumptions are supported by experimental data. For example, Brogden (1939) demonstrated formation of CS-CS associations between CSs presented together by showing that following presentations of A-B together when A is reinforced B elicits CR,

even though it has never been paired with the US (also see Rescorla & Durlach, 1981). Rescorla (1984) found that a CX can also be used as a CS in a sensory preconditioning design which suggests that CSs form direct associations with CXs and vice versa (also see Marlin, 1982). According to the SLG model changes in the CSi-Cji associations, VCSi-CSj, are given by

$$dV_{CSi\text{-}CSj}/dt = K_7 X_{CSi} (\lambda_{CSj} - B_{CSj}) (1 - |V_{CSi\text{-}CSj}|), \qquad [4.9']$$

where X_{CSi} is the internal representation of CSi, λ_{CSj} is the intensity of CSj, and B_{CSj} is the aggregate prediction of CSj by all X_{CS}'s active at a given time.

2.4.6 Aggregate predictions of the US and CS

The output of Node 3 in Figure 2 is the aggregate prediction of the US by all present and predicted CSs, B_{US}, given by

$$B_{US} = \Sigma_{CS} B_{CS\text{-}US} = \Sigma_{CS} X_{CS} V_{CS\text{-}US}, \qquad [4.10]$$

where $B_{CS\text{-}US}$ is the prediction of the US by each CS and $V_{CS\text{-}US}$ is the association of each CS with the US. Consequently, B_{US} determines the magnitude of the CR. As mentioned before, although $V_{CS\text{-}US}$ can take negative (inhibitory) or positive (excitatory) values, B_{US} can only take positive values.

2.4.7 CR strength

Finally, the output of Node 3, B_{US}, directly controls the CR according to a non-linear function

$$CR = B_{US}^2 / (K_{11}^2 + B_{US}^2). \qquad [4.11]$$

Although the original model assumed that the orienting response (OR = Novelty') inhibits the CR by incorporating (1-OR) term to the CR equation, as suggested by Schmajuk and Larrauri (2006), this is not the case in some classical conditioning paradigms such as suppression in appetitive conditioning and when the CR is freezing in a fear conditioning paradigm.

2.4.8 Conditioned Inhibition

Similar to the Rescorla-Wagner (1972) model, the SLG model suggests that during A+/AX- training of conditioned inhibition, X becomes inhibitory while A stays excitatory based on the error term incorporated in the model (see Equation 4.9). Consequently, during a summation test, the strength of the CR is given by the aggregate prediction of the US (see Equation 4.10), B_{US} is based on the individual excitatory association of the transfer excitor and the inhibitory association of the conditioned inhibitor, X, as well as their respective internal representation values, X_{CS}. Therefore, during the summation test, the inhibitory associative value of the conditioned inhibitor

is subtracted from the excitatory associative value of the excitor which results in decreased B_{US} and CR relative to the external inhibition control. Notice that the expression of the excitatory and inhibitory associations is based on the attention modulated X_{CS} values. In other words, the amount of inhibition or excitation is given by the strength of the inhibitory association and the amount of attention directed to the inhibitory or excitatory CS (Table 4). Consequently, as depicted in Table 4, a well-attended inhibitory CS will perform more inhibitory power in a summation test than a poorly-attended conditioned inhibitor with the same $V_{CS\text{-}US}$ value. Same is true for the

Table 4. The SLG model's predictions regarding the summation test.

Summation Test		
Inhibitory Associations ($V_{X\text{-}US}$)	Strong	Weaker CR
	Weak	Stronger CR
Attention to the CI (z_X)	High	Weaker CR
	Low	Stronger CR
Excitatory Associations ($V_{B\text{-}US}$)	Strong	Stronger CR
	Weak	Weaker CR
Attention to the Excitor (z_B)	High	Stronger CR
	Low	Weaker CR

excitatory CSs. Similarly, a well-attended excitor will elicit more CR than a poorly-attended CS with the same strength of excitatory associations. The model assumes that the rate of conditioning of a conditioned inhibitor in a retardation test is also based on Equation 4.9 in which changes in the associative strength of a CS are computed. According to this equation (see Table 5), there are at least four factors that determine the

Table 5. The SLG model's predictions regarding the retardation test.

		Retardation Test
Inhibitory Associations ($V_{X\text{-}US}$)	Strong	More Retardation
	Weak	Less Retardation
Attention to the CI (z_X)	High	Less Retardation
	Low	More Retardation
Prediction of the US (B_{US})	Strong	More Retardation
	Weak	Less Retardation
Novelty'	High	Less Retardation
	Low	More Retardation

rate of conditioning and the strength of the CR in a retardation test. The first factor is the initial $V_{CS\text{-}US}$ value. According to the model, negative $V_{CS\text{-}US}$ values do not generate any CR. Thus, the CR will not be generated until $V_{CS\text{-}US}$ becomes a positive alue with relatively many reinforced trials and the rate of conditioning will be retarded compared to a CS with neutral $V_{CS\text{-}US}$ value. Secondly, the model assumes that with relatively large non-reinforced trials attention to a conditioned inhibitor after training will be lower than a neutral CS. Consequently, X_{CS} of the conditioned inhibitor will be smaller than the control CS and as mentioned above, X_{CS} controls both changes in the associative strength and the BUS value. Consequently, a conditioned inhibitor will take a relatively large number of reinforced trials to elicit CR also due to the low X_{CS} value. The model explains latent inhibition in similar terms. According to the model, the retardation of acquisition effect after the preexposure of a CS is a result of increased prediction of the CS by the CX during preexposure. This way internal representation of the CS, X_{CS} is decreased which lead to a slower conditioning even though the $V_{CS\text{-}US}$ is still zero.

A third factor is the size of the error term (λ_{US} - B_{US}) which is affected not only by $V_{CS\text{-}US}$ but also by CX-US associations. When the error term is small the acquisition of CS-US associations will be slower and lead to more retardation. Finally, the fourth factor is Novelty' which increases or decreases as a result of the presence or absence of a predicted or unpredicted CS (see equation 4.7). According to the model, as Novelty'

increases, the retardation should decrease as a result of increased z_{CS} and X_{CS} and faster forming $V_{CS\text{-}US}$ associations (see equation 4.9).

2.4.9 Extinction of Conditioned Inhibition and Predictions of the Model

As discussed above, in contrast to the Rescorla-Wagner model, the SLG model assumes that B_{US}, B_{CS} and B_{CX} take only positive values. Hence, the model prevents the elimination of inhibitory associations during non-reinforced presentations of the conditioned inhibitor, as demonstrated by Zimmer-hart and Rescorla (1974), and inhibitory associations becoming excitatory when the inhibitor is presented with a neutral CS, as demonstrated by Baker (1974). As depicted in the previous section, the model assumes that both summation and retardation test performances of a conditioned inhibitor are affected by attentional and associative components of a CS. Thus, although inhibitory associations are not eliminated during extinction treatment of a conditioned inhibitor it is still possible to decrease or increase the inhibitory power of a CS in a summation or a retardation test by manipulating the amount of attention directed to the inhibitor. Based on this idea the model makes two specific predictions regarding deactivation and re-activation of conditioned inhibitors.

First, according to the model during the extinction treatment of the conditioned inhibitor, $V_{CX\text{-}CS}$ associations are formed and therefore, the CS becomes strongly

predicted by the CX and Novelty' and z_{CS} decrease (Equations 4.4. and 4.8). The model predicts that the decreased z_{CS} values should result in less inhibition performed by the conditioned inhibitor in a summation test as the amount of inhibition is based on the amount of attention directed to the inhibitory CS (Equation 4.10). On the other hand, the decreased z_{CS} values should result in even slower conditioning in a retardation test (Equation 4.9) and therefore, the conditioned inhibitor should appear more inhibitory in a retardation test.

Second, according to the model, if the conditioned inhibitor is paired with a novel CS following extinction treatment of the inhibitor Novelty' and z_{CS} should increase because of the unpredicted presentation of the novel CS (Equation 4.4). Consequently, this will result in more inhibitory power in a summation test due to increased internal representation of the inhibitor, X_{CS}. In contrast, increased X_{CS} should result in faster conditioning (Equation 4.9). Hence, the conditioned inhibitor should appear less inhibitory in a summation test after being paired with a novel CS. These predictions will be tested in Chapter 4 using a human predictive learning paradigm.

2.4.10 Extinction and Recovery Effects

According to the SLG model, when λ_{US} is equal to prediction of the US (B_{US}), the error term is equal to zero (see Equation 4.9). Notice that this assumption suggests if an

excitatory CS is paired with an inhibitory CS in the absence of the US and the absolute values of their associative strengths are equal, B_{US} will be equal to zero (see Equation 4.10). Therefore, there will be no change in the associative strength of the neither CSs. In other words, the excitatory CS will not extinguish even in the absence of the US (Protection from Extinction, Chorazyna, 1962; Soltysik, 1985; Rescorla, 2003).

As shown in Figure 3 (Upper Panel), according to the SLG model, during extinction, CS-US associations decrease but stay excitatory because the CX becomes inhibitory and protects CS-US associations from extinction. However, both the CX and the CS become unattended because Novelty' decreases as a result of the repeated non-reinforced trials (Figure 3, Lower Panel). Based on these variables, the model explains spontaneous recovery. According to the model, during the delay that follows extinction, CX-CS associations extinguish and the CS becomes unpredicted by the CX. Following the delay, Novelty' increases when the now unpredicted CS is presented. This leads to (a) an early increase in attention to the excitatory CS, which results in the spontaneous reappearance of the CR, and (b) later to an increase in attention to the inhibitory CX which ends the CR. The model explains renewal in terms of the excitatory CS being able to elicit CR when it is presented outside the inhibitory context of extinction.

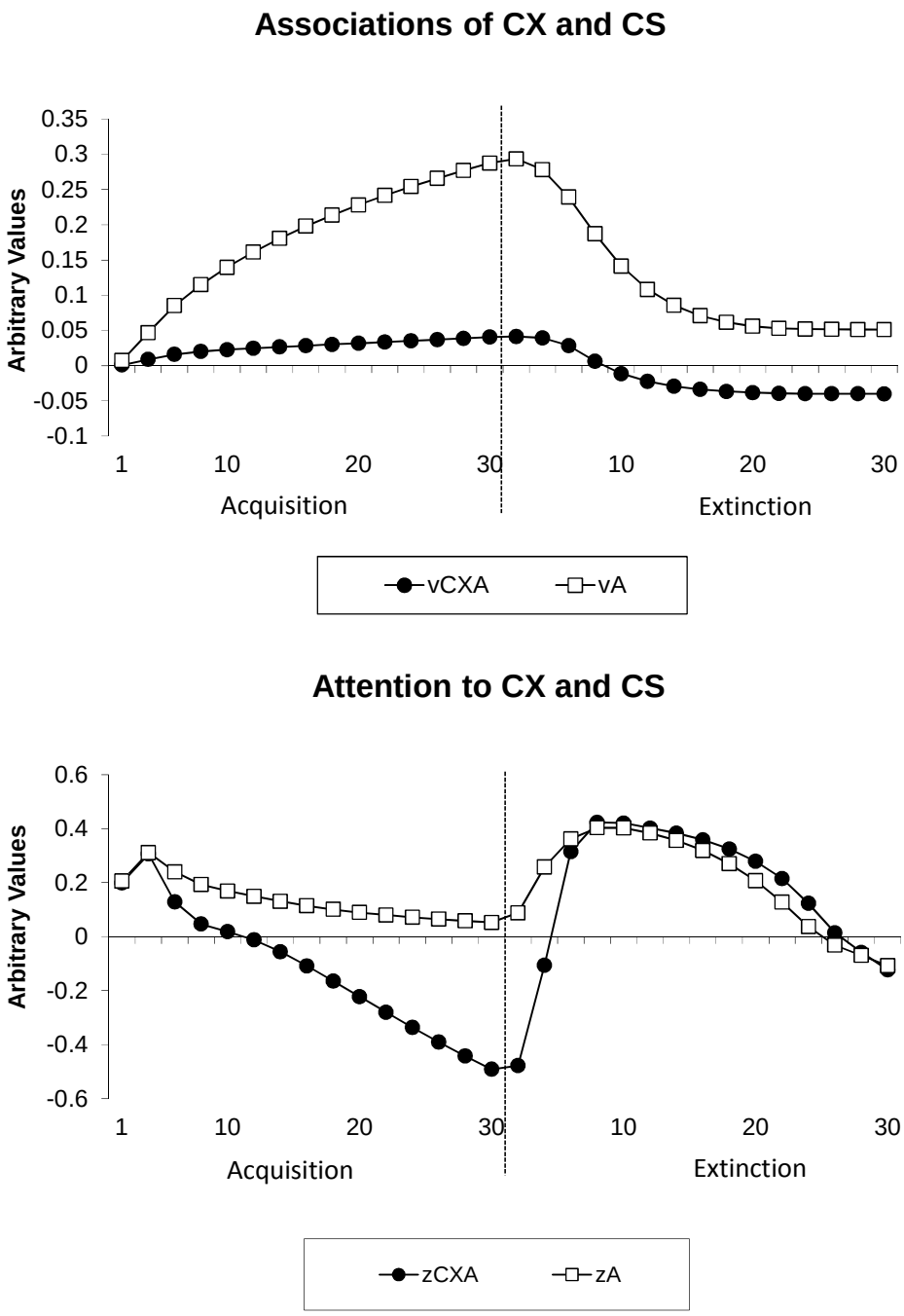

Figure 3. Simulations of the SLG model showing acquisition of extinction. Upper Panel: Simulations with the SLG model showing associations of CXB-US, $V_{CXB\text{-}US}$, and A-US, $V_{A\text{-}US}$. Lower Panel: Simulations with the SLG model showing attention to CXB, z_{CXB}, and A, z_A.

According to the model, reinstatement is the result of the extinction CX becoming neutral or excitatory during CX-US trials. In addition, the model explains a large number of experimental results related to extinction, including re-extinction; facilitation of extinction; the effects of varying the extinction-test interval, the acquisition-extinction interval, the presence of other conditioned stimuli, extinction cue effects, and repeated extinction on spontaneous recovery; external disinhibition; the effects of different procedures, context salience on renewal; the attenuation of renewal by previous extinction, massive extinction, and extinction cues; extinction, attenuation of reinstatement by erasure and massive extinction; reinstatement vs. partial reinforcement and vs. inflation, faster reacquisition with few extinction trials; slower reacquisition with many extinction trials, and slower reacquisition with few acquisition trials (Larrauri & Schmajuk, 2008).

2.5 Other Models of Extinction: Extinction Context as an Occasion Setter

According to Bouton (1993, 1994), the extinction CX does not become inhibitory but serves as a "negative occasion setter "which indicates that the CS will not be followed by the US. Negative occasion setters for a given excitatory CS do not attenuate responding to a different excitatory CS (that is not a target of another feature). That is, occasion setters do not pass a summation test (Morell & Holland, 1993). Also, occasion

setters' ability to modulate a CS-US association is not affected when they are directly paired with the US. That is, when a negative occasion setter is separately trained with a US and tested with its original target again, it still reduces CR to its target (Holland, 1989). This property of occasion setters can be observed when the US (e.g., food) elicits different CRs for each CS (e.g., rearing and head jerking), but it cannot be observed when both the CX (negative occasion setter) and the CS (target) contribute to the same CR. Therefore, the occasion setter view can explain reinstatement based on the direct CX-shock US associations. Only if the CR to the context could be differentiated from the CR to the CS, a confirmation of the property would be possible.

Bouton (1993, 1994) also proposed a memory structure to address the results that failed to detect direct CX-US associations. According to this memory structure, excitatory CS-US associations are formed during acquisition and these associations stay intact during extinction. Instead, during extinction, the CS forms a new inhibitory CS-US association in the absence of the US. Here, the meaning of the CS becomes ambiguous as it both predicts the presence and the absence of the US. Therefore, the CX acts on a CX-CS gate (becomes a negative occasion setter) and assumes control over the inhibitory CS-US association. Therefore, unless the CS and the extinction CX are active together this gated inhibitory association does not become activated and therefore, only the excitatory association to be expressed. Based on this memory structure, Bouton (1993) suggested

that renewal is the result of the gated inhibitory association not being active in a CX different from the extinction CX, reinstatement is the result of the extinguished CS being returned to a feature of the conditioning "context", and spontaneous recovery is explained because the time delay would remove the subject from a temporal extinction context controlling extinction performance. It is unclear, however, why repeated testing results in the elimination of spontaneous recovery (see Thomas, Larsen, and Ayres, 2003). According to the temporal context view, as time elapses during testing and the subject is further removed from the temporal extinction context, recovery should increase instead of decreasing. As mentioned above, the SLG model's notion of the CX becoming inhibitory provides an elegant explanation for spontaneous recovery.

The above-mentioned properties of occasion setters are explained by the Schmajuk, Lamoureux, and Holland (1998, SLH) model. The model consists of 3 layers: 1) direct inhibitory or excitatory CS-US and CX-US associations, 2) configural units (H) activated by the CSs and the CX, and 3) inhibitory and excitatory H-US associations. Therefore, CSs and the CX are directly (through direct associations) and indirectly (through configural units) connected to the US. According to the model, during extinction the CX assumes control over the CR mainly through the configural units but weakly through direct associations and, thereby, acts as an occasion setter. Also, during extinction, CS-US associations stay excitatory but the CS forms indirect inhibitory

associations through the configural units. According to the SLH model, renewal occurs because the CX forms inhibitory H-US associations during extinction and these inhibitory associations are deactivated in the absence of the extinction CX. Recently, Kutlu and Schmajuk (2012) offered an extension of the SLG model (the Schmajuk-Lam-Gray-Kutlu; SLGK model) that can describe occasion setting by assuming a hidden unit layer similar to the SLH model. According to the SLGK model, even though the CX gains occasion setting properties during extinction these properties have a minimal effect.

3. Clinical Implications of Conditioned Inhibition and Extinction

Although most of the discussion on inhibitory learning is fueled by the differences between predictions and assumptions of the dominant theoretical accounts, the importance of inhibitory learning for behavioral therapies is well established. Following sections aim to illustrate how conditioned inhibition and extinction are applied in the clinical field to treat anxiety and fear related psychopathologies.

