A STUDY OF CONDITIONED INHIBITION PROCEDURES IN RELATION TO INDIVIDUAL DIFFERENCES AND DISORDER

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ABSTRACT

Classical conditioning and conditioned inhibition are fundamental for cognitive processes in both animals and humans. Conditioned inhibition is involved in a wide range of normal behaviour – and its disruption could produce a wide range of behavioural deficits. For example, lack of inhibitory control has been argued to lie at the core of impulsivity (Buss & Plomin, 1975). Impulsivity is one of the core features in some of the clinical groups, such as schizophrenic patients and patients with cluster B personality disorders (PD), especially patients with PD within forensic populations (Hare et al., 1991; Munro et al., 2007). Previous research studied impulsivity by using some laboratory behaviour learning tasks (e.g. Go-NoGo tasks). People with higher impulsivity have difficulty withholding responding which is demonstrated by poor performances in these tasks. Such tasks measured participants' ability to inhibit pre-potent motor responses, and these tasks are usually thought to involve inhibition of stimulus-response (S-R) association. To date, little research has explored the inhibition of stimulus-stimulus (S-S) associations (formally 'conditioned inhibition', CI) in relation to individual differences, and no research has explicitly examined CI learning in any clinical groups.

The present study developed a suitable procedure to examine human participants' conditioned inhibition in a summation test and explored CI learning performance in relation to individual differences and disorders. Two hundred and thirty-seven participants in the University of Nottingham completed a set of questionnaires [BIS/BAS, UPPS, EPQ-RS, O-LIFE (short) and STB] to assess their individual differences and a computer-based experiment to test their excitatory and conditioned inhibitory learning. The results suggested various correlations between the scores of questionnaires

and the measures of excitatory and inhibitory learning, which confirmed that the higher impulsivity, neuroticism and schizotypy levels, the less evidence of the excitatory learning. At the same time, the higher anxiety, neuroticism and schizotypy levels, the less evidence of the conditioned inhibition.

Twenty-five schizophrenic patients in community-based and 24 patients with PD in forensic settings were also tested using the CI learning task. The results suggested that schizophrenic patients showed a clear reduction in their excitatory and inhibitory learning performance. Moreover, schizophrenic patients with higher negative scores on PANSS, perform worse on the CI learning task. For PD patients at Rampton hospital, the CI effect was abolished in the samples. There was also a significant difference in the CI effect between patients in the PD and the DSPD units. Specifically participants in the DSPD unit showed significantly less CI. Within the clinical samples used in the present study, it was unable to demonstrate any relationship between the levels of CI and medication. Implications of these findings for personality dimensions affect learning in normal populations and clinical groups would be discussed, and further research would be suggested in this thesis.

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Abbreviations

ADHD	Attention Deficit Hyperactivity Disorder
ASPD	Antisocial Personality Disorder
BAS	Behavioural Activation System
BIS	Behavioural Inhibition System
BIS-11	Barratt Impulsiveness Scale
BPD	Borderline Personality Disorder
CBT	Cognitive behavioural therapy
CC	Classical conditioning
CPZ	Chlorpromazine
CI	Conditioned Inhibition
CS	Conditioned Stimulus
CWI	The Colour-Word-Interference task
DA	Dopamine
DSM-IV	Diagnostic and Statistical Manual of Mental Disorder 4th Edition
DSPD	Dangerous and Severe Personality Disorder
EC	Evaluative Conditioning
EPQ	Eysenck Personality Questionnaire
EPQ-RS	Eysenck Personality Questionnaire – Revised short scale
ICD-10	the International Statistical Classification of Disease and Related Health Problems, 10th Revision
IPDE	International Personality Disorder Examination
IAPS	International Affective Picture System
KGV	Psychiatric Assessment Scale
LI	Latent Inhibition
NHS	National Health Service (UK)
OCD	Obsessive-Compulsive Disorder
O-LIFE	The Oxford-Liverpool Inventory of Feelings and Experiences short scale
PANSS	Positive and Negative Syndrome Scale (for schizophrenia)
PCL-R	The Psychopath Check List – Revised
PD	Personality Disorder
PDU	Personality Disorder Unit at Rampton Hospital
PPI	Prepulse Inhibition
RT	Reaction time
STA	Schizotypal Personality Scale
STB	Borderline Personality Scale
SSRT	Stop signal reaction time
UPPS	Urgency, Premeditation, Perseverance, Sensation-seeking scale
US	Unconditioned Stimulus
VTA	Ventral Tegmental Area
WCST	The Wisconsin Card Sorting task

Chapter I: General introduction

1.1 Introduction

In the 1890s, Ivan Pavlov first demonstrated classical conditioning, a procedure in which an initially neutral stimulus (conditioned stimulus or CS) is repeatedly paired with an unconditioned stimulus (US). Subjects can learn that the CS is a signal for the US (Pavlov, 1927). Classical conditioning is used as an important method for investigating how subjects learn about the stimuli. When a CS is associated with a US, it is called a conditioned excitor; but when a CS is associated with the absence of a US, it is called a conditioned inhibitor. That is to say that conditioned inhibition is a type of classical conditioning in which a stimulus (conditioned inhibitor) is used to signal the omission of an expected US. For example, if a conditioned stimulus A signals a US (A+), then after a number of training trials the conditioned stimulus A is paired with another stimulus B and signals the omission of a US (AB–), subjects can learn that B indicates no US (B is a conditioned inhibitor) (Pavlov, 1927). Both classical conditioning and conditioned inhibition are forms of associative learning, which is a ubiquitous process of evolutionary advantage. It is not only fundamental, being found in all vertebrates, but has been argued to underlie many more sophisticated cognitive processes in both animals and humans. Conditioned inhibition (CI) is therefore likely to be involved in a wide range of normal behaviour – and its disruption could produce a wide range of behavioural deficits. This research attempts to establish CI as a theoretical basis for clinical applications.

Lack of inhibitory control has been argued to lie at the core of impulsivity (Buss & Plomin, 1975). Individuals with high impulsivity fail to inhibit unwanted thoughts, emotions and actions. Impulsivity is also one of the core features in some mental disorders, such as schizophrenia (Enticott, Ogloff & Bradshaw, 2008; Hoptman et al., 2002), personality disorders

(cluster B) (Diagnostic and Statistical Manual of Mental Disorder IV; DSM-IV, American psychiatric association, 1992, 1994, 2004; Dougherty, Bjork, Huckabee, Moeller & Swann, 1999; Henry et al., 2001), especially PD within forensic populations (Hare, Hart & Harpur, 1991; Warren et al., 2002), and psychopathy (Munro et al., 2007; Ray, Poythress, Weir & Rickelm, 2009). Impulsive behaviours usually measured by established laboratory behavioural tasks - stimulus-response (S-R) association learning tasks (e.g. using variants of the Go-NoGo procedure, as described later in the chapter). Such tasks are usually thought to involve inhibition of S-R associations, which measure participants' ability to inhibit pre-potent motor responses. People with higher impulsivity have difficulty withholding responding which is demonstrated by poor performances in these tasks. However, as a construct, inhibition encompasses a diverse range of processes and should not be too narrowly identified with any one paradigm (Nigg, 2000). To date, little research has explored the inhibition of stimulus-stimulus (S-S) associations (formally 'conditioned inhibition', CI) in relation to individual differences, and no research has explicitly examined CI learning in disorders. Therefore, the present research will explore idea that CI might also be related to impulsivity, and thus be impaired in mental disorders where impulsivity is one of important symptoms for these patients.