3.1 Classical Conditioning and Behavioral Therapies

Behavioral therapy is a cluster of therapy techniques based on the idea that abnormal behaviors are learned through classical conditioning and unlearning these maladaptive associations alleviates symptoms related to the psychopathology (Butcher, Mineka, & Hooley, 2004). Wolpe (1969) defined behavior therapy (or conditioning therapy) as "the use of experimentally established principles of learning for the purpose of changing maladaptive behavior (p.VII)". Behavior therapy methods such as exposure therapy, aversion therapy, and modeling are used to treat patients with anxiety disorders including but not limited to panic disorders, generalized anxiety disorder (GAD), and post-traumatic stress disorder (PTSD).

Early 20th century behaviorists successfully demonstrated that a maladaptive behavior such as a phobia can be learned through classical conditioning (see Table 6 for classical conditioning concepts in exposure therapy for spider phobia). For example, in their famous "Little Albert" experiment Watson and Rayner (1920) successfully taught a child to be afraid of a white rat by pairing the sight of the rat with a clanging noise. In this situation, the fear eliciting noise serves as the US, initially neutral but then conditioned fear eliciting rat serves as a CS, and the fear response of the child serves as

Table 6. Classical conditioning concepts in exposure therapy for spider phobia.

Classical Conditioning Concept	Spider Phobia Example
CS	A toy spider
US	A real spider
CR	Heart palpitations
CX	Therapy room
Conditioned Inhibitor	Presence of the therapist
Extinction	Exposure therapy
Extinction Reminder	A painting similar to the one in the therapy room

the CR. Furthermore, Jones (1924) showed that a child's fear of rats can be counterconditioned by pairing the fearful stimulus with a positive US such as food (see Kazdin, 1978 for other examples of early behaviorist attempts). These initial attempts later helped other behaviorists to try counterconditioning anxiety eliciting stimuli through desensitization techniques (Wolpe, 1958). By the 1970s, along with what is called the Cognitive Revolution, behavior therapy changed. The idea was that the human thought is not automatic and it is influenced by personal verbal and cognitive abilities (O'Donohue, 1998). Therefore, newly developed therapies, namely Cognitive-Behavioral Therapy or CBT, integrated the principles of Cognitive Psychology and behavioral therapies. Today, CBT is used for the treatments of wide range of psychopathology including mood, personality and anxiety disorders as well as psychotic disorders. Interestingly, Cognitive-Behavioral therapies still use techniques, which are mostly based on classical conditioning paradigms. Next sections will review two of these techniques, using conditioned inhibitors as safety signals and extinction as a model of exposure therapy.

3.2 Conditioned Inhibitors as Safety Signals

People use safety signals on a daily basis. For example, a person who is afraid of dogs may not perceive a dog on a leash as a threat because the leash serves as a safety

signal. The idea behind safety signals is very similar to the conditioned inhibition mechanism (see Table 6). In our example, the dog serves as a fear eliciting stimulus or an excitor CS (A) because it has previously been associated with fear (analogous to A+ trials). On the other hand, when the dog is on a leash, the leash serves as an inhibitory CS (X) because the person has previously learned that a dog on a leash is not dangerous (analogous to AX- trials).

According to Barlow (1988), this mechanism is malfunctioning in people who have panic disorder. Panic disorder is a type of anxiety disorder and defined as recurrent and unexpected episodes of panic attacks in which the person experiences cognitive symptoms of depersonalization, fear of dying, or fear of losing control (Butcher et al., 2004). Barlow (1988, Barlow, Chorpita, & Turovsky, 1996) proposed a theory, known as the "alarm theory", of panic disorders based on classical conditioning. According to this theory, real dangerous events are "true alarms" but sometimes the individual may experience "false alarms" where a safe event is perceived as dangerous. True alarms trigger non-clinical panic or a flight-or-fight response which become associated with internal and external cues (A+ trials). During a false alarm, the individual learn to identify internal and external cues as conditioned inhibitors or safety signals (AX- trials). This way the individual will not experience anxiety and fear when he/she encounters the same situation again. However, according to Barlow, an

individual with panic disorder would fail to differentiate between cues that are associated with danger and safety or in other words, between A+ and AX- events. Usually these individuals are not able to tell if their internal bodily responses or a real dangerous event trigger panic (Williams, Johns, & Norton, 1998).

One of the treatment methods for panic disorders is based on helping individuals establishing safety signals or in other words, acquiring conditioned inhibitors which provide long-term reduction of stress by preventing direct confrontation with the anxiety eliciting stimuli or situations (Michelson et al., 1990; Demertzis & Craske, 2005). For example, Cox, Endler, & Swinson (1992) demonstrated that in the presence of a trusted friend or a therapist, individuals with panic disorder may perform stressful activities. In this case, the trusted individual serves as a safety signal. Furthermore, Carter, Hollon, Carson, & Shelton (1995) showed that CO_2 inhalation induced panic response was reduced when the subjects were with a trusted person that they identified as "safe" before the experiment.

Overall, the parallels between conditioned inhibitors and safety signals as defined in Clinical Psychology makes it very important to understand the inhibitory mechanisms in associative learning. Theoretically, similar inhibitory mechanisms play a very vital role in extinction (see Chapter 2). Next section reviews the relationship between inhibitory learning in extinction and exposure therapies.

3.3 Extinction as a Model of Exposure Therapy

Anxiety disorders are attributed to deficits in extinction learning (Craske, Liao, Brown, & Vervliet, 2012). As shown by Lissek, Powers, and McClure's (2005) meta-analysis of behavioral studies, patients with anxiety disorders show greater anxiety response (galvanic skin response, startle reflex, and US expectancy ratings) to the CS+ (the CS paired with the US during acquisition but not during extinction) during the acquisition phase and even during the extinction phase where the US presentations are omitted. Furthermore, these individuals show stronger response to CS-, the CS that is never paired with the US during differential conditioning. There are number of studies showing that extinction performance is delayed in the individual with anxiety disorders (Blechert, Michael, Vriends, Margraf, & Wilhelm, 2007; Craske, Waters, Henry, & Neumann, 2008; Michael, Blechert, Vriends, Margraf, & Wilhelm, 2007; Milad et al., 2009). Lissek et al. (2005) argued that individuals with anxiety disorders fail to learn inhibitory safety signals during extinction. Consequently, these individuals fail to learn that CS+ during extinction or CS- throughout the experiment serves as a safety signal. Critically and in line with safety signals as conditioned inhibitors idea discussed in the previous section, Liao and Craske (2013) demonstrated that healthy individuals showed impaired inhibitory learning after anxiety induction compared to healthy individuals

who did not receive the treatment. Finally, Craske et al. (2008a) found that children who show difficulties in learning inhibitory signals are at a higher risk of developing anxiety disorders when they become adults. These studies suggest a causal relationship between impaired inhibitory processing and anxiety disorders.

As discussed by Craske and her colleagues (Craske et al., 2008b, 2012) one way to treat anxiety disorders is to enhance inhibitory learning using repeated extinction treatment. Exposure therapies used for the treatment of anxiety disorders, drug addiction, and phobias (Bouton, 2000; Chambless & Ollendick, 2001) serve this purpose. Similar to extinction procedure, during exposure therapy the stimulus that is the source or the trigger of fear, anxiety or addictive behavior is treated as a CS that is being extinguished. For example, during exposure therapy for spider phobia, stimuli resemble spiders are presented to the patient in the absence of the aversive outcome to eliminate the association between these cues and fear. Otto, Smiths, and Reese (2005) called this procedure "safety learning". During this process a new association is learned by creating new mental representations without eliminating the old memory. In line with this idea, Foa and Kozak (1986) proposed a theory on the process of newly formed memory representations called "emotional processing theory". According to this theory, activation of the fear memory by external or internal cues during exposure is required to encode new information that is incompatible with the old memory. The initial activation

of the fear is followed by reduction of the fear response with repeated exposure and this new information suggesting that the feared consequence will not occur is integrated into what authors called a "fear network". Foa and Kozak (1986) suggested that reduced physiological response to the fear eliciting cues or habituation is an indicator of successful integration of the new safety memory into the system. According to Bouton (2004), this new learning occurs as a result of "expectancy violation". Bouton (2004) suggested that presentation of the CS leads the person to expect the occurrence of the US but this expectancy is violated in each extinction trial as the US occurrence is omitted. Similarly, in exposure therapy the patient expects the fearful outcome as a result of the presentation of a fear-eliciting stimulus. As this expectancy is violated, a new mental representation is encoded. All three ideas are compatible with the inhibitory learning hypothesis of exposure therapies as both theories suggest that a new safety memory which counteracts the old fear memory is learned during exposure therapy sessions.

Exposure therapy is also widely used to treat PTSD, an anxiety disorder caused by a traumatic event. Traumatic events are fairly common. Estimated 37% to 92% of the population experience traumas (Breslau et al, 1998). After a traumatic event the negative emotional response (e.g. re-experiencing, avoidance, and hyperarousal) usually extinguishes with time. In individuals with PTSD, this automatic extinction fails and the emotional response becomes persistent (Rothbaum & Davis, 2003). Jovanovic et al.

(2009) found that following the AX+/BX- training, veterans with PTSD fail to learn that B becomes inhibitory when tested in a summation test. Therefore, similar to the other anxiety disorders, the pathology behind PTSD is also believed to be related to the impaired inhibitory learning during extinction.

PTSD is different from specific phobias because the acquired fear is generally expressed to many different stimuli associated with the traumatic event. Instead, in specific phobias the acquired fear is usually associated with one stimulus or object (e.g. spider or snake). However similar to the therapy used for phobias, during exposure therapy, the PTSD patient is given exposure to the cues associated with the traumatic event in the absence of danger in order to successfully extinguish the negative emotional responses. In an exposure therapy session, PTSD patients are given "imaginal exposure" which requires repeatedly narrating the traumatic event, and "in vivo exposure" consisted of exposure to the trauma related situations and objects while the therapist gives emotional support to identify the therapy context as a safety cue (Rothbaum & Davis, 2003). Lately, computer generated virtual environments which provide a more realistic experience of the traumatic events using more consistent visual and audio stimulation are being tried for more effective exposure therapies (Rothbaum, Kozak, Foa, & Whitaker, 2001).

Exposure therapy alleviates PTSD symptoms in 60% to 80% of the trauma patients in average. However, as discussed in section 1.2, there is ample evidence showing that the extinction treatment does not eliminate excitatory associations between the CS and the US but forms a new inhibitory association, probably between the CX and the US, instead. Similar to the safety signals discussed in section 3.2 and in line with the SLG model, during exposure therapy, we can assume that the whole therapy context or individual contextual cues may be learned as a safety signal. Consequently, PTSD patients who received successful exposure therapies are vulnerable to the recovery of the fear response, relapse, in the absence of these safety signals. Therefore, the inhibitory properties of the extinction context become vital to determine the effectiveness of an exposure therapy.

3.4 Recovery Effects and Relapse in Anxiety Disorders

As mentioned above, one major problem with the extinction approach is the fact that the association between the trigger stimulus and fear cannot be eliminated. Similarly, even after a successful exposure therapy relapse is common (Craske, 1999). There are at least 3 main sources of relapse in anxiety disorders, spontaneous recovery, renewal, and reinstatement.

Spontaneous recovery of fear after an interval of time between extinction and retest is also observed in a clinical setting. Spontaneous recovery of fear is commonly observed when a fear-eliciting stimulus that is previously extinguished during exposure therapy is encountered some time after the completion of the therapy. (e.g., Craske & Rachman, 1986; Craske & Mystkowski, 2006). For example, a patient whose spider phobia is treated as a result of exposure therapy may experience fear when he/she goes back to therapy after some time and reencounters the same spider image used during the therapy. According to the SLG model, this happens because following the interval after the therapy the patient pays more attention to the spider image as the image is not predicted and therefore, the fear response recovers before the inhibitory CX becomes effective.

Renewal also arises as a source of relapse in a clinical context. Patients usually receive exposure therapy in one or two different contexts. Therefore, even after a successful exposure therapy session the fear may return when the patient encounters a fear-eliciting stimulus in a different context, such as home, in the absence of the contextual cues of the therapy room which are associated with the absence of the fear (safety signals or conditioned inhibitors). For example, a person with spider phobia may feel comfortable to view spider images in the presence of the therapist in the therapy room because these external cues serve as safety cues. In other words, the patient knows

that nothing bad happens as a result of viewing the previously fear eliciting images when he/she is in the therapy room (AX- trials). However, when the person encounters the same spider image at home he/she may experience fear (A alone trials) because the safety provided by the therapy room is missing. According to the SLG model, the renewed fear response is a result of missing inhibitory associations of the therapy context, which prevent the spider image eliciting fear during therapy. In addition to the animal fear-conditioning experiments renewal of various conditioned responses including alcohol craving among non-alcoholic drinkers (Collins & Brandon, 2002), speedball self-administration in rats (Crombag & Shaham, 2002), spider phobia (Mineka, Mystkowski, Hladek, & Rodriguez, 1999; Mystkowski, Craske, & Echiverri, 2002), and auditory fear (Hermans, Craske, Mineka, & Lovibond, 2006) in humans have been reported as a result of changing the extinction context.

Finally, reinstatement is another cause of recovery of fear after exposure therapy. Reinstatement of fear may occur if any negative emotion is experienced in the therapy context. For example, if a patient with spider phobia experiences an emotionally negative event during the exposure to a live spider, this may lead patient to experience fear even in the therapy context next time he/she encounters a fear eliciting image. According to the SLG model, the recovery of the fear to the spider image is a result of

the therapy context losing its inhibitory properties when the adverse event (the US) occurs in the same context.

In sum, there are several sources of relapse after exposure therapy and the underlying mechanism can be explained by attentional-associative terms. Even though, these mechanisms are still in debate, recently several methods derived from associative learning literature have been tried to reduce relapse in anxiety disorders. Next section discusses these methods, their results and potential problems.

3.5 Methods of Reducing Relapse

3.5.1 Extinction Manipulations

Since exposure therapy is established on classical conditioning mechanisms, several solutions based on extinction have been proposed to reduce relapse and experimentally tested in the laboratory environment. One of these methods is called "super extinction" which involves extinguishing not one but multiple excitors simultaneously which should result better and faster extinction (Rescorla, 2000). This method has been found to be effective in reducing renewal in animals but not in humans (Vervliet, Vansteenwegen, Hermans, & Eelen, 2007). Another method is called "deepened extinction". In this method multiple excitors are first extinguished separately and then combined for another extinction treatment (Rescorla, 2006). This method was

shown to reduce spontaneous recovery and reinstatement both in animals and humans (Culver et al., in sub cf. Craske et al., 2012). Similarly, "massive extinction" is a method where an extensive number of extinction trials are used to achieve better extinction learning. Denniston, Chang and Miller (2003; also see Tamai and Nakajima, 2000) demonstrated massive extinction treatment reduces renewal whereas Thomas, Vurbic, and Novek (2009; also Rauhut, Thomas, & Ayres, 2001) failed to replicate these findings. Finally, another method is to extinguish an excitor in multiple contexts. Gunther, Denniston, & Miller (1998) tested this idea and found that extinguishing an excitor in three different contexts yielded less renewal than the case in which the excitor is extinguished only in a single context.

Interestingly, all four methods aim to achieve better extinction learning by using conditioned inhibition mechanisms. Possibly, super extinction, deepened extinction, and massive extinction achieve a better extinction learning because these methods help the organism to better associate external cues with safety. On the other hand, in "extinction in multiple contexts" the excitor is released from protection from extinction effect (see section 2.1.2) because the CS-US association weakens in each extinction phase before the neutral context acquires inhibitory associations and net associative value becomes zero.

3.5.2 Extinction Reminders

Another way to decrease relapse is creating artificial safety signals or namely, "Extinction reminders (ERs)". Generally, ERs are either neutral stimuli deliberately presented paired with the CS that is being extinguished during extinction or contextual cues from the extinction CX such as a painting or a desk. Brooks & Bouton (1994) reduced renewal by training ERs during the extinction phase and presenting them with the extinguished CS after switching back to the acquisition context in rats. Furthermore, ERs were shown to be effective in attenuating the spontaneous recovery of alcohol tolerance (Brooks, Vaughn, Freeman, & Woods, 2004), reducing relapse of stimulus induced alcohol craving in social drinkers following exposure therapy (Collins and Brandon, 2002), and renewal of the conditioned fear to an extinguished stimulus in humans (Dibbets, Havermans, & Arntz, 2008). In summary, ERs may work as additional safety signals by reminding the extinction context. Massad and Hulsey (2006) suggested that other members in a group exposure therapy may also work as extinction reminders outside the therapy CX and reduce the chance of relapse. Therefore, the inhibition of the ERs replaces the inhibition of the extinction context and reduces renewal when subjects are returned to the acquisition context.

Extinction reminders may work both as conditioned inhibitors by directly becoming inhibitory and an occasion setters by exerting inhibition without becoming

inhibitory. Ross and Holland (1981, also Rescorla, 1985) found that in a feature negative discrimination training, A+/AX-, X becomes a conditioned inhibitor if A and X are presented simultaneously during compound trials (AX-) and X becomes a negative occasion setter if A and X are presented serially (X→ A-). As discussed in Chapter 2 (section 2.5), occasion setter extinction reminders do not pass the summation test as they cannot be transferred to another excitatory CS unless the excitor is the target CS of another negative occasion setter (Morell & Holland, 1993, Holland, 1986, 1989). Therefore, extinction reminders learned through occasion setting are only effective to a specific fear eliciting stimulus and they cannot be used for different fear eliciting stimuli. In contrast, conditioned inhibitors have an advantage over the occasion setters as they can be transferred to other excitors.

3.6 Activation and Deactivation of Discrete and Contextual Safety Signals

As discussed in previous sections, historically, clinical researchers have always considered inhibitory learning as a part of both etiology and treatment of anxiety disorders. Exposure therapy techniques that are used to treat fear and anxiety related disorders work through establishing external cues as safety signals and as explained in previous sections, acquiring safety signals is based on conditioned inhibition principles.

Therefore, unless they are learned as occasion setters, discrete safety signals such as auditory or visual stimuli are subject to the same limitations that the conditioned inhibitors are. Consequently, after Zimmer-Hart and Rescorla's (1974) findings we can assume that once learned, safety signals cannot be extinguished. However, the SLG model predicts that after using safety signals such as extinction reminders a number of times after the therapy, the patient should start paying less attention to these signals and therefore, safety signals should lose their inhibitory power and the patient becomes more prone to relapse. To avoid this potential problem the SLG model suggests that these safety cues should be presented with novel stimuli to increase attention to these cues and reactivate their inhibitory power. Thus, testing the SLG model's predictions regarding activation and deactivation conditioned inhibitors is crucial to understand the limits of safety signals.