Thus the present research aims to contribute to our understanding of the behaviours and cognitive processes in normal people and clinical patients, by focusing on the role of conditioned inhibition in individual differences and disorder. The introduction to this thesis first will describe the definition of impulsivity, and the relation of impulsivity and behavioural inhibition. Next, measurements of impulsivity are introduced, and impulsivity as a symptom of disorders is also explained. The details of different inhibitory

learning tasks and learning procedures are also described. After considering evidence for the relationship between individual differences and inhibitory learning, then previous studies of inhibitory processes in schizophrenic patients, personality disorders and psychopaths will be presented. Furthermore, earlier studies of CI learning procedures in humans will be reviewed. Finally, an improved design relative to previous studies of CI learning procedures for the present thesis will be introduced.

1.2 Impulsivity and inhibition

1.2.1 Definition of impulsivity

Impulsivity is a complex and multidimensional concept, which includes lack of inhibitory control, a desire to seek novelty, to act without foresight, and inability to delay gratification (Barratt, 1985; 1994). These behavioural impulsivity deficits can be characterized as "rapid-response impulsivity" and "reward-delay impulsivity" models (Evenden, 1999; Swann, Bjork, Moeller & Dougherty, 2002). The former model is related to behavioural inhibition and involves an inability to evaluate a stimulus fully before responding to it; and the latter requires an evaluation of consequences and indicates they respond immediately for a small reward rather than waiting to respond for a larger one.

1.2.2 Measurements of impulsivity

From a psychological approach, most studies attempt to measure impulsivity by relying on psychometric self-report questionnaires and behavioural laboratory inhibition tasks. The self-report measures include the Barratt Impulsiveness Scale (BIS-11) (Patton, Stanford & Barratt, 1995), the Eysenck Impulsiveness Questionnaire (Eysenck, Eysenck & Barrett, 1985), and the Urgency, Premeditation, Perseverence, Sensation-seeking scale (UPPS) (Whiteside & Lynam, 2001), which can help

researchers to gather information on a variety of types of acts and on whether these behaviours have long-term patterns. Recently the UPPS scale has been widely used to measure impulsivity in normal population and patients with mental disorders (Billieux, Van der Linden & Ceschi, 2007; Gay, Rochat, Billieux, D'Acremont & Van der Linden, 2008; Magid & Colder, 2007; Ray et al., 2009).

The self-report measures have been widely used for studying impulsivity and the inhibitory process, although some disadvantages were noticed during the research – the measures are unsuitable for repeated use, and need to rely on the veracity of the individual completing the questionnaires (Moeller et al., 2001). In fact, more recent evidence suggested that impulsivity itself is a complex concept and has several different facets (e.g. Parker, Bagby & Webster, 1993). Therefore, many studies combine both self-report questionnaires and behavioural inhibitory tasks for measuring impulsivity (Claes, Nederkoorn, Vandereycken, Guerrieri & Vertommen, 2006; Enticott, Ogloff & Bradshaw, 2006; Helmers, Young & Pihl, 1997; Reynolds, Ortengren, Richards & de Wit, 2006).

Behavioural measures of impulsivity include a range of established laboratory behavioural tasks (e.g. Go/NoGo, stop-signal, anti-saccadic eye movement procedures). These inhibitory learning tasks can be conducted in both animals and humans, allowing for comparative studies of the basic biochemistry and behaviours. Previous studies have suggested that an inability to tolerate delays of reinforcement could be an important aspect of impulsivity in both animals and humans (e.g. Logue, 1988; Logue et al., 1992; Thiébot, Le Bihan, Soubrié & Simon, 1985; Van de Bergh et al., 2006). Furthermore, deficits in the performances of such tasks have been demonstrated in clinical research, such as the deficits found in

schizophrenic patients, patients with PD, and psychopaths (e.g. Enticott et al., 2008; Grootens et al., 2008; Newman, 1987; Nigg, Silk & Stavor, 2005; Rentrop et al., 2007; Rubio et al., 2007; Ruchsow et al., 2008;).

1.2.3 Impulsivity and disorder

Impulsivity in psychiatric disorders can be described as: "a predisposition toward rapid, unplanned reactions to internal or external stimuli without regard to the negative consequences of these reactions to the impulsive individual or to others" (Moeller et al., 2001 p.1784). Impulsivity is one of the defining characteristics of many psychiatric diagnoses; and it is one of the core features of antisocial personality disorders, borderline personality disorders and psychopathy (Stein, Hollander & Liebowit 1993; Stein, Towney & Hollander, 1995; Johansson, Kerr & Andershed, 2005; Lesch & Merschdorf, 2000).

Impulsivity is also one of the main features of damage to the frontal lobe, which has been reported following frontal lobe lesions (Damasio, Tranel & Damasio, 1990; Paradiso, et al., 1999). Neurological evidence has shown that frontal lobe deficits can been found in many mental disorders, such as schizophrenia, antisocial and borderline personality disorders, and psychopathy (Allen, Goldstein & Weiner, 2001; Dinn, et al., 2004; Lapierre, Braun & Hodgins, 1995). It has been suggested that frontal lobe dysfunction may contribute to poor impulse control and impaired motor inhibition in these disorders (Enticott et al., 2008; Damasio, 2000; Newman, Patterson & Kosson, 1987).

1.2.4 Learning tasks and paradigms

Many learning tasks have been used in previous studies with clinical and normal populations to assess cognitive process, inhibition and/or

impulsivity (Nigg, 2000). These learning tasks and paradigms are introduced in this section to help understand previous research which will be discussed later in this chapter.

The established laboratory behavioural learning tasks such as variants of the Go-NoGo and Stop-signal procedure are conducted as the measurements of impulsivity and/or inhibitory control, which examine subjects' response to stimulus-response (S-R) association (Marsh, Dougherty, Mathias, Moeller & Hicks, 2002; Ruchsow et al., 2008). Stroop and negative priming tasks are employed to investigate frontal function, attention, cognitive flexibility, cognitive processing speed and inhibition (Lansbergen, Van Hell & Kenemans, 2007; Tipper, 1985). The Wisconsin Card Sorting Task (WCST) is used for examining impaired frontal lobe function, cognitive flexibility, set-shifting process, and abstract reasoning (Cadenhead, Perry, Shafer & Braff, 1999; Trestman et al., 1995). Prepulse inhibition (PPI) and latent inhibition (LI) learning paradigms are neurophysiological measures of disruption in sensorimotor gating, information processing abnormalities, attentional and associative deficits in schizophrenia (Geyer, Krebs-Thomson, Braff & Swerdlow, 2001; Swerdlow, Braff, Hartston, Perry & Geyer, 1996). The deficit of PPI and LI may reflect a biological correlate of sensory flooding and cognitive dysfunction in schizophrenia (Baruch, Hemsley & Gray, 1988a; Braff, et al., 2001; Braff, & Geyer, 1990). Furthermore, deficits of PPI and disruption of LI are also reported in personality disorder, Tourette's disorder and attention deficit hyperactivity disorder (ADHD) (Cadenhead, Geyer & Braff, 1993; Castellanos et al., 1996; Kumari et al., 2005; Ornitz, Hanna & De Traversay, 1992; Swerdlow, Magulac, Filion & Zinner, 1996).

1.2.4.1 Go/NoGo and Stop-signal tasks

A Go/Nogo task requires participants to respond as rapidly as possible by pressing a button for continuously positive stimuli (Go, >=75%), while withholding responses to infrequent negative stimuli (Nogo). Therefore, the task is providing a measure of the ability to inhibit a pre-potent response (Donders, 1868/1969). Go/no-go task has a high load on the response selection, due to the prior knowledge about whether or not to respond to a "Go" or "No-go" stimulus. The task demands high-level cognitive functions of decision making, response selection, and response inhibition.

A Stop-signal task contains majority go-signals and minority stop-signals, which requires participants to quickly withhold a motor response from a primary go task to secondary stop task. That is to say, participants should convert the majority go-signals to a stop signal, in which a stop signal reaction time (SSRT) is used as a measure of inhibitory control. SSRT is an estimation of the time an individual needs to stop their usual behaviour (i.e. pressing a key every time they see the symbol) in response to the stop signal. Generally speaking, response inhibition was more difficult in the Stop-signal than Go/Nogo task. It is because the processes involve the retraction of a response that has already been triggered by a go signal (Logan, 1994; Logan & Cowan 1984).

Both Go/NoGo and Stop-signal tasks are a form of rapid-decision task and have been suggested as valid and reliable measurements for impulsivity and behavioural inhibitory learning process (Asahi et al., 2004; Dougherty et al., 2003; Nigg, 2000). Both tasks aim to measure an association between behaviours and their consequences. In other words, the tasks are usually involving inhibition of the stimulus-response (S-R) association (Logan, 1994; Logan & Cowan, 1984). Previous studies have explored behavioural inhibition using Go/Nogo and Stop signal tasks in both the

normal population (Helmers et al., 1997; Schulz et al., 2007; Verbruggen, Liefooghe & Vandierendonck, 2004) and in clinical groups (Eagle et al., 2008; Kaiser et al., 2008; Ruchsow et al., 2008).

1.2.4.2 Stroop task

The Stroop task has become a well-known neuropsychological test in recent decades for measuring frontal function, attention, cognitive flexibility, cognitive processing speed and inhibition. In this task, individuals have to identify a word's ink colour, while ignoring the word's meaning. For example, for the first word from list B in figure 1.1, participants should read as "red" in response to the word "BLUE" in red ink. This is to say, participants should name the ink colour referred to by a Stroop word in the presence of interference a word written in a different colour from its name. It is required that participants attend to the ink colour and override the more automatic process of reading the word. In fact, participants find it more difficult to name the ink colours in list B than list A. The task measureed an increased reaction time (an inhibition effect) (Stroop, 1935). The Stroop effect is demonstrated by changes in reaction time. An increased Stroop effect is found in a variety of mental disorders such as schizophrenia, addictions and depression (Phillips, Woodruff & David, 1996; Dafters, 2006; Kertzman et al., 2009).

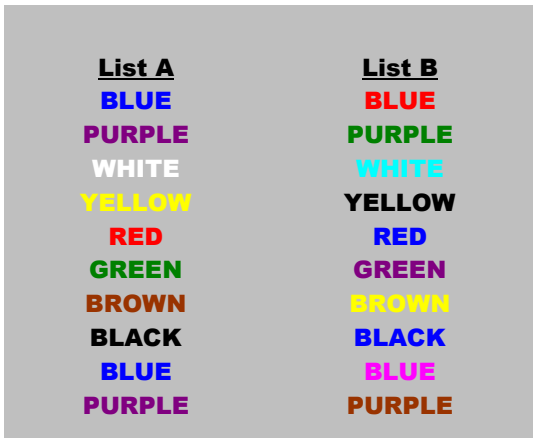


Figure 1.1 Illustration of Stroop colour words.

1.2.4.3 Negative Priming task

Negative priming can be based on the Stroop effect. Negative priming refers to the slowing of reaction time that occurs when a participant is required to respond to a target, but an immediately prior distractor is presented, which the participant has been instructed to ignore (Tipper, 1985; Neill, 1977). For instance, list B in figure 1.2, the first word is BLUE and the ink is GREEN, while the second word is RED, but the ink colour to be named is BLUE, and so on down the list. Participants find it more difficult to name the ink colours in list B than list A. It is because in list B, it is the same name between the ignored colour word in one stimulus, and the to-be-named ink colour in the next stimulus, thus the colour name participants are trying to produce was the word inhibited while responding to the immediately previous item. Therefore the negative priming emerges, because for each stimulus, people have to name the colour that is the same as the ignored word in the previous display. The slower response time to name the ink colours in list B is the negative priming paradigm (Tipper & Weaver, 2008).

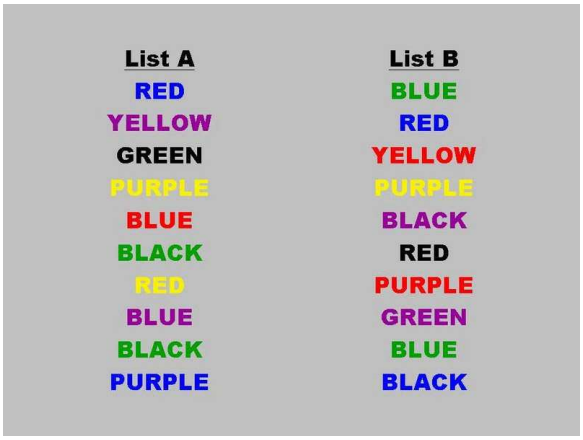


Figure 1.2 Illustration of negative priming using Stroop colour words (redrawn from Tipper & Weaver, 2008).