Another important aspect of exposure therapy is that the patient learns the therapy context as a safe environment or individual contextual cues as extinction reminders. Even though there are models that assume that the extinction context becomes inhibitory during non-reinforced presentation of the CS (e.g. the SLG model), several studies failed to show that the extinction context passes the summation test ((Bouton & King, 1983, Bouton & Swartzentruber, 1986, 1989). Therefore, Bouton (1991) argued that extinction contexts are occasion setters that do not acquire inhibitory

properties but set the occasion for the CS. Occasion setters and conditioned inhibitors are subject to different limitations (discussed in Chapter 5). For example, as suggested by the SLG model, negative occasion setters cannot be transferred to another excitor. Consequently, it is important to understand if the therapy context becomes a conditioned inhibitor or an occasion setter. If the therapy context becomes a conditioned inhibitor, then it will be activated and deactivated using the same methods suggested for discrete safety signals. By doing so, relapse based on lack of contextual inhibition may be better understood. Chapters 4 and 5 experimentally test the SLG model's predictions regarding the above-mentioned questions.

4. Deactivating and Activating Discrete Conditioned Inhibitors

4.1 Introduction

As mentioned in chapters 1 and 2, the Rescorla-Wagner (1972) model predicts that conditioned inhibitors lose their inhibitory associations through non-reinforced presentations. However, Zimmer-Hart and Rescorla's findings (1974) failed to support this prediction. Subsequent theories (e.g. Schmajuk, Lam, and Gray, 1996) incorporated this result into their models to avoid erroneous predictions. Therefore, although the SLG model assumes that the inhibitory associations are not eliminated during the non-reinforced presentations of a conditioned inhibitor as discussed in section 1.3, the model predicts that attention to the inhibitory CS should decrease as a result of such treatment. Furthermore, the model assumes that Novelty' and attention to a CS should increase when a novel CS is presented with that CS. Based on these assumptions the model predicts that extended extinction treatment should result in a) decreased inhibitory power in a summation test and b) weaker conditioning in a retardation test as a result of decreased attention. Furthermore, the model predicts that pairing the conditioned inhibitor with a novel CS after the extinction treatment should result in a) reactivated inhibitory power in a summation test and b) stronger conditioning in a retardation test as a result of increased attention. We simulated and tested the above-mentioned predictions of the SLG model in 3 experiments.

4.2 Simulation Method

All simulations used values for the independent variables: The saliences of the 20 time unit (t.u.) CSs were 1; the US strength was 1, and its duration was 5 t.u., overlapping with the last 5 t.u. of the CSs. The salience of the CX was 0.1, and the ITI was 1,500 t.u. The same results were obtained with a large range of different simulation values, such as CS, US durations, ITI, CS, US saliences, and trial numbers.

4.3 Experiment 1: Deactivation and Activation of Conditioned Inhibition in a Summation Test

4.3.1 Predictions of the SLG Model

According to the SLG model, a neutral CS that is paired with an excitatory CS in the absence of the US forms inhibitory associations with the US and becomes a conditioned inhibitor. With repeated non-reinforced presentations, attention to the conditioned inhibitor decreases while the inhibitory associations are not affected. The reason why Novelty' and attention decrease during repeated non-reinforced trials is that during these trials associations between the CX and CS and also between the CS and itself become stronger and the CS becomes predicted by the CX and by itself. Since the CS is predicted and present the novelty in the environment decreases. Also, the model assumes that when a conditioned inhibitor with a low z_{CS} value is paired with another

excitor during the summation test the amount of inhibition is reduced because the expression of an excitatory or inhibitory association is dependent on the amount of attention directed to that CS (Equation 4.10). Moreover, the model suggests that if a CS is paired with a novel CS, Novelty' and so the attention to both CSs increase because the novel CS is not predicted by either the CX or the CS. Therefore, after such a treatment, the inhibitory power of a conditioned inhibitor should be reactivated in a summation test where it is paired with an excitatory CS. We ran simulations with the SLG model to formally demonstrate these predictions of the model. Simulations for the acquisition phase used 10 A+, 10 AX–, and 10 B + intermixed trials followed by the first summation test which included BX (conditioned inhibition) or BZ (external inhibition) test trials. Following the acquisition phase summation test, simulations for the extinction/recovery (EXT/REC) and in the extinction/no-recovery (EXT/ NOREC) conditions 75 X– trials and 10 G + trials were given, while for the no-extinction/recovery (NOEXT/REC) condition 75 Y– trials were given instead of X- trials. Then, the second summation test, consisted of GX and GW presentations, was given. Following the extinction phase summation test, conditions EXT/REC and NOEXT/REC were given 3 non-reinforced XN trials where N was a novel CS whereas the EXT/NOREC condition received 3 ML- trials where both CSs were novel. Also, all three groups received 5 intermixed H+ trials. This phase was followed by a third and final summation test of HX and HR trials. Therefore, after each

phase a summation test was given where the CR to a different excitor, B, G, or H was measured in a pair either with the conditioned inhibitor X or a novel CS, Z, W, or R.

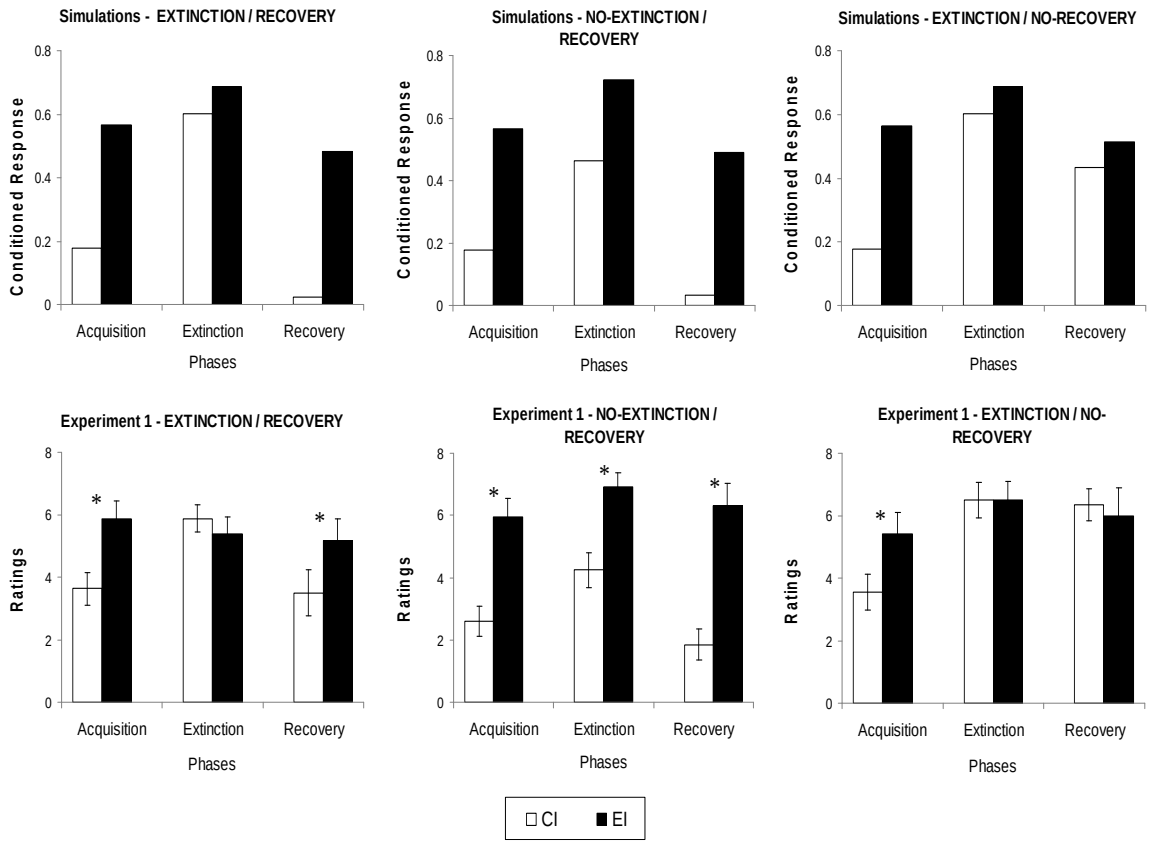

Figure 4. Experiment 1. Simulated CRs and Experimental Ratings in Conditioned Inhibition (CI) and External Inhibition (EI) groups in three summation tests following Acquisition, Extinction and Recovery. Upper Panels: Simulated conditioned responses. Lower Panels: Experimental ratings. Left Panels: Extinction/Recovery Condition. Mid Panels: No-Extinction/Recovery Condition. Right Panels: Extinction/No-Recovery Condition. Asterisks indicate a significant difference at the level of $p<.05$. Error bars show Standard Error of the Mean (SEM).

Simulations of the SLG model suggest that (Figure 4, Upper Panels) during acquisition all three groups should yield a significant conditioned inhibition effect or in other words, a significant difference between the CRs to BX and BZ. Then, the model predicts that this difference should disappear in the EXT/REC and EXT/NOREC conditions, which received X- trials due to decreased attention to X but not in the NOEXT/REC condition. Finally, the difference should resurface in the EXT/REC condition due to increased Novelty' during recovery trials but not in the EXT/NOREC condition while the effect should be slightly enhanced in the NOEXT/REC condition. Overall, the model predicts that conditioned inhibition should disappear with X- trials and be reactivated with XN recovery treatment.

4.3.2 Participants

The participants were 120 (40 in each of three conditions) Duke University undergraduate students who did not participate in any subsequent experiment in this study. Participants were randomly assigned to six experimental groups. Data from 2 of the participants were eliminated due to a program error, and data from 8 participants were eliminated because they failed to meet the learning criterion (see below for details). Ten new participants were then added to complete the groups. Their participation was

rewarded with course credits. Participants required approximately 15 min to complete the experiment.

4.3.3 Apparatus and Stimuli

Each participant was seated in front of a PC and was tested individually. A custom-made MATLAB 6.5.2 program was used for the cue presentations and obtaining the participants' responses. The participants used a regular PC keyboard to assign their responses. Thirteen different symbols from Microsoft Word (Ω, ¢, ∂, ξ, ≈, ω, #, ●, *, §, ۞, ∞, 🏛) were used as stimuli. We counterbalanced the role of conditioned inhibitors between different symbols.

4.3.4 Design and Procedure

Each trial in the experiment consisted of two separate response and outcome screens. Response screens (500 * 450 pixels) contained 1 or 2 symbols (270 × 280 pixels, centered on the screen) and two buttons (at the bottom of the screen) labeled as "High Bar–'H' key" and "Low Bar–'L' key." The participants were asked to assign their responses by pressing one of the keys on the keyboard. As soon as one key was pressed, the outcome screen (500 * 450 pixels) appeared, in which the symbols were still present but no response buttons were shown. Instead, either a high red bar (67 pixels wide and 467 pixels high) indicating the presence of an outcome or a very low red bar (67 pixels

wide and 10 pixels high) indicating a negligible outcome was presented on the right side of the screen. While the response screen stayed on for an unlimited time, the outcome screen was on for only 2 s, and there were no time gaps between screen presentations.

The experiment was divided into three phases: acquisition, extinction, and recovery (see Table 7). After each phase was completed, a test screen appeared, and participants were asked to rate each test symbol or combination of symbols on the basis of the information provided during the preceding phase. Specifically, participants were asked to indicate the likelihood of the symbol or combination of symbols predicting the high red bar on a rating scale between 0 (very unlikely) and 9 (very likely) shown at the bottom of the screen. Again, the participants indicated their ratings by using the keyboard.

Table 7. Experimental Design of Experiment 1. Letters indicate different symbols. (+) means an outcome (red bar), (-) indicates the absence of the outcome.

Conditions	Test Groups	Acquisition	Acquisition Summation Test	Extinction	Extinction Summation Test	Recovery	Recovery Summation Test
Extinction Recovery	CI --- EI	10 A+ 10 AX- 10 B+ 10 CD+ 10 E-	1 BX? --- 1 BZ?	75 X- 10 G+ 10 F+	1 GX? --- 1 GW?	3 XN- 5 H+	1 HX? --- 1 HR?
No-Extinction Recovery	CI --- EI		1 BX? --- 1 BZ?	75 Y- 10 G+ 10 F+	1 GX? --- 1 GW?	3 XN- 5 H+	1 HX? --- 1 HR?
Extinction No-Recovery	CI --- EI		1 BX? --- 1 BZ?	75 X- 10 G+ 10 F+	1 GX? --- 1 GW?	3 ML- 5 H+	1 HX? --- 1 HR?

At the beginning of the experiment, all the participants were presented the first set of instructions shown in Appendix 1. The experiment was a 3 × 3 × 2 design, where there were initially three conditions receiving different treatments: EXT/REC and EXT/NOREC conditions, which received non-reinforced trials of X during the extinction phase, and the control NOEXT/REC condition, which received non-reinforced trials of another CS, Y, during the extinction treatment. During the recovery phase, participants in the EXT/REC and NOEXT/REC conditions received non-reinforced X–novel-CS trials, whereas those in the EXT/NOREC condition received non-reinforced trials of two novel CSs. All conditions were divided into two different groups according to the test stimulus they would be asked to rate at the end of each phase. Whereas the conditioned inhibition (CI) groups were asked to rate excitors (B, G, and H) paired with the conditioned inhibitor X (BX, GX, and HX), the external inhibition (EI) groups were asked to rate excitors paired with novel CSs (BZ, GW, and HR). Therefore, there were a total of six groups: EXT/REC–CI, EXT/REC–EI, NOEXT/REC–CI, NOEXT/REC–EI, EXT/ NOREC–CI, and EXT/NOREC–EI. The ratings of CI and EI groups were compared in order to differentiate conditioned inhibition from external inhibition (see Melchers et al., 2006; Rescorla, 1969). During the acquisition phase, all the participants received 10 A+, 10 AX–, and 10 B + intermixed trials, as well as fillers, 10 reinforced compound trials, and 10 non-reinforced single element cue trials. After the inhibitory training, a

summation test was conducted for all participants in order to measure the level of conditioned inhibition following the instructions shown in Appendix 2. During this test, the CI groups were asked to rate (on a 0 to 9 scale) B in compound with the conditioned inhibitor, X, and the EI groups were asked to rate B in a compound with a novel cue, Z. During the extinction phase, the EXT/REC and EXT/ NOREC conditions were given 75 X– and 10 G + intermixed trials; cue G was used for the second summation test after the extinction phase. The NOEXT/REC condition was given 75 non-reinforced presentations of novel cue Y, instead of X– presentations, intermixed with 10 G + trials. Following the extinction phase, the second summation test was conducted with the new transfer cue, G. The CI groups were asked to rate GX, and the EI groups were asked to rate G with a novel cue, W. During the recovery phase, another cue, H, was trained as the predictor of the outcome. To recover the inhibition produced by X, X was paired with a novel cue N without the outcome in the EXT/REC condition. Participants in the EXT/REC and NOEXT/REC conditions were shown five trials of H + and three trials of XN–. Participants in the EXT/NOREC condition were shown five trials of H + and three trials of ML– (two novel CSs). Finally, the last summation test was conducted. Again, the CI groups rated HX, and EI groups rated H with a novel cue, R.

4.3.5 Results and Discussion

As is shown in the lower panel of Figure 4, the experimental results closely match the predictions of the model for summation tests in the different phases of the experiment. Following conditioned inhibition training (acquisition), the inhibitory CS decreased responding to a conditioned excitor in a summation test, but the inhibitory effect disappeared following repeated non-reinforced presentations (extinction) and reappeared following presentations of the inhibitory CS with a novel CS (recovery). Instead, when another CS was repeatedly not reinforced, the extinction treatment had no effect. Finally, when a CS (different from the CI) was paired with a novel CS, no recovery was observed in the summation test (however, such a procedure has an effect in a retardation test; see the Discussion section for Experiment 3).

Figure 4 (lower panels) shows the mean ratings for the test trials of excitor with the conditioned inhibitor X, (BX, GX, and HX) and the excitor with a novel CS, BZ, GW, and HR (test group: CI, or EI) for the EXT/REC, NOEXT/REC, and EXT/NOREC conditions (condition) during three summation tests, after the acquisition, extinction, and recovery phases, respectively (phase). Eight participants were eliminated (5 in the EXT/REC–CI condition and 3 in the NOEXT/REC–CI condition) because they assigned a rating larger than 7 to the BX compound, which indicates that they did not acquire conditioned inhibition when compared with the responses to the BZ compound.

Together with the 2 other participants eliminated due to program error, ratings from 120 participants were included in our statistical analysis.

A 3 × 3 × 2 repeated measures ANOVA yielded a significant interaction between condition (EXT/REC vs. NOEXT/REC vs. EXT/NOREC), phase (acquisition vs. extinction vs. recovery), and test group (CI vs. EI), $F(4, 226) = 2.54$, $p < 0.05$. The aim of the following sections is to identify the source of the interaction between each condition.

4.3.5.1 EXT/REC and NOEXT/REC Conditions

A two-way ANOVA did not yield a significant interaction between test group (CI vs. EI) and condition (EXT/REC vs. NOEXT/ REC) for the acquisition phase, $F(1, 76) = 1.32$, $p > 0.05$, indicating that there was no significant difference between the levels of conditioned inhibition of these four groups. Additional two-tailed t-tests showed that both EXT/REC and NOEXT/REC conditions rated CI lower than EI, $t(38) = 3.38$, $p < 0.05$, and $t(38) = 4.40$, $p < .001$, respectively. These results demonstrate that conditioned inhibition was learned by both groups during the acquisition phase.

After the extinction phase, a repeated measures ANOVA showed that a three-way interaction for the acquisition and extinction phases of test group (CI vs. EI), phase (acquisition vs. extinction), and condition (EXT/REC vs. NOEXT/REC) was significant, $F(1, 76) = 4.54$, $p < 0.05$. A two-way ANOVA yielded a significant interaction between test group (CI vs. EI) and condition for the extinction phase, $F(1, 76) = 11.81$, $p < 0.05$.

This result indicates that CI decreased in the EXT/REC condition, but not in the NOEXT/REC condition during the extinction phase. Furthermore, two separate repeated measures ANOVAs yielded a significant interaction between test group (CI vs. EI) and phase (acquisition vs. extinction phase) for the EXT/REC condition, $F(1, 38) = 14.35$, $p < 0.05$, while that interaction was not significant for the NOEXT/REC condition, $F(1, 38) = 1.09$, $p > 0.05$. Moreover, additional two-tailed t-tests showed that the participants in the NOEXT/REC condition, but not in the EXT/REC condition, rated CI lower than EI, $t(38) = 3.64$, $p < 0.05$, and $t(38) = 1.04$, $p > 0.05$, respectively. These results demonstrate that X lost its inhibitory power after the extinction phase in the EXT/REC condition, but not in the NOEXT/REC condition.

Note that even when the ratings for both test groups were lower in the acquisition than in the extinction phase for the NOEXT/REC condition, the interaction between test group (CI vs. EI) and phase (acquisition vs. extinction phases) was not significant for that condition. This result was also predicted by the model as follows. The larger ratings after extinction in the NOEXT/REC condition are the consequence of the increased Novelty' and attention to the transfer excitor H used in the summation test because Y is absent but expected.

After the recovery phase, a repeated measures ANOVA showed that the three-way interaction of test group (CI vs. EI), phase (extinction vs. recovery phases), and

condition was not significant, $F(1, 76) = 1.00$, $p > 0.05$. The interaction between test group (CI vs. EI) and condition (EXT/REC vs. NOEXT/REC) was not significant, $F(1, 76) = 2.68$, $p > 0.05$. Furthermore, after recovery, two-tailed t-tests showed that participants in both the EXT-REC and NOEXT/REC conditions rated CI lower than EI, $t(38) = 2.36$, $p < 0.05$, and $t(38) = 4.54$, $p < .001$, respectively. However, the interaction between test group (CI vs. EI) and phase (extinction and recovery phases) was significant for the EXT/REC condition, $F(1, 38) = 8.93$, $p < 0.05$, but not for the NOEXT/REC condition, $F(1, 38) = 2.84$, $p > 0.05$. These results demonstrate that the inhibition was recovered after the recovery phase for the EXT/REC condition, but it was not significantly increased for the NOEXT/REC condition.

4.3.5.1 EXT/REC and EXT/NOREC Conditions

A two-way ANOVA did not yield a significant interaction between test group (CI vs. EI) and condition (EXT/REC vs. EXT/ NOREC) for the acquisition phase, $F(1, 72) = 0.10$, $p > 0.05$, indicating that there was no significant difference between the levels of conditioned inhibition of these four groups. Additional two-tailed t-tests showed that participants in both the EXT/REC and EXT/NOREC conditions rated CI lower than EI, $t(38) = 3.38$, $p < 0.05$, and $t(34) = 2.64$, $p < 0.05$, respectively. These results demonstrate that conditioned inhibition was learned by both groups during the acquisition phase.

After the extinction phase, a repeated measures ANOVA showed that a three-way interaction for the acquisition and extinction phases of test group (CI vs. EI), phase (acquisition vs. extinction), and condition (EXT/REC vs. EXT/NOREC) was not significant, $F(1, 72) = 0.61$, $p > 0.05$. A two-way ANOVA did not yield a significant interaction between test group (CI vs. EI) and condition for the extinction phase, $F(1, 72) = 0.39$, $p > 0.05$. This result indicates that CI decreased in both the EXT/REC and EXT/NOREC conditions during the extinction phase.

After the recovery phase, a repeated measures ANOVA showed that the three-way interaction of test group (CI vs. EI), phase (extinction vs. recovery phases), and condition was significant, $F(1, 72) = 4.62$, $p < 0.05$. The interaction between test group (CI vs. EI) and phase (extinction and recovery phases) was significant for the EXT/REC condition, $F(1, 38) = 8.93$, $p < 0.05$, but not for the EXT/ NOREC condition, $F(1, 34) = 0.11$, $p > 0.05$. Furthermore, two-tailed t-tests showed that participants in the EXT/REC condition rated CI lower than EI, $t(38) = 2.36$, $p < 0.05$, but not in the EXT/NOREC condition, $t(34) = 0.82$, $p > 0.05$. These results demonstrate that the inhibition was recovered after the recovery phase for the EXT/REC condition, but not for the EXT/NOREC condition.

In sum, supporting the predictions of the SLG model, summation tests in Experiment 1 show that X was deactivated after non-reinforced trials. In addition, also

supporting the predictions of the SLG model, Experiment 1 shows that X, which had been deactivated after non-reinforced trials, was reactivated by pairing X with a novel stimulus. The three-way interaction is significant after the recovery phase because the EXT/REC, but not the EXT/NOREC, condition is affected by the treatment.

While at the end of the extinction phase, Experiment 1 indicates that X– trials result in a decreased inhibitory effect, thereby supporting the SLG model's prediction of a decreased attention z_X and X_X, it is still possible that, as suggested by the Rescorla and Wagner (1972) model, the inhibitory association V_{X-US} also decreases. However, the reinstated inhibition at the end of the recovery phase is consistent with the SLG model assumption that the V_{X-US} association had been preserved.

4.4 Experiment 2: Deactivation of Conditioned Inhibition in a Retardation Test

4.4.1 Predictions of the SLG Model

The SLG model suggests that while inhibitory power of a conditioned inhibitor is decreased with repeated non-reinforced presentations it also takes longer to be conditioned in a retardation test. This is because according to the model, with extended non-reinforced presentations, attention to the CS, z_{CS} decreases and the decreased z_{CS} results in slower changes in V_{CS-US} (see equation 4.9). To demonstrate this effect we ran simulations with the SLG model.

Simulations for the acquisition phase consisted of 10 A+, 10 AX–, and 10 B + intermixed trials which was followed by a summation test of B, BX, and BZ in order to validate that X was learned as a conditioned inhibitor. This phase was first followed by 75 X- trials for the Extinction group and 75 Y- for the No-Extinction group. Then, a conditioning phase of 3X+/3J+ intermixed trials where J was a novel CS were given.

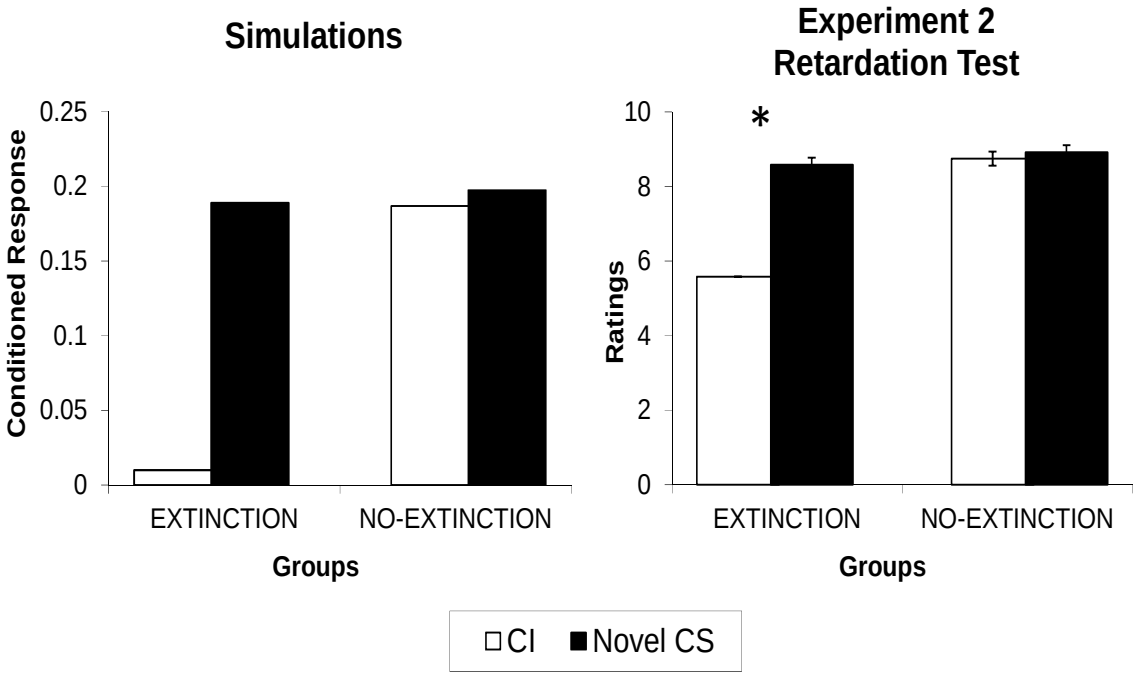

Figure 5. Experiment 2. Simulated CRs and Experimental Ratings after conditioning trials of the Conditioned Inhibitor (CI) and a Novel CS in a retardation test following Extinction or No-Extinction. Left Panel: Simulated Conditioned Responses to the conditioned inhibitor (CI) and a Novel CS, for Extinction and No-Extinction groups. Right Panel: Experimental ratings of conditioned inhibitor (CI) and a Novel CS, for Extinction and No-Extinction groups. Asterisks indicate a significant difference at the level of $p<.05$. Error bars show Standard Error of the Mean (SEM).

Finally, X and J were tested individually during the retardation test. Simulations of the SLG model suggest that conditioning of X was retarded compared to the Novel CS, J, in the Extinction group but not in the No-Extinction group (Figure 5, left panel).

4.4.2 Participants

The participants were 24 Duke University undergraduate students that had not taken part in any other experiment in this study. Their participation was rewarded with course credits. They were randomly assigned to two experimental groups.

4.4.3 Apparatus and Stimuli

The apparatus and stimuli were identical to those in Experiment 1.

4.4.4 Design and Procedure

Acquisition and extinction phases were identical to those in Experiment 1, except that instead of a summation test after the extinction phase, a retardation test was conducted (see Table 8). Ten F + trials during the extinction phase were kept as fillers. The first summation test, where the participants were asked to rate all stimuli (B, BX, and BZ), was run to verify that a significant level of conditioned inhibition was achieved. Escobar, Arcediano, and Miller (2003) successfully achieved retardation of a CS that was previously preexposed in a human predictive learning task without a

Table 8. Experimental Design of Experiment 2. Letters indicate different symbols. (+) means an outcome (red bar), (-) indicates the absence of the outcome.

Conditions	Acquisition	Acquisition Summation Test	Extinction	Conditioning	Retardation Test
Extinction Treatment	10 A+ 10 AX- 10 B+	1 B? 1 BZ? 1 BX?	75 X- 10 F+	1 X+	X?
				1 J+	J?
No-Extinction Treatment	10 CD+ 10 E-		75 Y- 10 F+		

masking task by using only a single acquisition trial and testing in the absence of the outcome. In line with this procedure, for the retardation test, initially, one reinforced novel CS trial, J+, and one X + trial were presented to the participants in order to condition X and J. Then, after the retardation phase, the participants were asked to rate J and X only once. The order of the test trials was counterbalanced.

4.4.5 Results and Discussion

After the acquisition phase, a repeated measures ANOVA did not yield a significant interaction between test stimuli (CI vs. EI) and condition (extinction vs. no-extinction), $F(1, 22) = 0.19$, $p > 0.05$, indicating no significant difference between the levels of conditioned inhibition in extinction and No-Extinction conditions in the

summation tests. Additional two-tailed t-tests showed that both conditions rated CI lower than EI, $t(11) = 4.60$, $p < 0.05$, and $t(11) = 5.30$, $p < .001$, respectively. These results show that conditioned inhibition was achieved for both groups during the acquisition phase.

Figure 5 (Right Panel) shows the mean ratings for the retardation test of a novel CS, J, and the conditioned inhibitor, X, for Extinction and No-Extinction conditions following the extinction phase. After the extinction phase, a repeated measures ANOVA yielded a significant interaction between test stimuli (CI vs. novel CS) and condition, $F(1, 22) = 8.43$, $p < 0.05$, in the retardation tests. Two-tailed t-tests showed that participants in the Extinction condition, but not in the No-Extinction condition, rated the CI lower than the novel CS, $t(11) = 3.12$, $p < 0.05$, and $t(11) = 1.00$, $p > 0.05$, respectively. According to these analyses, the conditioned inhibitor X in the Extinction condition showed significantly more retardation than did the novel CS, J. A similar result was reported by Pearce et al. (1982, Experiment 3) who showed that after X- trials retardation was stronger than the AX- and CX- controls.

The data support the predictions of the model, suggesting that, after the extinction procedure, due to the decreased attention to X, X in the Extinction condition does not show inhibition in a summation test (Experiment 1), but it shows increased retardation. In addition, the data also support the model's prediction (Figure 5, Left

Panel) that retardation is not observed for X in the No-Extinction condition, due to the fast learning (one reinforced trial) that occurs in a predictive learning preparation (Escobar, Arcediano, & Miller, 2003).

4.5 Experiment 3: Reactivation of Conditioned Inhibition in a Retardation Test

4.5.1 Predictions of the SLG Model

As demonstrated in Experiment 1, when the conditioned inhibitor X is paired with a Novel CS the inhibitory power of that conditioned inhibitor returns in a summation test. According to the SLG model, this is a result of increased attention to the inhibitory CS due to also increased novelty in the environment. The model suggests that when attention to a conditioned inhibitor is increased, the rate of conditioning also increases. In other words, increased attention results in decreased retardation of acquisition in a retardation test.

Simulations of the SLG model was identical to the ones introduced for Experiment 2, except following the extinction treatment, the Recovery group received 3 trials of non-reinforced XN presentations where N was a novel CS while the No-Recovery group received 3 trials of non-reinforced CX presentations. Presentations of ML as used in the control group of Experiment 1were replaced by CX only presentations in the No-Recovery group because our simulations showed that even ML presentations

are enough to disrupt retardation effect. Finally, as in Experiment 2, 3 X+/ 3 J+ trials were given which were followed by non-reinforced test trials of X and J. Simulations show that in the Recovery group, retardation disappeared when a recovery treatment was added after the extinction trials whereas retardation effect was intact in the No-Recovery group (Figure 6, Left Panel). Therefore, the simulations show that the increased retardation effect as a result of repeated non-reinforced presentations of the conditioned inhibitor can be reversed with the presentations of a novel CS in pair with

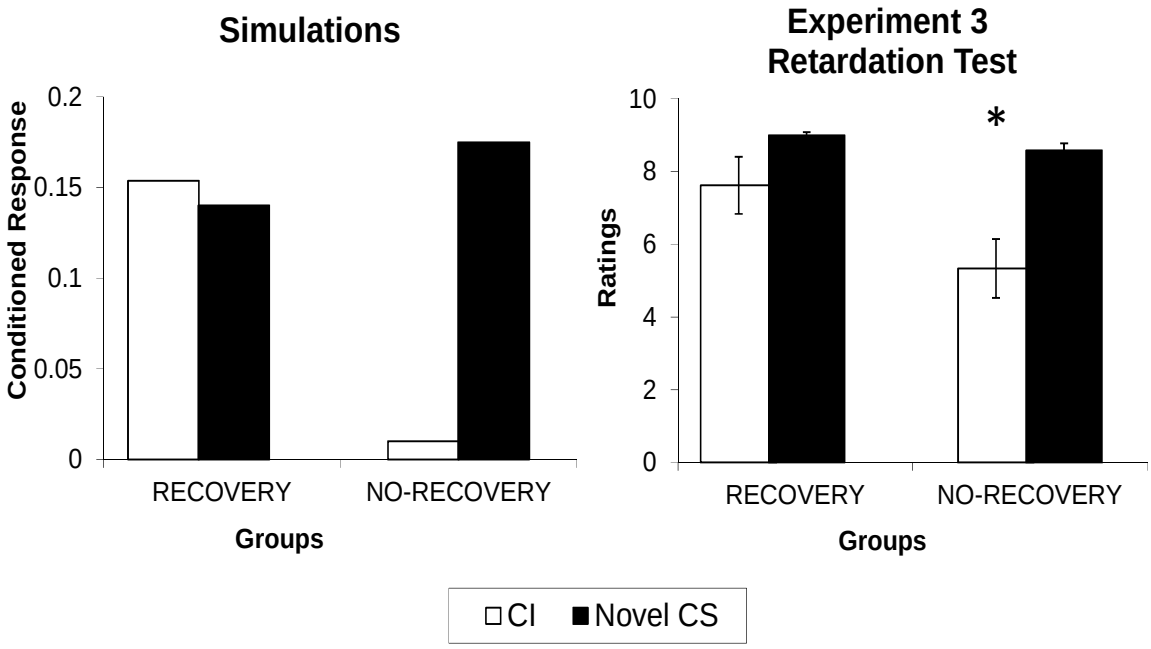

Figure 6. Experiment 3. Simulated CRs and Experimental Ratings after conditioning of the Conditioned Inhibitor (CI) and a Novel CS in a retardation test following Recovery and No-Recovery treatments. Left Panel: Simulated Conditioned Responses to the conditioned inhibitor (CI) and a Novel CS, for Recovery and No-Recovery conditions. Right Panel: Experimental ratings for the conditioned inhibitor (CI) and a Novel CS, for Extinction and No-Extinction groups. Error bars show Standard Error of the Mean (SEM).

the inhibitory CS.

4.5.2 Participants

The participants were 24 Duke University undergraduate students who had not taken part in any other experiment in this study. Their participation was rewarded with course credits. They were randomly assigned to two experimental conditions.

4.5.3 Apparatus and Stimuli

The apparatus and stimuli were identical to those in Experiment 1.

4.5.4 Design and Procedure

In Experiment 3, acquisition, extinction, and retardation test phases were identical to those in Experiment 2, except this time, as in Experiment 1, a recovery or no-recovery phase was added before the retardation test (see Table 9). As in Experiment 2, we kept the first summation test, where the participants were asked to rate all stimuli (B, BX, and BZ), to verify that a significant level of conditioned inhibition was achieved. here were two conditions, recovery and no recovery. During the recovery phase, X was paired with a novel cue N without the outcome for the Recovery condition. Participants in this condition were shown three trials of XN–. For the No-Recovery condition, participants were shown only the context, which was the white screen where the

symbols were presented for the duration of three trials (6 s). As was mentioned above, exposure to the context (instead of exposure to ML) was used in the No-Recovery condition, because the model predicts that if two novel stimuli (ML) are used in the control condition, attention to X increases during retardation. After the recovery phase, the retardation test consisted of one novel CS + and one X+. Then participants were asked to rate the novel CS and X. The order of the test trials was counterbalanced.