Research has suggested that individuals with schizophrenia, or schizotypal tendencies, have more difficulty ignoring irrelevant distracting information,

and exhibit reduced levels of negative priming (Beech, Powell, McWilliams & Claridge, 1989). Reduced negative priming has also been observed in other diseases or mental disorders, such as Parkinson's disease (Filoteo, Rilling & Strayer, 2002; Wylie & Stout, 2002), Alzheimer's disease (Sullivan, Faust & Balota, 1995; Vaughan et al., 2006), obsessive-compulsive disorder (OCD) (McNally, Wilhelm, Buhlmann & Shin, 2001) and depression (MacQueen, Tipper, Young, Joffe & Levitt, 2000).

1.2.4.4 Wisconsin Card Sorting Task

The original Wisconsin Card Sorting Task (WCST) was introduced by Grant and Berg (1948). During the task, participants are instructed to match and separate piles of cards according to varying decision rules (colour, number, and design). Participants are usually not told how to match the cards, but they must figure out the sorting rule on the basis of feedback. After a number of consecutive correct sorts, the sorting rule changes without warning and participants have to learn the new rules. The errors are the number of responses that do not match the sorting principles. The Wisconsin Card Sorting Task has been widely used to assess the "frontal" lobe functions (e.g. strategic planning, organized searching, inhibition, and modulating impulsive responding) in neurodegenerative diseases and mental disorders, such as schizophrenia (Manoach et al., 2002; Meyer-Lindenberg et al., 2002), personality disorder (Cadenhead et al., 1999; Trestman et al., 1995), and psychopathy (Gorenstein, 1982; Sutker & Allain, 1987).

1.2.4.5 Prepulse inhibition (PPI)

Prepulse inhibition (PPI) of the startle response is a measure of inhibitory function by which a relatively weak version of a pre-stimulus (prepulse) inhibits the elicitation of the startle response caused by a strong startle

stimulus (Graham, 1975). The stimuli are usually acoustic, but other stimuli have also been used in PPI research, such as tactile, light and airpuff. The startle response is measured in startle chambers in animals or by eye-blink response in humans to detect bodily reactions, and the degree of startle is compared on pulse alone and prepulse + pulse trials. The percentage of the reduction in the startle reflex represents prepulse inhibition. PPI has been widely used in numerous species, and disruptions of PPI have been studied in humans and other species. Most notably it is disrupted in several psychiatric diseases, such as schizophrenia, as well as personality disorder (Braff et al., 1978; Braff & Geyer, 1990; Braff, Grillon & Geyer, 1992; Braff, Swerdlow & Geyer, 1999; Geyer, Swerdlow, Mansbach & Braff, 1990; Grillon, Ameli, Charney, Krystal & Braff, 1992; Herpertz & Koetting, 2005; Kumari, Soni, Mathew & Sharma, 2000; Weike, Bauer & Hamm, 2000).

1.2.4.6 Latent inhibition (LI)

Latent inhibition (LI) has been defined as a decrement in learning performance which takes place when the conditioned stimulus (CS) is given non-reinforced "pre-exposure" (Lubow & Moore, 1959). An LI procedure is one in which a CS is pre-exposed alone for a number of training trials, and then subjects are given the CS paired with the US. Compared to controls (not pre-exposed to the CS), the subjects are slow to learn the required association, and this retardation of learning constitutes LI. However, this retarded learning performance is not same as true inhibition. The simple pre-exposure does not cause the CS to acquire inhibition. For example, a latently inhibited stimulus is slower to become a conditioned inhibitor as well as a conditioned excitor. LI can develop in the absence of an expectancy of a US. One explanation is that non- reinforced pre-exposure to the CS may cause the subjects to pay less attention to the same CS

later (Reiss & Wagner, 1972). Despite its name, LI assesses stages of information processing possibly related to attentional filtering, and LI is viewed as an attentional phenomenon (Lubow, Schnur & Rifkin, 1976), rather than a test of inhibitory learning. In contrast, conditioned inhibition (CI) is an effect that is more closely related to an intuitive notion of inhibition.

1.2.4.7 Conditioned inhibition (CI) and its procedures

Compared with S-R learning (e.g. using variants of the Go-NoGo procedure, as described above), conditioned inhibition can be referred to stimulus-stimulus (S-S) learning, because participants learn to associate a conditioned stimulus and an unconditioned stimulus after a number of training trials. However, when a CS is associated with the absence of the US, it is called a conditioned inhibitor, where the US is the absence of the expected outcome (Dickinson, 1985).

As mentioned before, in CI procedures, the expectation of an outcome is normally inhibited by the presence of a qualifying stimulus. Building on the basic design for classical conditioning in which a conditioned stimulus (CS) signals an outcome (unconditioned stimulus, US), an additional stimulus (the conditioned inhibitor) signals the omission of the otherwise expected US (Pavlov, 1927). For example, training subjects a number of reinforced trials (A+), then pairing A and B in compound without reinforcement (AB–), subjects can learn B indicates non-reinforcement. Therefore B is a conditioned inhibitor (e.g. Marchant, Mis & Moore, 1972; Rescorla & LoLordo, 1965; Wagner, 1971).

Rescorla (1969) suggested two methods for measuring conditioned inhibition, one is called the summation test (training A+, C+ and AP–, test

C and CP, if CP is significantly lower than C, then P is a CI); another is retardation–of–acquisition test – after the summation test, if P is paired with a US, then the responding to P will develop very slowly compared with learning about a neutral CS. Hammond and Daniel (1970) confirmed similar results which were conducted by both methods. Besides, differential conditioning also establishes CI effect. Differential conditioning refers to the situation in which subjects are trained with random alternating trials, A+ and B–, and usually this is sufficient for subjects to regard B as a reliable inhibitor (Konorski & Szwejkowska, 1952; LoLordo, 1967; Rescorla & LoLordo, 1965). However, it has been argued that differential conditioning may not be the most effective procedure for establishing CI.

To date, little research has explored CI in relation to individual differences, and no research has explicitly examined CI learning in any clinical groups. The present study designed better controlled CI testing procedures than previous studies to assess CI performance in normal and clinical populations. Furthermore the current study has not chosen any unpleasant pictures as CSs or USs, so the experiment could test in clinical groups conveniently.

1.3 Individual differences and inhibitory learning

1.3.1 A founder of individual differences

Pavlov (1928, 1955) not only pioneered the study of the phenomenon of the conditioned learning in animals, but also established the concept of individual differences that he found among his animal subjects. During his famous conditioned reflex experiments, Pavlov discovered that not all of the dogs acquired or inhibited their conditioned reflexes at the same rate. He further stated that these differences seemed to be related behaviourally to the temperamental characteristics of the animals; later he proposed the

theory of nervous types which suggested that the brain was the centre of the individual variation.

1.3.2 Eysenck's theory

Following in the steps of Pavlov, Eysenck proposed a dimensional approach to analyse and clarify personality differences. According to Eysenck, there were two basic dimensions after factor analysis for a set of personality data – introversion-extraversion (I-E), and neuroticism (N). Introverts tend to be more reserved, less outgoing, and less sociable; in contrast, extraverts tend to be gregarious, assertive, and interested in seeking out excitement. Individuals who score high on neuroticism are predisposed to suffer strong, changeable mood, and to overreact in emotional situations (Eysenck, 1957; Eysenck & Eysenck, 1976a, 1976b).