Table 9. Experimental Design of Experiment 3.Letters indicate different symbols. (+) means an outcome (red bar), (-) indicates the absence of the outcome.

Conditions	Acquisition	Acquisition Summation Test	Extinction	Recovery	Conditioning	Retardation Test
Recovery Treatment	10 A+ 10 AX- 10 B+	1 B? 1 BZ? 1 BX?	75 X- 10 F+	3 XN-	1 X+ 1 J+	X? J?
No-Recovery Treatment	10 CD+ 10 E-			3 CX-		

4.5.5 Results and Discussion

After the acquisition phase, a repeated measures ANOVA showed no significant interaction between test stimuli (CI vs. EI) and condition (recovery vs. no recovery), $F(1, 22) = 0.7$, $p > 0.05$, in the summation test following the acquisition phase. Two-tailed t-tests showed both conditions rated CI lower than EI ($t(11) = 5.23$, $p < .001$, for the

Recovery condition, and $t(11) = 6.42$, $p < .001$, for the No-Recovery condition). These results demonstrate that conditioned inhibition was equally achieved by both groups during the acquisition phase.

Figure 6 (Right Panel) shows the mean ratings for the retardation test of a novel CS, J, and the conditioned inhibitor, X, for the Recovery and No-Recovery conditions subsequent to the recovery phase. Following the recovery phase, a repeated measures ANOVA showed that the interaction between test stimuli (CI vs. novel CS) and condition (Recovery vs. No recovery) was significant, $F(1, 22) = 7.75$, $p < 0.05$, after the retardation test. Furthermore, two-tailed t-tests showed that in the No-Recovery condition, there was a significant difference between CI and novel CS ratings, $t(11) = 4.00$, $p < 0.05$, but not in the Recovery condition, $t(11) = 1.91$, $p > 0.05$. Overall, these results show that the inhibitory power of X is recovered in the recovery condition, but not in the No-Recovery condition. That is, the recovery treatment reinstates attention to X, which now conditions faster in the retardation test.

In sum, Experiment 3 supported the predictions of the model that even though X shows inhibition when it is tested in a summation test after a recovery phase (Experiment 1), it shows less retardation due to its increased attention when it is compared with a novel CS. As discussed above, the CI in the Recovery condition shows

no retardation, even when they are initially inhibitory, due to the fast conditioning that takes place in our preparation.

4.5 General Discussion

The results of Experiment 1 confirmed the predictions of the SLG model suggesting that a) the inhibitory power of a conditioned inhibitor should be deactivated in a summation test with repeated extinction treatment and b) it should be re-activated when the conditioned inhibitor is paired with a novel CS. According to the model, these are the results of decreased attention to the conditioned inhibitor, X, during repeated extinction trials and increased attention to X when it is paired with a novel CS. Interestingly, our results are not in line with Zimmer-Hart and Rescorla (1974), and Pearce et al. (1982, Experiment 1) results which found no effect of X- trials. According to the SLG model, this may be because when the conditioned inhibitor is tested with an excitor in a summation test, Novelty' is low due to strong prediction of the inhibitor by the CX. Therefore, low Novelty' in the environment decreases attention to both the excitor and inhibitor resulting in no change in the aggregate CR. In contrast, in Experiment 1 strongly decreased attention to the inhibitor due to extended extinction trials cannot be compensated by the decrease in attention to the excitor.

Also, the results of Experiment 2 and 3 confirmed the model's predictions that suggest a) the retardation of acquisition should increase after a repeated extinction trials and b) the retardation should decrease if the conditioned inhibitor is paired with a novel CS even after repeated extinction treatment. According to the model, with decreased attention to X the rate of conditioning decreases and in contrast, when X is paired with a novel CS, attention to X and the rate of conditioning increases in a retardation test. These results are also in line with Ricker & Bouton's (1996) results demonstrated that prolonged extinction of an excitor resulted in slower reacquisition. Importantly, increased retardation as a result of extinction treatment of a conditioned inhibitor has previously been shown by Pearce et al. (1982, Experiment 3) but our study also successfully reversed this effect by pairing the conditioned inhibitor with a novel CS. Interestingly, our results are also in line with previous studies showing decreased CR as a result of extended conditioning trials of CS (Bouton, Frohardt, Sunsay, Waddell, & Morris, 2008; Heth, 1976). According to the SLG model, both results are due to decreased Novelty' as a result of CS being predicted by the CX and by itself.

Notice that while other attentional-associative models (e.g. SOP, see Chapter 2) can explain our results showing decreased inhibition as a result of extended extinction treatment, only the SLG model predicts the re-activation of the inhibitory power when the inhibitor is paired with a novel CS. This is because only the SLG model includes a

mechanism in which all the CSs present are affected by the novelty in the environment. Kutlu and Schmajuk (under review) argued that the novelty mechanism implemented in the SLG model subsumes all the attentional rules of the previous models such as Pearce and Hall (1980), Mackintosh (1973), and Wagner (1981).

Taken together, confirming the SLG model's predictions, our results offer a method to deactivate and re-activate the inhibitory power of a conditioned inhibitor in a summation test based on the level of attention to the inhibitory stimulus. The attentional interpretation of the model is further supported by the confirmation of the model's predictions using retardation tests.

5. Deactivating and Activating Contextual Inhibition

5.1 Introduction

As described in Chapter 1, extinction refers to the non-reinforced presentations of a CS that was previously paired with a US, in order to decrease or eliminate the CR elicited by that CS (Pavlov, 1927). One possible explanation of extinction is that the excitatory associations between the CS and the US are unlearned during the non-reinforced presentations of the CS. Against the "unlearning hypothesis", experimental evidence such as spontaneous recovery indicates that some excitatory CS-US associations stay intact after extinction (Rescorla, 2004). This result suggests that the initially established excitatory CS-US associations are counteracted by newly formed inhibitory CS-US associations during extinction (Konorski, 1967, p. 315; also Konorski, 1948). Other experimental results like renewal, the recovery of the extinguished CR when the CS is tested in a CX that is different from the extinction CX (Bouton and King, 1983), and reinstatement, the recovery of the extinguished CR as a result of isolated presentations of the US in the extinction context (Rescorla and Heth, 1975) suggest that extinction is context-specific and the CX may form direct inhibitory associations with the US and therefore counteracts the excitatory CS-US associations during extinction.

There have been attempts to detect direct inhibitory associations formed between the CX and the US during extinction but these studies failed to do so (Bouton & King,

1983, Bouton & Swartzentruber, 1986, 1989). For example, Bouton and Swartzentruber (1989) showed that the extinction CX fails to pass the summation test which suggests it does not form direct inhibitory associations with the US. Because the attempts to demonstrate direct CX-US associations failed, as an alternative to the inhibitory context view, Bouton (1993, 2004) suggested that the extinction CX becomes a "negative occasion setter" which controls the CS-US associations without forming direct associations with the US.

As mentioned in section 2.4.10, according to the SLG model, during extinction, CS-US associations decrease but stay excitatory because the CX becomes inhibitory and protects CS-US associations from extinction. However, according to the SLG model (see Larrauri & Schmajuk, 2008, page 666), the inhibitory associations of the extinction CX cannot be detected in a summation test when attention to the CX decreases during non-reinforced CS presentations in that CX when the intertrial interval (ITI) is long. Notice that when ITI is long subjects receive longer exposure to the CX, which decreases attention to the CX. This effect is consistent with experimental data that demonstrated the CX does not appear inhibitory when the ITI is long (Bouton and Swartzentruber, 1989, Experiment 3).

Larrauri and Schmajuk (2008) made several specific predictions on how to detect inhibitory properties of the extinction CX in a summation test. First, Larrauri and

Schmajuk (p. 669, 2008) suggested replicating Bouton and Swartzentruber's (1989) Experiment 3 with a modified design with relatively few extinction trials. According to the SLG model, with many extinction trials attention to the CX decreases and the inhibitory power becomes undetectable. However, the model predicts that with fewer extinction trials attention to the CX will stay high and therefore, it will be possible to detect the inhibitory power of the CX in a summation test. Second, Larrauri and Schmajuk (p. 669, 2008) also predicted that presenting a novel CS in the extinction CX will increase novelty and reinstate attention to the CX and therefore, it will appear inhibitory in a summation test even after many extinction trials. Our Experiment 1 results also support these predictions. The present study tests Larrauri and Schmajuk' (2008) predictions that (a) the extinction CX will pass the summation test with few but not with many extinction trials and (b) if a novel CS is presented in the extinction CX prior to the summation test, the CX will appear inhibitory in the summation test, even after many extinction trials.

5.2 Simulation Method

All simulations used values for the independent variables: CS salience 1, CS duration 20 time units (t.u.), US strength 1, US duration 5 t.u., inter-stimulus interval (ISI) 15 t.u. and ITI 200 t.u. We have used similar values in most of our previous papers.

The experiments reproduced the sequence of type of trials (e.g., CS paired with the US, CS alone) used in each simulation, but used fewer number of trials of each type because of the faster learning shown by humans in predictive learning paradigms (Escobar et al., 2003; also Experiment 1 in this dissertation). Like Larrauri and Schmajuk (2008), the salience of the CX was set to 0.9. This relatively large value is justified by (a) Rosas, Callejas –Aguilera, Ramos-Alvarez, & Fernández Abad 's (2006) suggestion that the CX should be salient in order to get a context-switch effect in a human predictive learning paradigm, (b) Richards, and Sargent's (1983) finding that a nonsalient CX does not become inhibitory and does not protect the CS from extinction (a result easily accommodated by our model, see Larrauri and Schmajuk, 2008), and c) Thomas, Larsen, and Ayres' (2003) demonstration that renewal needs distinctive contextual cues such as odors.

5.3 Experiment 4: Deactivation and Activation of Contextual Inhibition using Visual Cues as Contexts

5.3.1 Predictions of the SLG Model

As mentioned above, Larrauri and Schmajuk (2008) predicted that the CX becomes inhibitory during extinction (Figure 7, Upper Panel). However, the inhibitory power of the extinction CX can be detected in a summation test after relatively few extinction trials when attention is still high but not after relatively many extinction

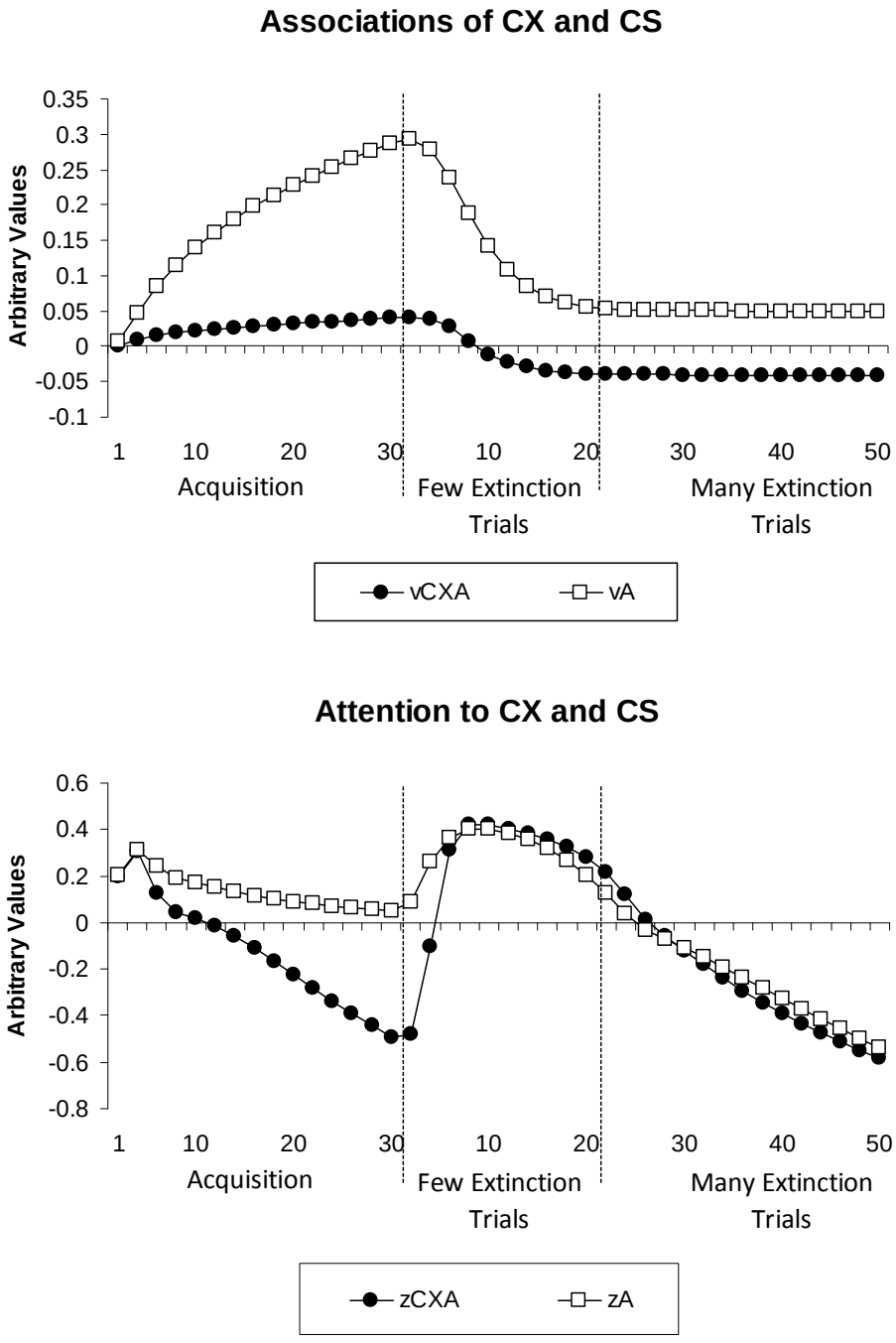

Figure 7. Simulations of the SLG model with either few or many extinction trials. Upper Panel: Simulations with the SLG model showing associations of CXB-US, $V_{CXB\text{-}US}$, and A-US, $V_{A\text{-}US}$. Lower Panel: Simulations with the SLG model showing attention to CXB, z_{CXB}, and A, z_A.

trials when attention is low (Figure 7, Lower Panel). Simulations for all groups consisted of 20 A+ in CXA during the acquisition phase. During the extinction phase, the SAME-MANY group received 80 A- extinction trials in CXB, while the DIFF-MANY group received the same number of extinction trials in CXC. Both groups also received 20 B+ trials in CXA. The SAME-FEW and DIFF-FEW groups received 20 A- trials in CXB and CXC, respectively as well as 20 B+ trials in CXA. Finally, all groups were given 5 test trials of B in the extinction context, CXB.

As shown in Figure 8 (Left Panel), simulations of the SLG model indicate that the extinction context will appear inhibitory after few but not after many extinction trials. According to the SLG, model this is because a) CX-US associations, $V_{CX\text{-}US}$, become inhibitory during extinction and b) attention to the CX, z_{CX}, and Novelty' stay high after few extinction trials but decrease after many extinction trials as the CX and the CS become predicted by each other and by themselves. Therefore, after few extinction trials, the extinction CX appears inhibitory in a summation test because z_{CX} is high thereby increasing the inhibitory power of the CX (see Equation 2a). In contrast, because z_{CX} is decreased with many extinction trials, the extinction CX does not pass the summation test. Experiment 4 tested these predictions of the SLG model in a human predictive learning paradigm.

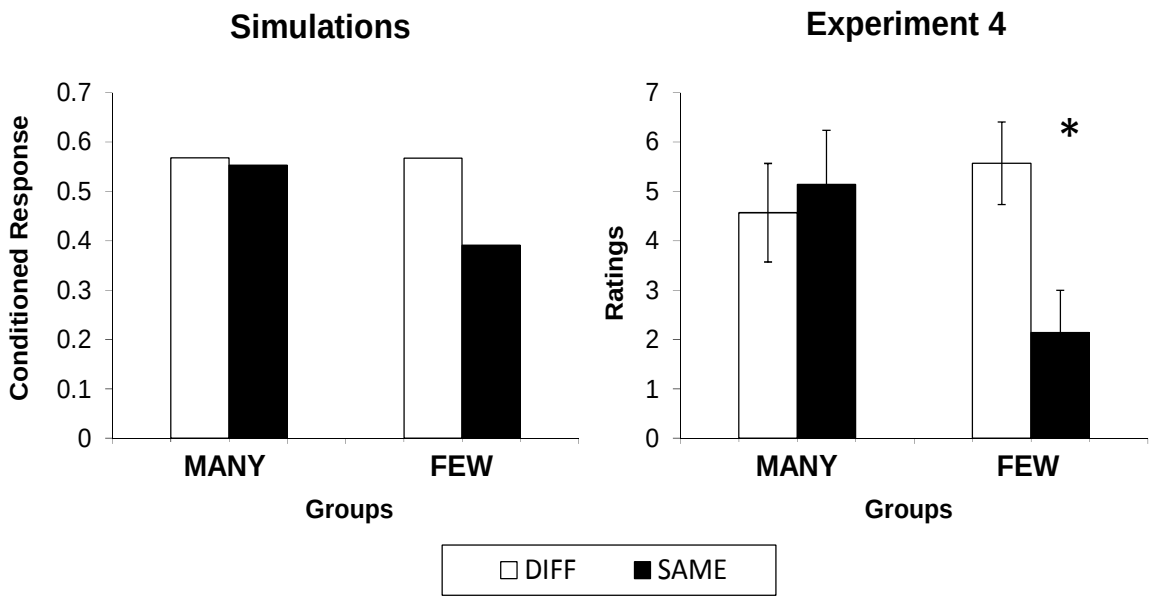

Figure 8. Experiment 4. Simulated CRs and Experimental Ratings during the summation test of the extinction context, CXB for the SAME groups and a novel context, CXC for the DIFF groups after many (20 A-) or few (5 A-) extinction trials in CXB. Left Panel: Predictions of the SLG model showing simulated Conditioned Responses. Right Panel: Experimental ratings. Error bars show Standard Error of the Mean (SEM). Asterisk indicates a significant difference at the level of $p < .05$.

5.3.2 Participants

The participants were 56 (14 in each of four conditions) Duke University undergraduate students who did not participate in any subsequent experiment in this study. Their participation was rewarded with course credits. Participants required approximately 5 min to complete the experiment.