Eysenck's (1957) research has provided a biological explanation of individual differences. His theory suggested that the nervous systems differ between introverts (I) and extraverts (E), because introverts have more 'excitable' brains than extraverts. The theory also tried to explain why different groups of people could develop different psychiatric symptoms: because the differences in central nervous excitability would shape different conditioned responses for different people. In 1967, Eysenck proposed his second theory, which suggested that central nervous excitability depended on two brain circuits, and each of these showed functional variation across individuals. The first is the limbic system and the other is the ascending reticular activating system (ARAS). The different combination levels between the two biological systems have formed individual differences. For example, neuroticism is due to differences in the responses of the limbic system, and introversion and extraversion are based on variability in the ARAS. Eysenck pioneered the biological theory

for the individual difference, although his research did not classify the different types of personality disorders associated with personality dimensions in practice.

Later Eysenck introduced his third dimension – Psychoticism (P) (Eysenck & Eysenck, 1991). Psychoticism does not imply psychosis, but individuals scoring high on the P scale are more likely to exhibit aggressive, tough-minded, and impulsive characteristics than average people. Historically, sociability and impulsivity have been handled as two components for defining extraversion by other personality theorists. However, Eysenck also defined impulsivity as one of the core features in his P dimension. Therefore, impulsivity is critical for understanding how Eysenck extended his two-dimensional scheme to three dimensions, and how others developed their own models of personality based on Eysenck's scales.

The dimensional approach also tried to describe and explain psychological disorders. For example, in the dimensional I-E and N scales, people scoring high on neuroticism indicate that they respond more poorly to environmental stress, and are more likely to interpret ordinary situations as threatening, and also find minor frustrations hopelessly difficult. They are also more likely to experience anxiety, anger, guilt, and clinical depression (see figure 1.3). Eysenck suggested that anxiety neurosis was the clinical counterpart of neurotic introversion, and disorders with antisocial behaviours could be regarded as the clinical counterpart of neurotic extraversion.

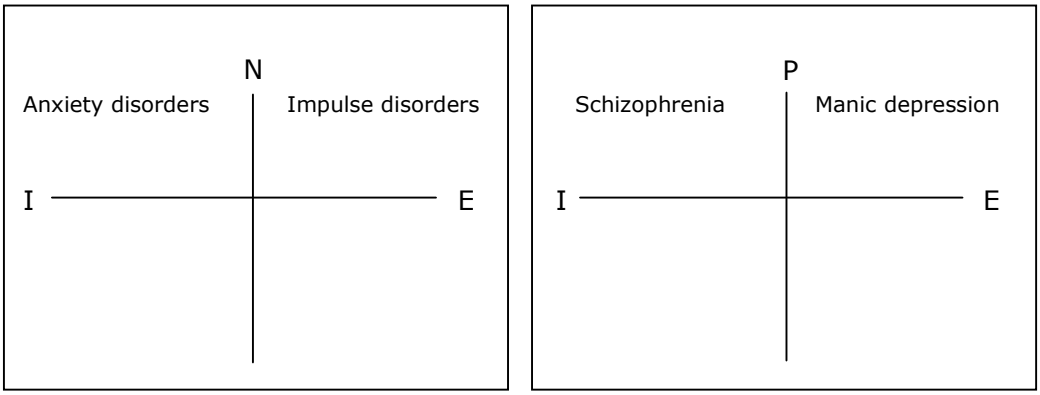


Figure1.3 Eysenck's location of disorder in P, I-E and N. Redrawn from Claridge and Davis (2003).

Unstable extraverts could become psychopaths because they are prone to have a hypersensitive negative emotional response and lack remorse or guilt; furthermore they usually fail to learn society's rules. These personality features and learning deficits could lead to aggressive and violent behaviours, which can be presented as impulsive personality and difficulty in response inhibition (Barratt, 1985, 1994; Horn, Dolan, Elliott, Deakin & Woodruff, 2003).

1.3.3 Gray's theory

Gray (1981) revised the Eysenckian two-dimensional (I-E and N) personality framework and proposed two rotated dimensions theory which is adapted from Eysenck's theory. Gray proposed his scheme as two rotated lines relative to the location of disorder in P, I-E and N (figure 1.3). One new dimension "anxiety" was between I and N; another new dimension "impulsivity" was between E and N (see figure 1.4). Gray's revision of Eysenck's model enriched the understanding of biosocial mechanism underlying individual differences. A further step in this revision was to propose a motivational theory of anxiety and impulsivity based on two dimensions in the sensitivity to reinforcement. Individuals who have a high sensitivity to signals of punishment fall along the anxiety dimension,

whereas those who have a high sensitivity to signals of reward fall along the impulsivity dimension.

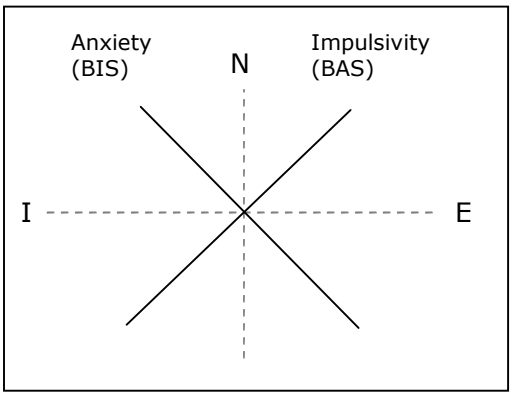


Figure 1.4 Gray's revision of Eysenck's theory. Redrawn from Claridge and Davis (2003)

Hence, Gray envisaged a behavioural model with two components – a behavioural inhibition system (BIS) and a behavioural activation system (BAS), which respectively corresponded to anxiety and impulsivity in the personality or temperament domain (Pickering & Gray, 1999). BIS provides account why individuals will experience an increase in central nervous system arousal and enhanced attention, as well as a 'freezing' of behaviour in anticipation of possible danger when they face certain inputs, such as a punishment (and non-reward), novel stimuli, and fear-producing stimuli. Compared with these who scored lower on the BIS scale, people with higher BIS scores would experience great anxiety about an impending punishment. The signals of punishment, non-reward, and innate fear stimuli would be as significant inputs for these people, and result in an increase in attention and arousal, and greater behavioural inhibition. In the extreme, heightened BIS sensitivity may relate to anxiety or depressive disorders (Fowles, 1993); thus BIS is particularly relevant to the understanding of some disorders, e.g. anxiety and phobias. The BAS aims to explain the reward-directed behaviours seen in highly hedonistic or pleasure-seeking individuals. People with high BAS scores are drawn strongly to desired stimuli which could be related to impulsive or antisocial

tendencies. This is to say, people with high BIS scores learn better about aversive outcomes (punishment, and absence of positive outcome), and these with high BAS scores learn better about pleasant outcomes (reward and absence of negative outcomes).