5.3.3 Apparatus and Stimuli

Each individual was seated in front of a PC and was tested individually. A custom-made MATLAB 6.5.2 program was used for the cue presentations and obtaining the participants' responses. The participants used a regular PC keyboard to assign their responses. The stimuli were similar to those used by Rosas & Callejas-Aguilera (2006), who demonstrated renewal in a human predictive learning task. Two different food items were used as CSs (beef and chicken) and 3 different colored squares with the name of the restaurant (Restaurant 1, Restaurant 2, or Restaurant 3) were used as the contextual stimuli. The CSs were presented as pictures of the particular food items in the squares that represented Context. We counterbalanced the role of the CSs between different food items.

5.3.4 Design and Procedure

We adopted the predictive learning scenario used by Rosas & Callejas-Aguilera (2006). According to this scenario, participants were asked to play the role of a medical doctor and review the records of a patient who got sick after eating some food items at different restaurants but not after eating other food items in some other restaurants.

Therefore, participants asked to learn which restaurant-food combination resulted in food poisoning.

Each trial in the experiment consisted of sequence of three separate screens. All screens stayed on for 2 s, and there were no time gaps between screen presentations. First, the CX-alone screen appeared with only the restaurant name, its corresponding color square, and on the right side of the screen a very low red bar (30 pixels wide and 10 pixels high) indicating no food poisoning were presented. Then, an outcome screen (600 * 451 pixels) which contained a food item (203 * 203 pixel food pictures, centered on the screen), a context item (290 * 280 pixel colored squares around the food item), and on the right side of the screen either a high red bar (28 pixels wide and 287 pixels high) indicating the presence of the severe food poisoning or a very low red bar indicating no food poisoning were presented. Finally, another CX alone screen appeared with the corresponding CX item and a low bar. We adopted Bouton and Swartzentruber's (1989) Experiment 3 design where the extinction context was tested in a summation test with a transfer excitor (see Table 10). At the beginning of the experiment, all participants were presented the first set of instructions shown in Appendix 3. The experiment was a 2 × 2 design with two initial conditions receiving many (MANY) or few (FEW) extinction trials and two groups receiving the test trial either in the extinction context (SAME) or a different context (DIFF). Participants were randomly assigned to each of the four

Table 10. Experimental Design of Experiment 4. Letters indicate different food items. (+) means an outcome (red bar), (-) indicates the absence of the outcome.

Conditions	Groups	Acquisition	Extinction	Test
MANY Condition	SAME	5 A+ in CXA	20 A- in CXB 5 B+ in CXA	1 B? in CXB
	DIFF		20 A- in CXC 5 B+ in CXA	
FEW Condition	SAME		5 A- in CXB 5 B+ in CXA	
	DIFF		5 A- in CXC 5 B+ in CXA	

groups, SAME-MANY, SAME-FEW, DIFF-MANY, or DIFF-FEW. During the acquisition, phase all groups received 5 A+ trials in CXA. Then the subjects in the SAME-MANY group received 20 A- extinction trials in CXB, while the DIFF-MANY group received the same number of extinction trials in CXC. The FEW groups (SAME-FEW and DIFF-FEW) received only 5 A- trials in their corresponding contexts. During this phase all groups also received 5 B+ trials in CXA alternated with the A- trials.

After acquisition and extinction phases were completed, a test screen appeared, and participants were asked to rate each food item on the basis of the information provided during the preceding phases. Specifically, participants were asked to indicate

the likelihood of the food item in a given restaurant predicting the severe food poisoning on a rating scale between 0 (very unlikely) and 9 (very likely) shown at the bottom of the screen (see Appendix 4). The participants indicated their ratings by using the keyboard. During the test phase, all participants received a single test trial of a summation test where the transfer excitor B was presented in CXB to measure the inhibitory power of the extinction context, CXB.

5.3.5 Results and Discussion

Dependent variable for the following analysis was the likelihood ratings obtained during testing. A Two-Way-ANOVA showed that Interaction between GROUP (DIFF vs. SAME) and CONDITION (MANY vs. FEW) was significant ($F(1,52)= 5.14$, $p<0.05$) but the main effect of CONDITION ($F(1,52)= 2.62$, $p>0.05$) or GROUP ($F(1,52)= 1.25$, $p>0.05$) was not significant. Furthermore, independent sample t-tests yielded a significant difference between DIFF-FEW and SAME-FEW groups ($t(26) = 3.10$, $p < 0.05$), but not between DIFF-MANY and SAME-MANY groups ($t(26) = 0.41$, $p < 0.05$). Also, the difference between SAME-MANY and SAME-FEW ($t(26) = 2.33$, $p < 0.05$) groups was significant.

As shown in Figure 8 (Right Panel), these results demonstrate that the extinction context passed the summation test in the FEW condition, as SAME group ratings were

lower than the DIFF group ratings, but not for the MANY condition, thereby confirming the predictions of the SLG model shown in Figure 8 (Left Panel). These results also suggest that the extinction CX does not act as an occasion setter after few extinction trials. It is still possible that the CX becomes an occasion setter with repeated extinction trials. In that case increasing attention to the CX after many extinction trials should not re-activate the CX inhibitory power. If the CX is still inhibitory but unattended it would be possible to detect its inhibitory power in a summation test after many extinction trials by increasing attention to the CX. This prediction will be tested in Experiment 5.

5.4 Experiment 5: Reactivation of Contextual Inhibition using Visual Cues as Contexts

5.4.1 Predictions of the SLG Model

Larrauri and Schmajuk (2008, page 669) also predicted that, if attention decreases after many extinction trials and the CX is inhibitory, it would be possible to reactivate the inhibitory CX-US associations by increasing Novelty. Simulations for both Recovery and No-Recovery groups consisted of 20 A+ in CXA during the acquisition phase and 80 A- extinction trials in CXB, and 20 B+ trials in CXA during the extinction phase. During the recovery phase, the Recovery group received 4 of each recovery trials in which a novel CS was presented in the extinction context, CXB. The No-Recovery group received

12 CX only trials instead. Finally, all groups were given 5 test trials of B in the extinction context, CXB.

As shown in Figure 9 (Left Panel) simulations of the SLG model indicate that the extinction context will appear inhibitory even after many extinction trials when the attention to the context is recovered by presenting a number of novel CSs in that CX. Experiment 2 tested these predictions in a human predictive learning paradigm.

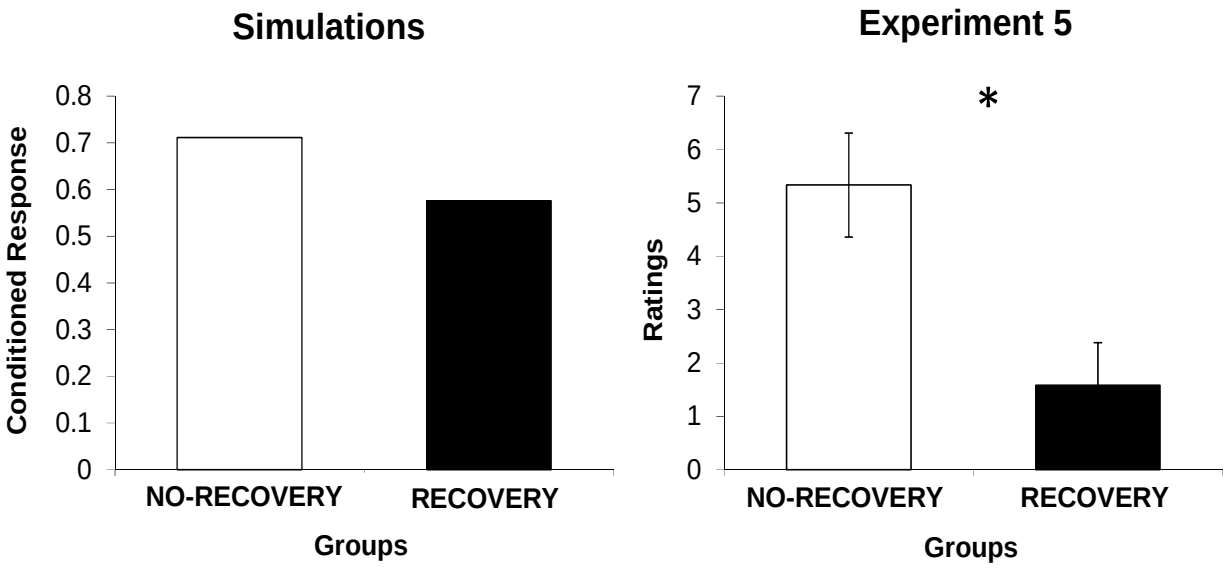

Figure 9. Experiment 5. Simulated CRs and Experimental Ratings during the summation test of the extinction context, CXB following Recovery or No-Recovery trials. Left Panel: Predictions of the SLG model showing simulated Conditioned Responses. Right Panel: Experimental ratings. Error bars show Standard Error of the Mean (SEM). Asterisk indicates a significant difference at the level of $p < .05$.

5.4.2 Participants

The participants were 24 (12 in each of two conditions) Duke University undergraduate students who did not participate in any previous experiment in this study. Their participation was rewarded with course credits. Participants required approximately 5 min to complete the experiment.

5.4.3 Apparatus and Stimuli

Apparatus and stimuli were identical to those in Experiment 1 except three more food items (hotdog, pizza, and pasta) were added for the recovery trials.

5.4.4 Design and Procedure

Designs of both Recovery and No-Recovery groups were identical to the MANY-SAME Group of Experiment 1 except that, before testing, the Recovery group received single presentations of each C-, D-, and E- recovery trials in CXB whereas No-Recovery group were given only exposure to CXB trials (see Table 11). As in Experiment 1, after the recovery phase, participants were asked to indicate the likelihood of the food item predicting the severe food poisoning on a rating scale between 0 (very unlikely) and 9 (very likely) shown at the bottom of the screen. The participants indicated their ratings by using the keyboard. During the test phase, all participants received a single test trial

of a summation test where the transfer excitor B was presented in CXB to measure the inhibitory power of the extinction context, CXB.

Table 11. Experimental Design of Experiment 5. Letters indicate different food items. (+) means an outcome (red bar), (-) indicates the absence of the outcome.

Conditions	Groups	Acquisition	Extinction	Test
RECOVERY	5 A+ in CXA	20 A- in CXB 5 B+ in CXA	1 C- in CXB 1 D- in CXB 1 E- in CXB	1 B? in CXB
NO-RECOVERY			3 CXB-	

5.4.5 Results and Discussion

Dependent variable for the following analysis was the likelihood ratings obtained during testing. A One-Way-ANOVA showed that the main effect of GROUP (No-Recovery vs. Recovery) was significant ($F(1,22)= 9.15$, $p<0.05$). As shown in Figure 9 (Right Panel), these results demonstrate that the extinction context appeared inhibitory in the MANY condition when novel CSs presented in the extinction context. Confirming the SLG model's predictions shown in Figure 9 (Left Panel), these results show that

inhibitory power of the extinction CX can be reactivated even after many extinction trials by presenting novel CSs in the CX. Importantly, this outcome rules out an alternative explanation for the results of Experiment 1, namely, that the extinction CX becomes an occasion setter with many, but not with few, extinction trials. If the CX were an occasion setter, it is impossible to understand why presentation of novel neutral CSs confers inhibitory power to the extinction CX.

Our results are in line with the data from Experiment 1 showing the decreased inhibitory power of a conditioned inhibitor after repeated non-reinforced exposure can be recovered by presenting it in pair with a novel CS. The results are also consistent with Reberg's (1972) data, showing that two CSs maintained their excitatory properties when tested in compound following prolonged individual extinction, and with Bottjer's (1982) finding that presenting a novel CS immediately before a previously extinguished CS produce renewed responding (external disinhibition). As in our experiment, the model explains these results in terms of attention to the CSs decreasing during extinction and increasing again when (a) both CSs are presented in compound during testing in Reberg's experiment, or (b) the CS is preceded by a novel CS in Bottjer's study.

5.5 Experiment 6: Measuring Overt Attention during Activation and Deactivation of the Context

5.5.1 Predictions of the SLG Model

Results of Experiment 4 confirmed the SLG model's predictions suggesting that the extinction CX should appear inhibitory after few but not after many extinction trials. According to the model, this is a result of decreased attention to the CX after many extinction trials. Therefore, according to the model the amount of attention directed to the CX should be smaller in the MANY group than in the FEW group. As the simulations for Experiment 4, simulations for all groups consisted of 20 A+ in CXA during the acquisition phase. During the extinction phase, the MANY group received 80 A- extinction trials in CXB, while the FEW group received 20 A- trials in CXB as well as 20 B+ trials in CXA. Finally, all groups were given 5 test trials of B in the extinction context, CXB.

As shown in Figure 10 (Left Panel), simulations of the SLG model indicate that during testing attention to the CX, z_{CX}, should be smaller than attention to the CS, z_{CS} in the MANY group while these values should be equal for the FEW group. Also, the model suggests, z_{CX} in the Few group should be higher than z_{CX} in the Many group. These predictions were tested in Experiment 6 using an eye-tracking device.

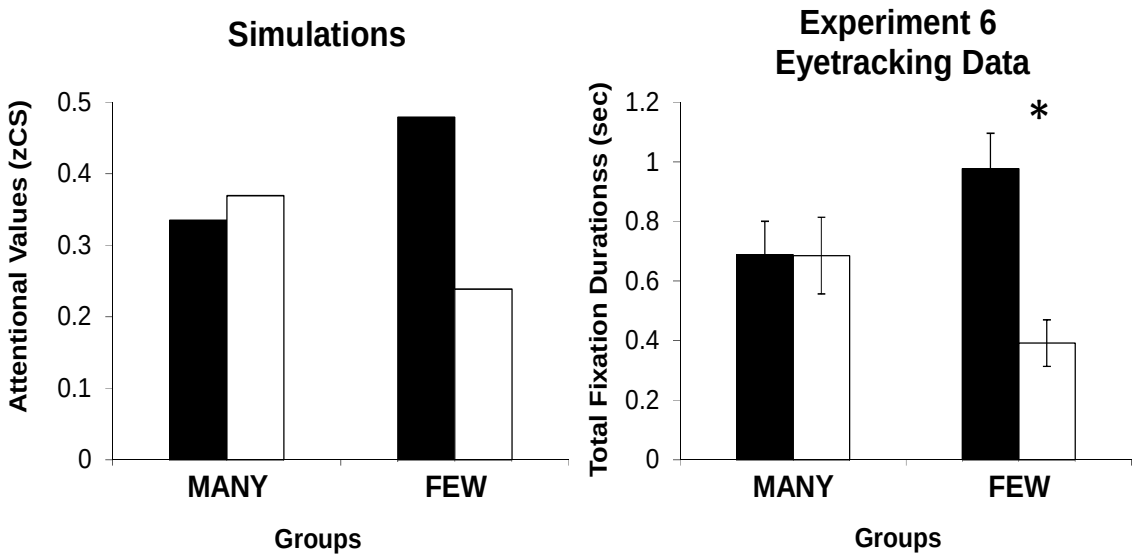

Figure 10. Experiment 6 Eyetracking Data. Simulated attentional values and Experimental Total Fixation Durations in seconds during the summation test of the extinction context, CXB for the MANY and FEW groups after many (20 A-) or few (5 A-) extinction trials in CXB. Left Panel: Predictions of the SLG model showing simulated attentional Values z_{CS}. Right Panel: Experimental Total Fixation Durations in seconds. Error bars show Standard Error of the Mean (SEM). Asterisk indicates a significant difference at the level of $p < .05$.

5.5.2 Participants

The participants were a total of 35 Duke University undergraduate students who did not participate in any previous experiment in this study. Data from 9 subjects were eliminated as they did not meet the learning and sampling criteria (see below) which resulted in total 26 participants (13 in each of two conditions). Their participation was rewarded with course credits. Participants required approximately 5 min to complete the experiment.

5.5.3 Apparatus and Stimuli

Apparatus and stimuli were identical to those in Experiment 1 except the CX used for the DIFF cases were not used. Also, for this experiment an eye tracking device, Tobii 2.2 was used to record participants' eye movements during the experiment.

5.5.4 Design and Procedure

Upon arriving, participants were seated in front of a PC and instructed to look straight to the computer screen and an automatic calibration of the eye movement detection was done by asking participants to follow a red ball on the screen with their eyes for 5 seconds. Once the calibration was achieved participants were given the instructions identical to the ones used in Experiment 4.

Designs of MANY and FEW groups were identical to the SAME-MANY and SAME-FEW groups in Experiment 4 (see Table 11) except that, the MANY group received 40 instead of 20 A- trials during extinction to increase the attentional decrement effect. Also, during testing, participants received 1 test trial of B in CXA and 1 test trial of A in CXA to validate that participants learned food items A and B as the cause of the food poisoning in the acquisition CX. During each test trial, the food item in a restaurant picture appeared and stayed on the screen for 2 seconds instead of waiting for the participant's response like in Experiment 4 and 5. This way we aimed to equalize the

length of exposure to the test stimuli between participants. After the presentation of the test stimuli, the participant was asked to rate the likelihood of the food item-context combination to cause food poisoning by pressing a number key on the keyboard as in the previous experiments.

5.5.5 Results and Discussion

We used two learning criteria in which participants have to rate food items A and B in their acquisition CX higher than 5 and one criterion for successful eye gaze recording in which the sampling percentage (successful detection of eye gazing during a given test trial) should be higher than 85%. We eliminated 6 participants from statistical analysis because they could not meet the learning criteria as they rated A or B equal or lower than 5 in their acquisition CXs and further 3 participants because their sampling percentage was lower than 85%. The dependent variables chosen for this experiment were total fixation durations in seconds which indicates how long the participants' gaze fixated to the chosen areas of interests (AOI) and likelihood ratings. There was one AOI for each item presented in a test trial, the CS which was the food item picture and the CX consisted of the colored square placed around the food picture and the restaurant's name.

First, as shown in Figure 11, a One-Way ANOVA yielded a significant main effect of GROUP (MANY vs. FEW) for the likelihood ratings as MANY group participants rated B in CXB higher than the FEW group participants did ($F(1,24)= 5.06$, $p < 0.05$). This result replicates our Experiment 4 results showing decreased inhibitory power of the extinction CX after many extinction trials. Second, a Two-Way- Repeated Measures ANOVA using total fixation durations in seconds showed that interaction

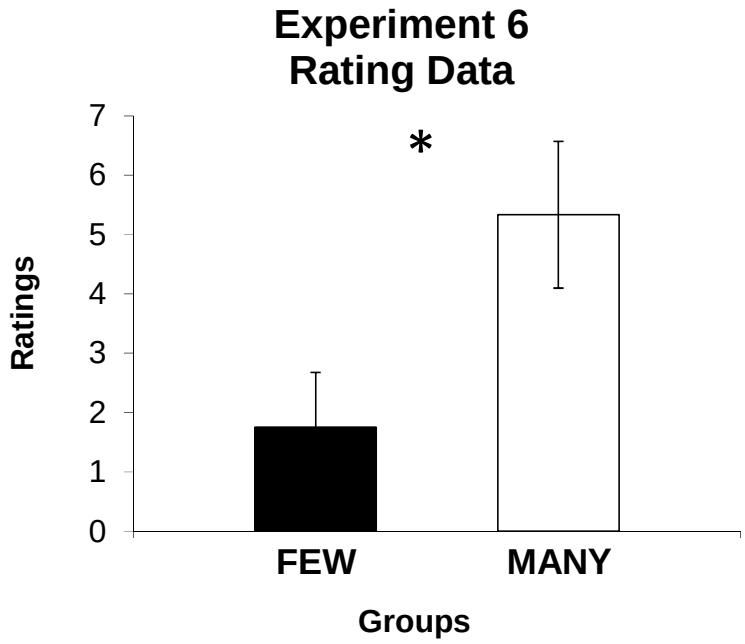

Figure 11. Experiment 6 Rating Data. Experimental Ratings during the summation test of the extinction context, CXB for the MANY and FEW groups after many (20 A-) or few (5 A-) extinction trials in CXB. Experimental ratings. Error bars show Standard Error of the Mean (SEM). Asterisk indicates a significant difference at the level of $p < .05$.

between GROUP (MANY vs. FEW) and TEST ITEMS (CS vs. CX) was significant ($F(1,24)= 4.34$, $p<0.05$). Furthermore, paired sample t-tests yielded a significant difference between TEST ITEMS ($t(12) = 3.45$, $p < 0.05$) in the MANY group but not in the FEW group ($t(24) = 0.96$, $p > 0.05$).

As shown in Figure 10 (Right Panel), these results suggest that the participants in the FEW condition paid equal amount of attention to the CX and the CS while the amount of attention directed to the CX was significantly reduced in the MANY group participants relative to the amount of attention directed to the CS. These results support and confirm the SLG model's explanation of the Experiment 4 results which predicted that longer extinction reduces attention to the CX which in turn, decreases the inhibitory power of the extinction CX in a summation test.

5.7 General Discussion

The present study confirmed the SLG model's prediction that (a) extinction CX only appears inhibitory in a summation test after few extinction trials but not after many extinction trials (Experiment4) and (b) the inhibitory power of the extinction CX can be reactivated when novel CSs are presented in that CX even after many extinction trials (Experiment 5). Also, the results of Experiment 6 showing that with many extinction

trials the participant's attention to the CX decreases, confirm the explanation provided by the SLG model for the results of Experiment 4.

According to Bouton (2002), extinction of a previously trained CS assigns 2 meanings to the same CS which results in an ambiguity because the same CS predicts both the absence and the presence of the US. Contexts help solving this ambiguity by specifying the meaning of the CS. For example, in Renewal subjects are first trained with A+ trails in CXA and then with A- trials in CXB. In this case A signals the presence of the US in CXA and the absence of the US in CXB. There are at least two ways for contexts to solve this problem. First, as proposed by Bouton (1993, 1994), the extinction CX may become a negative occasion setter and therefore, signal the absence of the US without forming direct associations with the US.

The second possibility, as suggested by the present results, the CX can solve the ambiguity by forming direct inhibitory associations with the US. According to the "direct inhibitory association" view, contexts directly become inhibitory during extinction and therefore, help the CS predicting the absence of the US. Similarly, the SLG model suggests that the inhibitory associations of a discrete conditioned inhibitor cannot be detected in a summation test when that CS is presented extensively in the absence of the US. This is because during these trials the CS becomes well-predicted by itself and the CX thereby decreases Novelty and attention to that CS.

Results of our Experiment 1 also confirm these predictions by showing decreased inhibitory power of the inhibitory CS after extensive non-reinforced presentations. More importantly, as in the present study, Experiment 1 results showed that this effect can be reversed by presenting a Novel CS in pair with the conditioned inhibitor which increases novelty and attention to the inhibitory CS.

6. General Discussion

6.1 Summary and Theoretical Implications of the Results

6.1.1 Deactivation and Reactivation of Discrete Conditioned Inhibitors

The present study confirmed the SLG model's prediction that extended non-reinforced presentations of a conditioned inhibitor results in a decreased inhibitory power in a summation test (Experiment 1) but in an increased effect in a retardation test (Experiment 2). Furthermore, in agreement with the model's predictions, presentations of the "extinguished" inhibitor with a novel stimulus before testing restored its inhibitory behavior in a summation test (Experiment 1) but accelerated its conditioning in a retardation test (Experiment 3). According to the model, these results are explained in terms of (1) the decreased attention to the inhibitory CS during non-reinforced trials and (2) the increased attention to the inhibitory CS following a few presentations of that CS with a novel CS. In other words, whereas extended non-reinforced presentations of the inhibitory CS decreases XCS and results in less inhibition in a summation test (Experiment 1) but increased retardation (Experiment 2), presentation of the inhibitory CS with a novel CS before testing increases X_{CS} and results in more inhibition in a summation test (Experiment 1) but decreased retardation (Experiment 3).

Note that our explanation of increased retardation following X– presentations is similar to the model's explanation of data showing that prolonged extinction of an

excitor results in slower reacquisition (Bouton, 1986; Bouton & Swartzentruber, 1989; Ricker & Bouton, 1996) and of latent inhibition (Schmajuk, Lam, & Gray, 1996). Another related result, also explained in attentional terms, is the finding that responding decreases with extended conditioning (Bouton et al., 2008; Heth, 1976). Similarly, Pearce et al. (1982) indicated that exposure of X– "may have had an effect analogous to that found in latent inhibition." In all cases, the SLG model explains these results in terms of decrements in attention with repeated CS presentations with or without the US.

Some associative theories address the results presented in this article. As indicated by Baetu and Baker (2010), extinction of a conditioned inhibitor is consistent with the Rescorla and Wagner (1972) associative model. However, the fact that inhibition can be reinstated following the presentation of the extinguished inhibitory CS with a novel (non-excitatory) CS suggests that non-reinforced presentations decrease attention to the conditioned inhibitor but does not eliminate the inhibitory association. This result is inconsistent with the Rescorla–Wagner model.

According to the SOP model (Wagner, 1981), inhibition is the result of the target CS acquiring inhibitory associations with the US when presented with the excitatory CS in the absence of the US. Although an extinction treatment does not decrease the inhibitory CS–US associations, the treatment results in the strengthening of CX–inhibitory-CS associations, thereby moving the inhibitor from the A1 state to the A2

state. State A2 is less effective in activating the association of the inhibitory CS during summation tests and increases retardation during conditioning. Even if SOP can describe the results of the non-reinforced presentation of the inhibitory CS, the model cannot describe the inhibition being "reinstated" by the absence of the novel CS during testing. According to the model, strong CX–inhibitory-CS associations are formed during the extended extinction phase and block the formation of novel CS–inhibitory-CS associations. Therefore, the inhibitory CS will be perfectly predicted by the CX during testing, thereby being unable to enter the A1 state.

According to the comparator hypothesis (Miller & Mantzel, 1988; Stout & Miller, 2007), inhibition is the result of the target CS having a lower expectation of the US than its comparator, the excitatory CS. Therefore, non-reinforced presentations of the inhibitory CS would eliminate its association with the excitatory CS, thereby decreasing its inhibitory value. It is unclear how the model would predict the recovery of the inhibitory power of a CS when it is paired with a novel CS.

Finally, and as indicated by Baetu and Baker (2010), our results are inconsistent with inferential theories of learning (De Houwer, Beckers, & Vandorpe, 2005). According to these views, just as people do not think that aspirin loses its antipyretic effects when taken in the absence of fever, inferential theories expect that X does not lose its

inhibitory power during the extinction phase. In sum, it seems that at present the SLG model is the only model capable of explaining the results presented in this study

6.1.2 Deactivation and Reactivation of Contextual Conditioned Inhibitors

Our study also confirmed the SLG model's predictions regarding the extinction CX that (a) extinction CX only appears inhibitory in a summation test after few extinction trials but not after many extinction trials (Experiment4) due to decreased attention to the CX following repeated extinction treatment (Experiment 6) and (b) the inhibitory power of the extinction CX can be reactivated when novel CSs are presented in that CX even after many extinction trials (Experiment 5). In line with Bouton's (2002) ambiguity idea, our results suggest that the CX clarifies the meaning of an extinguished CS. However, in contrast to Bouton's "negative occasion setter" idea, these results suggest that the CX solves the ambiguity by becoming inhibitory and helping the CS to predict the absence of the US. However, as suggested by the SLG model this inhibition cannot be detected in a summation test unless attention to the CX is relatively high. Similarly, the SLG model suggests that the inhibitory associations of a discrete conditioned inhibitor cannot be detected in a summation test when that CS is repeatedly presented in the absence of the US. This is because with repeated extinction trials CX and CS form strong CX-CS and CS-CX associations and thereby, strongly predict each

other. As a result, Novelty' and attention to the CX decrease and the inhibitory power of the extinction CX becomes undetectable in a summation test.

In addition, the "direct inhibitory association" view also predicts that, in line with Polack, Laborda, and Miller's (2012) Experiment 2 results, the extinction CX will appear inhibitory in a summation test with a short extinction ITI (6 sec) but less or no inhibitory with a long extinction ITI (23 mins). Just as in the case of many extinction trials, the SLG model expects that longer exposure to the extinction CX during the long ITI decreases attention to the CX, and thereby preventing the CX from expressing its inhibitory power in a summation test. Furthermore, the "direct inhibitory association" is consistent with Harris et al. (2000) results showing that changing the CX in which extinction has occurred produces renewal, even if the change is to a context in which extinction of another CS had taken place, a result that seems to suggest that the CX is not inhibitory. According to the model, renewal is present in the second CX because, even when that CX is inhibitory, attention and responding to the excitatory CS strongly increase in the new CX, but they rapidly decrease in the old CX.

Overall, the present results are in line with the inhibitory view of extinction by showing that extinction CXs may or may not appear inhibitory depending on the attention level of the contextual stimuli but not consistent with the occasion setting view of the extinction CX. Experiment 4 demonstrated that with few extinction trials the CX

becomes inhibitory and passes a summation test. Experiment 5 demonstrated that, with many extinction trials, the context is still inhibitory and has not become an occasion setter. Importantly, the view that the extinction CX becomes inhibitory allows the SLG model to explain spontaneous recovery (because attention to the excitatory CS increases before attention to the inhibitory CX), renewal (because the inhibition provided by the extinction CX disappears) and reinstatement (the inhibitory CX becomes neutral or excitatory), as well as a large number of other experimental results related to extinction.

6.2 Clinical Implications of the Results

Our results demonstrate 2 main outcomes: a) it is possible to manipulate the effectiveness of an inhibitor by increasing and decreasing attention to that inhibitor and b) extinction contexts become directly inhibitory and therefore, they are subject to the same attentional manipulations as discrete inhibitors. There are several implications of these results in the clinical domain regarding how we can maximize and sustain the positive effects of the discrete and contextual safety cues acquired during exposure therapy.

First, as discussed previously, the associative learning theory suggests that learning extinction reminders as conditioned inhibitors rather than as occasion setters is more advantageous because only conditioned inhibitors effectively reduce the CR to

other excitors. However, in line with our results (Experiments 1, 2, and 3), the SLG model suggests that conditioned inhibitors should lose its inhibitory power with repeated presentations. For example, according to the SLG model and our results presented here, a safety signal acquired during exposure therapy should lose its effectiveness with repeated use because the patient would pay less attention to the inhibitory cue as it becomes less novel. The solution the SLG model suggests is to present the safety signal with novel stimuli to make the inhibitory cue regain its novelty. Unfortunately, there are only a limited number of studies that have examined the efficacy of extinction reminders using clinical populations; therefore more research is needed to test the predictions of the SLG model in the clinical domain.

Second, as opposed to the theories proposing that the exposure therapy CXs are merely occasion setters, our results (Experiment 4) indicate that the CX becomes directly inhibitory during extinction. As previously discussed, the patient learns the therapy context as a safe environment during an exposure therapy session. As suggested by Bouton (2002), it is also important to note that individual contextual cues that are both common to the therapy CX and a novel CX may work as extinction reminders and reduce relapse. Therefore, it would be beneficial to connect as many common contextual cues between the therapy CX and other CXs as possible. Larrauri and Schmajuk (2008) added a generalization CX, CXg, in their SLG model simulations of extinction and

recovery effects to capture this notion. Supporting this idea, Gunther et al. (1998) demonstrated that extinction in multiple CXs can effectively reduce renewal potentially by increasing the number of inhibitory common contextual cues. Being conditioned inhibitors contextual cues from the therapy environment can effectively reduce fear response to multiple fear eliciting cues. This is very important for the treatment of anxiety disorders such as PTSD in which the acquired fear is generally expressed to many different stimuli associated with the traumatic event. However, our results also demonstrate that the contextual cues may lose their ability to inhibit fear responses when the patients are given too much exposure to the inhibitory stimuli. This suggests that therapists who consider using contextual cues as extinction reminders to prevent relapse should control for the amount of exposure to the inhibitory cues.

Finally, as suggested by Moscovitch, Antony, & Swinson (2009), during exposure therapy, it is important for the therapist to direct his/her patient's attention to the environmental cues (safety cues) that yield outcomes opposite to the anxiety/fear eliciting stimuli. In line with this idea, our results (Experiments 5) suggest that inhibitory learning during exposure therapy is responsible for the ameliorative effects of the exposure therapy and increasing attention to the inhibitory cues such as safety cues, extinction reminders and the cues from the therapy context should promote the effectiveness of the therapy. Also supporting this interpretation, Wells and

Papageorgieu (1998) instructed individuals with social phobia to pay attention to the external cues and examine the environment including social cues during exposure therapy. Results suggest that paying attention to the environmental cues effectively reduced social anxiety in these individuals. Furthermore, Mystkowski, Craske, and Echiverri (2006) asked their participants with spider phobia to mentally rehearse the extinction CX before testing in another and found that activation of the extinction CX memory decreases renewal of the spider fear. This result also show that internal representation of the inhibitory CX may not be active after the extinction treatment and reactivating this representation helps attenuating relapse in anxiety disorders. Our results suggest that the inactivation of the memory representation of the inhibitory CX may be due to the number of exposure during the exposure treatment and decreasing the number of exposures may help solving this problem. Also, results of Experiment 5 suggest that increasing novelty in the exposure therapy CX can also reinstate the inhibitory power of the contextual cues. Therefore, our results suggest that adding novel items (e.g. different flowers, changing painting on the wall) to the therapy CX for therapy each session will help preventing relapse by maintaining attention to the common contextual cues.

Although, our results make clear suggestions to develop more effective exposure therapies, there are number of limitations to a direct translation between laboratory and

clinical settings. One problem is the number of possible contexts. Even though, most of the studies concerning with the effects of the extinction CX (e.g. Gunther et al., 1998) use only a few number of distinct CXs, in real life we deal with many different CXs at the same time. Therefore, the effectiveness of the contextual safety cues might be diminished by the overall number of CXs the patient might encounter. It would also be very difficult the increase the number of potential common contextual cues between the therapy room and other CXs if these CXs are yet to be identified. Nevertheless, it is still worth trying to promote the number of common contextual cues between the therapy and the CX that the patient encounters the most such as his/her home. Another limitation to the suggestions proposed by our experiment is the fact that in real life there might be a greater generalization between virtually endless number of discrete cues. Thus, it is very difficult to determine when the patient will need the ER to prevent the unwanted response. Still, our results and the SLG model suggest that this might be a problem only if the safety cue is learned as an occasion setter as they are expected to precede the conditioned excitor. According to the SLG model, conditioned inhibitor safety cues will still intervene with the conditioned response and reduce it.

Overall, present findings suggest that discrete and contextual cues become safety signals during exposure therapy and it is possible to increase or decrease their inhibitory power by manipulating the amount of attention directed to these stimuli. Further

studies with real exposure therapy settings and clinical populations are required to connect these findings with real world situations.

6.3 Neurobiological Mechanisms in Conditioned Inhibition and Extinction

6.3.1 Neural Mechanisms of Extinction as Inhibitory Learning

Even though the underlying neural mechanisms of fear acquisition are well-known (see Maren, 2001 for a review), the "opposite" process "extinction" and its neural correlates are more controversial. As discussed in Chapter 1, the experimental evidence such as reinstatement, spontaneous Recovery, renewal show that extinction does not eliminate the CS-US association but inhibits the expression of these associations (Myers & Davis, 2007). In line with this idea and our results of experiments 4,5, & 6, there is evidence to support that extinction is the conditioned inhibition of the context.

In accordance with the "inhibitory learning hypothesis of extinction" some researchers suggested that the prefrontal cortex (PFC) is responsible for inhibiting the previously learned maladaptive behaviors. Morgan, Romanski, and LeDoux. (1993) showed that while the lesions of the ventral medial PFC (vmPFC) do not affect acquisition of fear to an auditory CS, they disrupt the extinction of these memories in rats. Furthermore, lesions to the dorsomedial PFC (dmPFC, primarily the middle frontal gyrus) were shown to slow down the extinction of fear related stimuli (Morgan &

LeDoux, 1995). In humans PFC is argued to have a key role for the inhibition of emotional responses such as anxiety (Milad, Rauch, Pitman, & Quirk, 2006). In addition, using imaging techniques Gottfried and Dolan (2004) found an increased activation of vmPFC and medial orbitofrontal cortex (moPFC) during the extinction of an olfactory CS in humans. A model for fear acquisition-extinction by Le Doux and his colleagues (Sotres-Bayon, Cain, & LeDoux, 2006) suggests that LA (Lateral Amygdala) is the structure responsible for CS-US associations and it relays this information to CeA (Central Nucleus of the Amygdala) for the expression of CR. Interestingly, this model argues that after extinction, vmPFC interferes with this communication between LA and CeA and inhibits the CS to control the fear response. This link is also modulated by the contextual information coming from the hippocampus which is essential to explain the contextual shift effect in Renewal (Ji & Maren, 2007). There is neurobiological evidence showing that when the hippocampus is lesioned or temporarily inactivated extinction is slower and incomplete (Benoit, Davidson, Chan, Trigilio, & Jarrard, 1999; Corcoran, Desmond, Frey, & Maren, 2005; see Bouton, Westbrook, Corcoran, & Maren, 2006 for a review). These results suggest that the CX may contribute to acquisition of extinction by becoming inhibitory and predicting the absence of the US.