Within Gray's model, introverts have a strong BIS and weak BAS, extraverts a strong BAS and weak BIS; emotional stability reflects a weak BIS and weak BAS, and emotional instability a strong BIS and strong BAS. In 1994, Carver and White developed BIS/BAS scales measuring behavioural sensitivity to punishment, non-reward, and novelty, which has become established scales to assess BIS/BAS traits. People with high BIS sensitivity tend to suffer from anxiety and depression; while these with high BAS sensitivity are related to impulsive or antisocial tendencies (Diaz & Pickering, 1993; Flowles, 1980, 1993; Franken & Muris, 2006; Gray, 1985; Poythress et al., 2008).

1.3.4 Individual differences and a dimensional model of disorder

1.3.4.1 An alternative model for disorder: continuum of personality, from healthy individual variation to mental illness

Eysenck and Gray's theories proposed a link between personality dimension and psychological disorder which has helped to foster an alternative perspective on personality and illness. For Eysenck, mental illnesses and personality disorders represented the end-points of normal personality dimensions. The theory helps to bridge the first gap between personality as healthy individual variation and illness as malfunction, and also helps to understand the continuity of the illness and mental diseases, such as people suffering from mild depression, odd behaviour and thinking, unconventional beliefs, or antisocial attitudes. For example, anxiety illnesses (e.g. phobias, panic, PTSD) could stem from an existing anxious

personality trait which increases a tendency to state anxiety. The changes in thoughts and behaviours in mental illness show continuity with temperamental variation in the normal population; thus researchers proposed the idea of continuity in serious mental illnesses.

1.3.4.2 An example of dimensional model of disorder: from schizotypal personality trials to schizophrenia

In psychiatric clinical practices, Rado (1953) and Meehl (1962) first introduced "schizotaxic" people and "schizotypy". These people were described as having some features of lower anxiety, physical vigour, and general resistance to stress. However, they never manifest symptoms of mental illness, so they just remained as a normal person with high schizotypal scores. In 1987, McGlashan suggested a definition of schizotypal personality disorder as noticeable oddities in perceiving, communicating and behaving, but not serious enough to warrant the diagnosis of schizophrenia. Schizotypal personality disorder is a vulnerability to schizophrenia, which has a genetic link to chronic schizophrenia (Spitzer, Endicott & Gibbon, 1979; Siever & Gunderson, 1983).

During the 1980s, a schizotypy traits questionnaire was developed by Claridge and his colleagues to identify 'schizotypal' traits within the normal population. The questionnaire contains two scales, a schizotypal personality scale (STA) and a borderline personality scale (STB) (Claridge & Broks, 1984; Rawlings, 1983). The two scales respectively measure schizotypal and borderline personality disorder levels in the normal population. Later, based on STA, a more convenient and reliable scale was established for measuring schizotypal levels in the general population – the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE) short scale

(Mason, Linney & Claridge, 2005). O-LIFE short scale only has 43 yes/no questions, and their internal consistency was calculated by alpha coefficient. The alpha coefficient range was from 0.63 to 0.80 in all sub-scales, which suggested a good reliability. According to Nunnally (1978), the alpha coefficient = 0.7 is ideal, but the alpha coefficient = 0.6 is an acceptable level of measurement error in psychological/social science.

1.3.5 Individual differences in schizotypy and inhibitory processes

Beech and Claridge (1987) were the first to investigate the correlation between individual differences in schizotypy and inhibitory processes. Participants were 32 male volunteers (no history of psychiatric illness), and the individual differences were measured by STA, STB and the Eysenck Personality Questionnaire (EPQ). The inhibitory learning was assessed by a negative priming paradigm. The negative priming experiment investigated both simultaneous interference and successive priming effects. In the simultaneous interference situation, participants were asked to respond to a target while ignoring a distractor; in the successive selection, experiment investigated what happens when participants had to respond to a previously ignored distractor (see details as above). The study found that participants with a high schizotypy score showed less inhibition than those with a lower score. The study also found that there was a significant negative correlation between the schizotypy score and the amount of inhibition shown.

These findings indicated that the measured inhibition effect decreases with the degree of schizotypal traits in the normal population, which may provide a necessary link for understanding some specific cognitive abnormalities in schizophrenic patients (Frith, 1979; Marcel, 1983). For example, dysfunctions of information processing in schizophrenia –

schizophrenics' information processes can be affected by a defect in the inhibition of further processing of unwanted material, or a failure to inhibit at a preconscious level.

1.4 Inhibitory learning and disorder

Previous studies suggested that normal people who scored higher on impulsive or schizotypal scales, would show lower level of inhibition (Enticott et al., 2006; Helmers et al., 1997; Migo et al., 2006). These findings suggest that the relevant clinical groups will show impaired inhibitory learning performance. The following sections provide evidence of inhibitory dysfunction in schizophrenia (1.4.1), personality disorder (1.4.2) and psychopathy (1.4.3).

1.4.1 Schizophrenia and inhibitory dysfunctions

1.4.1.1 Definition and symptoms of schizophrenia

Kraepelin (1919) distinguished dementia praecox from other mental disorders, and he proposed that when individuals displayed certain unusual symptoms they would be diagnosed with dementia praecox. These unusual symptoms included inappropriate emotional responses, such as smiling in pain, crying in a comedy; stereotyped motor behaviour, such as clapping on the chair repeatedly before sitting down; attentional difficulties, such as being unable to hold a conversation because of shifting shadows; sensory experiences in the absence of appropriate stimuli, such as hearing voices when the environment is silent; and beliefs that are sustained in spite of overwhelming contrary evidence, such as insisting that one is a famous or a historical personage like Queen Elizabeth I.

Kraepelin's view was taken up by Bleuler, who used the term "schizophrenia", and he believed that schizophrenics' unusual behaviour

was due to brain biological disease. Bleuler (1911) and Kraepelin (1919) proposed that schizophrenia was characterized by a dysfunction of the capacity for associative thought and cognitive processes. Since then there has been a notable increase in attempts to characterise the cognitive dysfunction that underlies schizophrenia. Bleuler and Kraepelin's ideas were further developed in the early 1960s by Venables (1960, 1964) who proposed the concept of "flooding" or sensory inundation in schizophrenia. It indicated their cognitive dysfunctions were due to the patients' brain has lost its ability to control the flood of sensory information into higher levels of processing areas. At the same time, McGhie & Chapman (1961) suggested that schizophrenic patients showed attention, sensory and perception abnormalities. For over five decades, a variety of studies have reported that patients with schizophrenia present with information-processing abnormalities.