Bouton et al. (2006,) showed that hippocampal lesions interfere with the context-dependency of extinction learning. Moreover, Kalisch et al. (2006) demonstrated

hippocampal activation during extinction in humans. This evidence suggests that the hippocampus modulates the inhibitory effect of the vmPFC on the amygdala by creating representation of the context amygdala (Quirk & Mueller, 2008). Finally, BN (Basal Nucleus of the Amygdala) is thought to be only partially involved as it helps modulating the contextual information. In support of the model depicted in Figure 12, recording studies (Quirk, Garcia, & Gonzalez-Lima, 2006) showed that extinction-like presentations of the CS results in LTP induction in the pathways between medial PFC (mPFC) and thalamus, and hippocampus. Furthermore, some studies showed that increasing sensitivity of mPFC (Herry & Garcia, 2002; Milad & Quirk, 2002) neurons by high-frequency stimulation prior to extinction trials increased the efficiency of extinction and in the latter case it leads to a decrease in CR to a non-extinguished CS. Finally, Quirk et al. (2006) suggested that PFC interferes with the LA-CeA connection by activating GABAergic intercalated cells (ITC) between BN and CeA which in turn inhibits the LA-CeA connection.

PFC is important for the recall of extinction as well as for learning extinction as an inhibitory connection (Milad et al., 2006). Consistent with the inhibitory learning hypothesis, Philips and LeDoux (1992) showed increased BOLD (Blood-Oxygenation

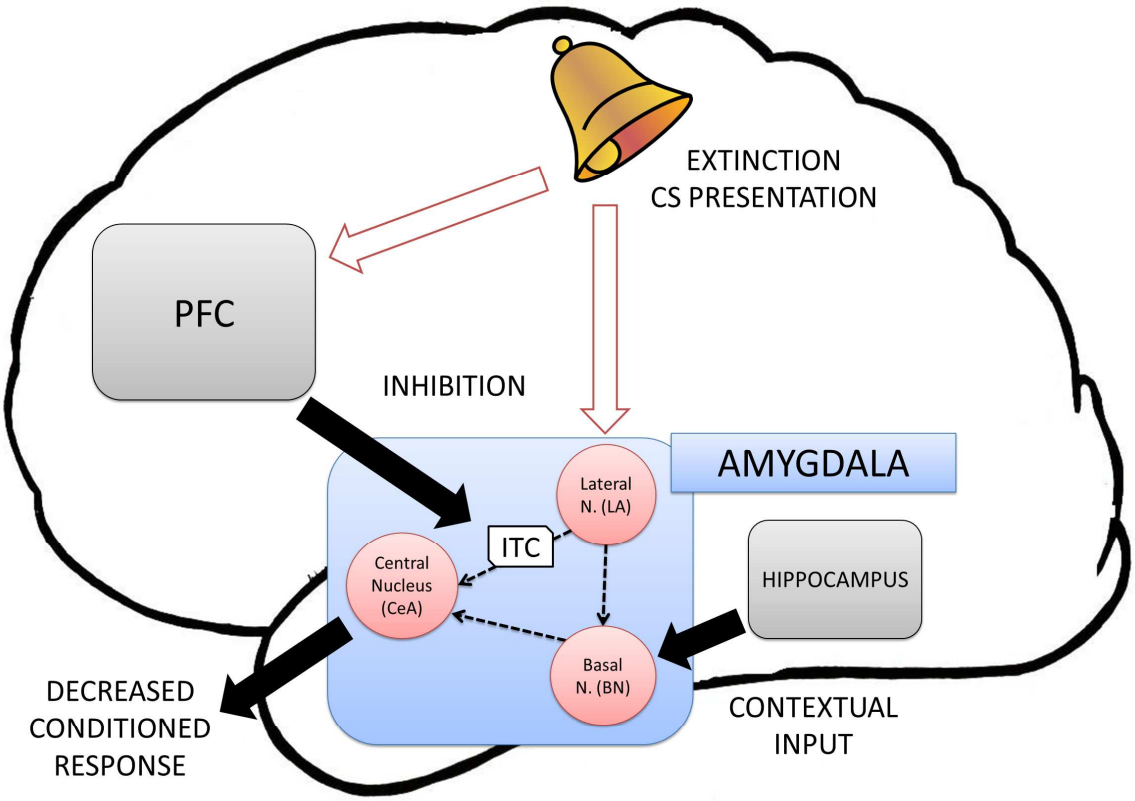

Figure 12. A model for the role of PFC in inhibition of the CR after extinction(drawn based on Sotres-Bayon et al., 2006 and Quirk et al., 2006).

Level Dependent) response in vmPFC in fMRI (functional magnetic resonance imaging) during the recall of extinction during recovery phases .Also, Milad et al. (2005) demonstrated that the cortical thickness of the vmPFC region measured in a structural MRI is positively correlated with how well the individuals retain extinction. In line with these results, Quirk, Russo, Barron, and Lebron (2000), lesioned vmPFC prior to acquisition of fear and showed that these lesions cause full recovery of CR after

extinction in a spontaneous recovery design. Interestingly vmPFC-lesioned animals showed normal extinction, which suggests vmPFC is particularly important for the recovery of fear. This study also differentiates between different vmPFC lesions. The results show that among vmPFC lesions the ones that IL was spared showed a low level of recovery, whereas the ones IL was lesioned showed great levels of recovery which identify IL as the central sub-region for the consolidation of the extinction learning.

Overall, this neurobiological model suggests that learned associations are altered by inhibitory connections between PFC and the Amygdala. In the absence of these inhibitory connections extinction cannot be consolidated and totally reversible by time or the reminders of fear. These results clearly support the inhibitory learning interpretation of extinction by suggesting inhibitory pathways in the brain.

Given that the SLG model is a neural network model, it is possible to implement some of the critical mechanisms on the model. Importantly, Dunsmoor and Schmajuk (2009) showed that the attentional variable in the model seems to correlate well with the activation of specific brain regions when Novelty increases as reported in fMRI studies during classical conditioning. Furthermore, the findings showing that hippocampal lesions disrupt the storage of CX-CS, and CS-CX associations in the cortex and affect Latent Inhibition (LI) were described using the SLG model simulations (Schmajuk, Buhusi, & Gray, 1998). In addition, based on CX-CS associations, Schmajuk, Larrauri, &

LaBar, (2007) showed that the model can also describe the results indicating impaired reinstatement but intact spontaneous recovery and ABA renewal in hippocampal lesioned rodents and human amnesics. Therefore, the model can capture the contextual effects of the hippocampus on the extinction, which is represented as CX-CS associations.

Importantly, Schmajuk, Buhusi, & Gray (1998) could also replicate the results showing that vmPFC selective dopaminergic lesions retard extinction by Morrow, Elsworth, Rasmusson, & Roth, (1999) and the results showing lesions of vm-PFC impairing spontaneous recovery but not reinstatement by Gewirtz, Falls, & Davis (1997). The model assumes that Novelty' increased and decreased by dopamine neuron activity is responsible for the attention and decreased attention to the CS following vm-PFC lesions. Finally, the model can also capture the Harris and Westbrook (1998) data showing the erasure of the contextual inhibition by γ-Aminobutyric acid (GABA) antagonists assuming GABAergic activity is a part of CX-US inhibitory processing. Interestingly, the model can also replicate the data showing GABA antagonists have no effect on LI. The model can replicate these results as LI is controlled by decreased Novelty' and attention, even though it is context dependent which suggests LI is controlled by dopamine but not by GABA activity in the brain. In sum, even though the

SLG model is a "behavioral" model different neurobiological mechanisms that are responsible for extinction can be mapped on the different nodes of the model.

6.3.2 Neurobiology of Conditioned Inhibition and Extinction of Conditioned Inhibition

Other than the neurobiological studies of the conditioned inhibition of the context in the form of extinction, there is only a limited number of studies investigated neurobiological mechanisms of conditioned inhibition of a discrete CS. Using an immediate-early gene c-fos, a neural activity marker, Campeau et al. (1997) found several regions of activations potentially responsible for conditioned inhibition including the Bed Nucleus of the Stria Terminalis, Septohypothalamic Nuclei, some tegmental nuclei, and the Locus Coeruleus. However, several studies failed to find any effect of the lesions of the brain regions that were previously identified to have a role in fear conditioning on conditioned inhibition such as CeA (Falls & Davis, 1995), Perirhinal Cortex (Falls, Bakken, & Heldt, 1997), and mPFC (Gewirtz, Falls, & Davis, 1997). In contrast, Rhodes & Killcross (2007) showed that the lesions of the Infralimbic Cortex in the mPFC which are also identified as critical for the inhibitory mechanisms in extinction (Milad & Quirk, 2002), disrupted retardation test performance but did not affect summation test performance. Furthermore, Fendt (1998) found attenuated expression of conditioned inhibition as a result of the blockage of the GABAA receptors

within the dorsal Periaqueductal Gray. There are also studies demonstrating that lesions of the superior colliculus (Waddell, Pistell, Heldt, & Falls, 2000) and medial geniculate body (Heldt & Falls, 1998) interfere with the feature-negative discrimination (A+/AX-) during conditioned inhibition training. Nicholson & Freeman suggested that (2002) there are three possible neurobiological mechanisms proposed for conditioned inhibition. First, conditioned inhibition might be a process which has an effect on the expression of the behavioral output; second, conditioned inhibition might have an effect on the CS input or third, underlying mechanisms of conditioned inhibition and conditioned excitation might be the same. Still, new studies are needed to identify critical brain regions for Conditioned Inhibition of a discrete CS.

Although it is possible that most of the underlying neurobiological mechanisms of both extinction of a conditioned excitor and extinction of a conditioned inhibitor are similar, there is virtually no direct evidence on the latter. As shown below, it is attempted to describe some potentially important regions in the attentional process which is identified as an essential mechanism for extinction of conditioned inhibition in the previous chapters.

As mentioned above, Dunsmoor & Schmajuk (2009) found that the activity patterns which are defined as percent area under the hemodynamic response curve (AUC) as a result of different reinforcement levels in a fear conditioning paradigm

previously reported by Dunsmoor, Bandettini, and Knight (2007) can be replicated in the different variables of the SLG model. For example, simulations showed that the activity in the Amygdala and Anterior Cingulate Cortex correlate with the level of prediction of the US. Interestingly, the activity pattern found in the dorsolateral PFC (dlPFC) and Insula correlates with attention modulated representation of the CS, X_{CS}, in the model. Importantly, the activity in the dlPFC and the X_{CS} decreased during full-reinforcement or full non-reinforcement of the CS and increased when the CS was partially reinforced. In line with the simulations provided above for the extinction of a Conditioned Inhibitor through X- trials and Dunsmoor & Schmajuk (2009) results, the SLG model assumes a decreased level of attention to both fully reinforced or non-reinforced neutral CS and a continuously non-reinforced Conditioned Inhibitor (see Figure 12). This suggests a dorsal pathway including dlPFC as suggested in Dunsmoor & Schmajuk (2009), might be responsible for the effects described for the extinction of a Conditioned Inhibitor. The subregions of PFC are thought to have different functions. For example, using an event-related fMRI, D'Esposito, Postle, Ballard, and Lease (1999) showed that vmPFC is activated during a simple maintenance task in which the participants asked only to remember the task items whereas more dl-PFC activation was observed when the participants were asked to reorganize the task items. Also several studies found vmPFC activity during inhibition tasks like go/no-go or cognitive set shifting in Wisconsin Card

Sorting Test which suggests that vmPFC plays a filter role where it leaves out the irrelevant information (Konishi et al., 1998, 1999). These findings support the view of dlPFC being responsible for the manipulation and updating of the items (representations of the items) that are currently being held in the working memory (D'Esposito et al., 1999; D'Esposito , Postle, & Rypma, 2000) whereas vmPFC inhibiting the irrelevant information (Konishi et al., 1999). In line with this distinction between PFC subregions, using fMRI, Yamasaki, Labar, and McCarthy (2002) identified an attentional dorsal stream (from posterior parietal cortex to dorsal PFC) and an emotional/arousal ventral stream (from the Amygdala to ventral PFC, see also Wood & Grafman, 2003). Even though there are no direct connection between dl-PFC and Amygdala it is still possible that the decreased attention to an inhibitory CS can be dictated through the top-down dlPFC-vmPFC-Amygdala connections (see Schiller & Delgado, 2010).

As depicted in Figure 13, the decreased attention to an inhibitory CS during non-reinforced trials may be mediated through dl-PFC while inhibitory associations are still intact. Even though there are several studies suggesting dissociable attentional and inhibitory streams within PFC, more experiments are needed to clarify the role of these regions in extinction of Conditioned Inhibition.

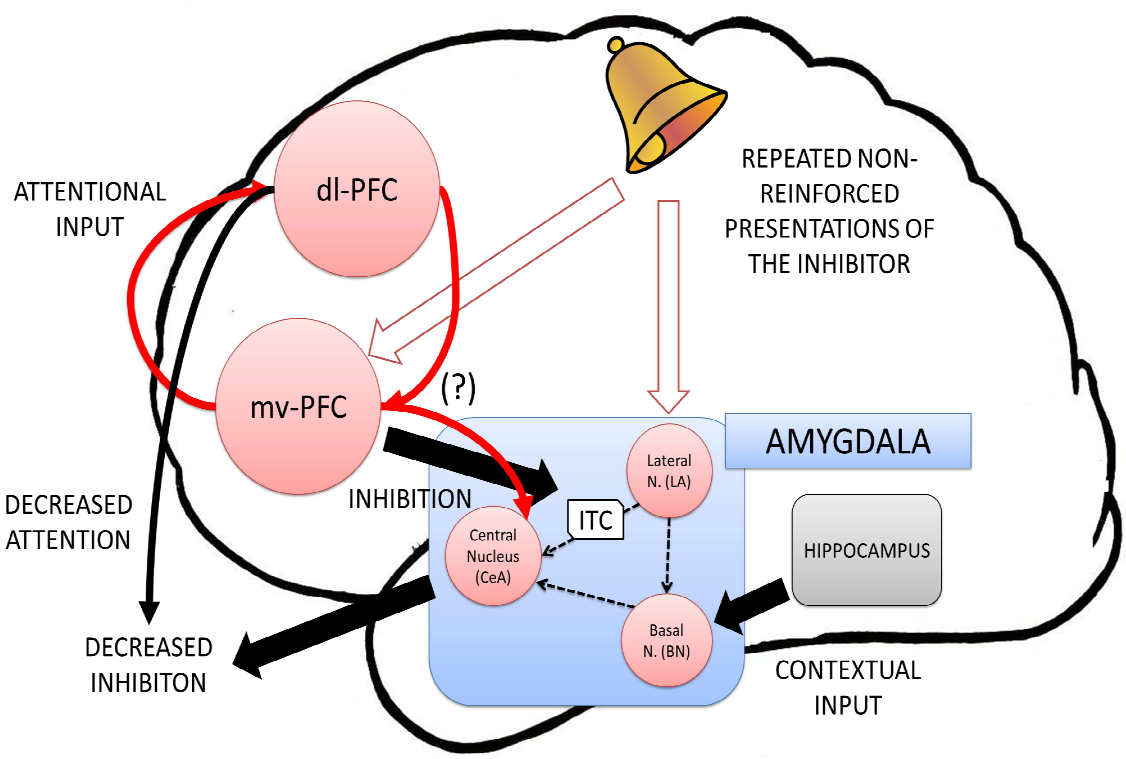

Figure 13. A model for the role of PFC in attention in Extinction of Conditioned Inhibition.

6.3.3 Conclusion and Future Directions

As conclusion, our results pose a challenge for most of the associative learning models, which do not include an attentional mechanism driven by Novelty like the SLG model. Therefore, the present study demonstrates that the importance of developing better computational models to derive predictions and test them in order to improve exposure therapies. Future studies testing our predictions using real life contexts and

clinical populations are essential to understand the real implications of our results in Clinical Psychology field.

Appendix 1

"In this experiment you will be shown one or two symbols at a time. These symbols predict either a HIGH BAR or a LOW BAR. Your task is to learn which symbols predict a HIGH BAR and which ones predict a LOW BAR. To do that, you need to guess whether the symbols predict the HIGH bar or not, by pressing "H" for the high bar and "L" for the low bar on your keyboard. On each trial, the computer will display one or two symbols and a red bar: HIGH BAR or LOW BAR. You will be shown the information in 3 separate parts. After each part, you will have to judge how likely the symbols predict a "HIGH BAR". In this task it is imperative that you are as accurate as possible. *Press the space bar to continue.*"

Appendix 2

"Now you have to indicate how likely the symbols are to predict a HIGH BAR. You have to judge on a rating scale ranging from 0 (the symbols are very unlikely to predict a HIGH BAR) to 9 (the symbols are very likely to predict a HIGH BAR), using the keyboard numbers from 0 to 9. *Press the space bar to continue.*"

Appendix 3

"Imagine that you are a medical doctor who tries to discover the cause of food poisoning in people. In order to evaluate a new patient, you will see the test results with different foods eaten at one of the three restaurants, (Restaurant 1, Restaurant 2, or Restaurant 3) *Press the space bar to continue.*

On each trial, the computer will display a record of your patient's condition with a food picture and "a food poisoning diagnostic bar" stating: whether food poisoning occurred or no food poisoning occurred. *Press the space bar to continue.*

You will see the test results of your patient for 2 days. After you reviewing all the information about your patient, you will judge the likelihood of the food items to cause food poisoning in your patient. *Press the space bar to start the experiment*"

Appendix 4

"Now you have to indicate how likely the food items are to predict "FOOD POISONING". You have to judge on a rating scale ranging from 0 (the food item is very unlikely to predict Food Poisoning) to 9 (the food item is very likely to predict Food Poisoning), using the keyboard numbers from 0 to 9. *Press the space bar to continue.*"

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