Since Kraepelin and Bleuler's proposals, their view has powerfully influenced succeeding generations of psychiatrists. Nowadays, schizophrenia is viewed as a genetic disorder, in the sense that it occurs much more often among biological families than adoptive families. Schizophrenia can also be viewed as a biological disorder, because it seems to be characterised by neurotransmission disorders and structural brain deficits. Schizophrenics are categorized according to their symptoms. Positive symptoms reflect marked departures from ordinary cognition, which include "delusions; hallucinations; disorganized speech (e.g. frequent derailment or incoherence); grossly disorganized or catatonic behaviours". Negative symptoms reflect the absence or diminution of normal daily functions, which is characterized "affective flattening, alogia, or avolition" (DSM-IV, 1992, 1994, 2004).

1.4.1.2 Response inhibition tasks in schizophrenia

Thoma and her colleges explored cognitive flexibility and response inhibition tasks among schizophrenia and comparison groups (Thoma, Wiebel & Daum, 2007). The study compared four groups (schizophrenia with and without substance use disorder, patients suffering from alcoholism or major depression, and healthy controls) in a German card version of the Colour-Word-Interference task (CWI, Bäumler, 1985) which is based on the Stroop task and a Go/NoGo task. The CWI task required participants to read out colour names printed in black ink, name the colours of coloured bars, and name the ink colour while ignoring the word's meaning. As the Stroop task, reaction time (RT) was measured to determine the levels of inhibition. The Go/NoGo task ("Neurobat": Wiebel, Happe & Weber, 2002), required participants to respond a Go stimulus or ignore a NoGo stimulus. The Go/NoGo stimuli were counterbalanced in two parts of the task. RTs and the number of errors were recorded. The results showed that schizophrenic patients had a significantly higher RT than the rest of groups during the CWI task, and the patients generally responded more slowly than healthy controls during the Go/NoGo task. The results indicated that schizophrenic patients had severe cognitive flexibility and response inhibition deficits, although there was no clear evidence of a differential impairment of the two schizophrenic groups.

1.4.1.3 LI and PPI procedures in schizophrenia

Since the schizophrenic patients (either with positive or negative symptoms) have prominent attentional difficulties and thought disorder, schizophrenia can be considered as a cognitive dysfunction. Many studies have investigated LI (Baruch et al., 1988; Cohen et al., 2004; Moser, Hitchcock, Lister & Moran, 2000; Swerdlow et al., 2005; Weiner, 2003), and PPI (Bolino et al., 1994; Braff et al., 1978, 1992, 2001; Kumari et al.,

1999, 2000; Kunugi et al., 2007; Grillon et al., 1992; Weike et al., 2000) in schizophrenic patients, and the studies confirmed that LI and PPI were reduced in the patients.

LI is an important model for understanding the cognitive dysfunction in schizophrenic disorders. Baruch et al. (1988) first reported a disturbance of LI in schizophrenic patients. During the LI learning task, there were three groups (26 acute schizophrenics, 27 chronic schizophrenics and 53 normal controls), and each group was randomly subdivided into two experimental conditions - preexposure or non-preexposure. The preexposed subjects first heard 30 bursts of white noise, and then had to listen to a series of nonsense syllables and count the frequency of one of them; the non-preexposed subjects listened to the nonsense syllables without the white noise. All the participants had the opportunity to learn that the noise signalled increments in a visually displayed number in both conditions (preexposed and non-preexposed). The study found the evidence of LI in normal controls and chronic schizophrenics: the preexposed two groups learned the association more slowly than non-preexposed participants. The results also showed that there was no significant difference between the two conditions in acute schizophrenic patients which indicated that the acute schizophrenic patients failed to display the LI effect.

Later many studies reported similar findings; for example an anomaly in LI in schizophrenic patients, especially in acute and/or unmedicated schizophrenic patients (Gray, Hemsley & Gray, 1992; Guterman et al., 1996; Kathmann, von Recum, Haag & Engel, 2000; Rascle et al., 2001; Sitskoorn, Salden & Kahn, 1991; Vaitl et al., 2002). These studies suggested that psychotic patients may have deficits in the early stages of

information processing (e.g. sensory "flooding" or registration). Because of these deficits, patients may pay less attention to the pre-exposed stimulus, so reduced or abolished LI effects were found in the clinical groups. Those dysfunctions in the information processing in patients also cause the deficits in cognitive process (Braff & Geyer, 1990; Braff et al., 1999; Venables, 1960).

Prepulse inhibition (PPI) is another paradigm to assess cognitive functions in schizophrenic patients. PPI has been extensively explored in schizophrenia (e.g. Bolino et al., 1994; Braff et al., 1978, 1992, 1999; Kumari et al., 2000; Weike et al., 2000), and it has been suggested that the deficient PPI is a clinically important feature of schizophrenia. Meanwhile, the PPI deficits have been particularly valuable for understanding the neurobiology of schizophrenia, as the PPI may reflect a biological correlate of sensory flooding and cognitive fragmentation in the patients. Many studies investigated PPI startle response in schizophrenia and reported that schizophrenic patients showed inability to filter out the unnecessary information (Braff & Geyer, 1990; Geyer et al., 1990; Grillon et al., 1992). Impaired PPI in the patients suggested abnormalities of sensorimotor gating in central nervous system. However, problems with PPI are not only found in schizophrenic patients. There are other disorders or diseases characterized by PPI deficits, such as ADHD (Castellanos et al., 1996; Ornitz, Hanna & De Traversay, 1992), Huntington's disease (Swerdlow et al., 1995), Tourette's syndrome (Castellanos et al., 1996; Swerdlow et al., 1994), OCD (Swerdlow et al., 1993; Swerdlow et al., 1994), and PD (Herpertz & Koetting, 2005; Kumari et al., 2005).

1.4.2 Personality disorders and inhibitory dysfunctions

1.4.2.1 The definition and diagnosis of personality disorders

Personality disorder (PD) is a broad term used to cover a set of heterogeneous conditions that have in common a tendency to be deviant, troublesome and persistent. Sartorius et al. (1993) stated that PD is generally less well described in the classification than any other group of disorders. Currently, DSM-IV (1992, 1994, 2004) is the most commonly cited classification of this disorder, which introduces the concept of operational criteria, and diagnostic core features of the condition. According to DSM-IV, PDs are categorised according to 3 clusters: the odd and eccentric (Cluster A), the emotional and erratic (Cluster B) and the anxious and avoidant (Cluster C) (see table 1.1 in details)

Table 1.1 DSM-IV descriptions of the three clusters in personality disorders.

Cluster A includes Paranoid personality disorder: irrational suspicions and mistrust of others. Schizoid personality disorder: lack of interest in social relationships, avoiding others. Schizotypal personality disorder: odd behaviours or thinking.
Cluster B includes Antisocial personality disorder: disregard for the law and the rights of others. Borderline personality disorder: instability in relationships and self-image, impulsivity. Histrionic personality disorder: excessive emotionality and attention-seeking. Narcissistic personality disorder: grandiosity, need for admiration, and a lack of empathy.
Cluster C includes Avoidant personality disorder: social inhibition, feelings of inadequacy, hypersensitivity to negative evaluation and avoidance of social interaction. Dependent personality disorder: pervasive psychological dependence on other people. Obsessive-compulsive personality disorder: rigid conformity to rules, moral codes and excessive orderliness.

Cluster B in particular includes PDs characteristic of offenders, particularly antisocial personality disorder (ASPD), borderline personality disorder (BPD), though paranoid PD found in Cluster A is also characteristic, and offenders show a high degree of comorbidity across PDs. ASPD and BPD have inspired a considerable amount of research; moreover, impulsivity is one of core features for ASPD and BPD, and especially it is a core feature for patients with PD in forensic settings, so the present study focuses on these two types of PD.

1.4.2.2 Antisocial personality disorder and inhibitory dysfunctions

Antisocial personality disorder (ASPD) is a potentially dangerous disorder, characterized by poor impulse control, and destructive and antisocial behaviours that have begun by adolescence, and continue in a variety of behavioural problems during adulthood (DSM-IV). There are many impulsivity related items included in the diagnostic criteria for ASPD; for example, impulsivity or failure to plan ahead; reckless disregard for safety of self or others; consistent irresponsibility, etc. It is clear that impulsivity is a core feature of this type of disorder; however, little research has measured impulsivity quantitatively in ASPD. Furthermore, few studies have explored the relationship between the trait of impulsivity and response inhibition in ASPD.

In a study by Swann and colleagues (Swann, Lijffijt, Lane, Steinberg & Moeller, 2009); 34 ASPD patients and 30 healthy controls took part in the experiments. The Barratt Impulsiveness Scale (BIS-11) (Barratt & Patton, 1983) was used for measuring impulsivity in ASPD patients. The scale included three factors: attentional, motor and non-planning impulsiveness (Patton et al., 1995). Compared with healthy controls, the study found that ASPD patients showed differences in motor and non-planning impulsiveness. Three behavioural inhibitory learning tasks were conducted – the immediate memory task (IMT), the single key impulsivity paradigm (SKIP), and the two choice impulsivity paradigm (TCIP). The IMT task aimed to assess impulsivity, measure attention and rapid-response impulsivity. Participants were required to respond as quickly as possible when they saw a five-digit number that matched the previous one. The RT and the number of responding errors were measured. The SKIP and the TCIP tasks measured their ability to delay response for a larger reward. Participants' short-delay responses to a small reward were taken as

impulsive responses. The results showed that ASPD patients had increased IMT commission error (4 of 5 digits matched) reaction times, which may suggest their response inhibition was impaired. However, there was no significant difference between the groups in the other tasks.

Rubio et al., (2007) examined varieties of impulsivity in patients with ASPD, BPD and alcohol-dependent personality disorder (APD), and used the stop-signal task as a behavioural inhibitory task measuring rapid-response impulsivity. The differential reinforcement for low-rate responding task (DRL task) assessed participants' ability to refrain from responding, which measured their impulsive control. The study also used one of the Barratt impulsiveness scales (BIS-11) as a psychometric measurement for impulsivity, and found patients with APD comorbid with BPD had the highest scores on BIS subscales and BIS total scales. Rubio et al.'s study also found that patients with ASPD and BPD had poorer performance (more errors) across all behavioural tasks than those with APD and controls, and patients with BPD showed behavioural disinhibition (more errors and longer SSRT).

1.4.2.3 Borderline personality disorder and inhibitory dysfunctions

Knight (1953) used the term of "borderline" for a sub-schizophrenic disorder applied to patients at the border of schizophrenia. Since Knight published his pivotal paper, there have been a large number of descriptive studies of borderline patients (Frosch, 1964; Gunderson, 1984; Kernberg, 1975). Borderline personality disorder is now viewed as a serious mental disorder with a characteristic pervasive pattern of affective disturbance, disturbed cognition, impulsive and potentially self-damaging, unstable and intense interpersonal relations, and a chronic feeling of emptiness (DSM-IV). Many studies have suggested that the impulsivity and dysregulated

behaviour are core features of BPD (Gunderson & Singer, 1975; Lieb, Zanarini, Schmahl, Linehan & Bohus, 2004; Zanarini, Gunderson & Frankenburg, 1990) which are correlated with poor performance on response inhibition (measured by stop signal reaction time) in BPD patients (Nigg et al., 2005; Rubio et al., 2007).

Nigg, Silk and Stavor, (2005) used a set of cognitive tasks to compare inhibition rate, perseverative errors, and mental set shifting in patients with BPD, other disorders (e.g. ADHD, ASPD), and controls. The following cognitive tasks were included: Stop Task which measured SSRT to assess participants' response of inhibition; the WCST Task measured participants' perseverative errors; the Trail Making Task examined participants' mental shifting (required participants to draw a line between letters or numbers as quick as they can); and the Tower of London Task which asked participants to rearrange balls to match a predetermined pattern on a series of pegs. The performance on the Tower of London task was related to participants' IQ and the ability of time planning. The study found that BPD patients showed significantly poorer response inhibition than controls (longer SSRT), even poorer than in other personality disorders (such as ADHD, ASPD) on Stop Task, the WCST Task and the Tower of London Task.

The research findings of Grootens et al.'s study (2008) further supported Nigg et al.'s (2005) experiment. Grootens and his colleagues used a pro-saccadic (requires participants to make an eye movement in the direction to the light-emitting diodes) and anti-saccadic (requires participants to make an eye movement in the direction opposite to the light-emitting diodes) eye movement task. The percentage of error responses in the anti-saccadic task measured as the percentage of inhibition errors. The study compared the results in three groups (recent onset schizophrenic patients,

BPD patients and controls), and found that schizophrenic patients showed significantly more inhibition errors during the anti-saccade task than BPD patients and controls, whereas BPD patients significantly showed more inhibition errors than controls. The data revealed a clear evidence of inhibition deficits in these two clinical groups.

Up to date, many studies suggested that patients with ASPD and BPD showed higher impulsiveness and impaired behavioural inhibition (Grootens et al., 2008; Nigg et al., 2005; Rubio et al., 2007; Swann et al., 2009). However, not all studies find inhibition deficits in BPD patients. Herpertz and Koetting (2005) compared PPI startle response in a sample of 28 unmedicated BPD patients and 28 controls (24 female and 2 male participants in each group). The experiment measured skin conductance response and eye-blink component of startle reflex, however, the study found no deficit in PPI startle response in BPD patients. The inconsistent findings questioned the relationship between psychotic symptoms and inhibition deficits in the clinical patients.

1.4.3 Psychopathy and inhibitory dysfunctions

1.4.3.1 Definition of psychopathy

In the nineteenth century, psychopaths were regarded as people who were afflicted by moral insanity. Prichard (1837) distinguished psychopathy from other psychotic disorders. In his view, the mind of a psychopath was "strangely perverted and depraved", and the power of a psychopath's "self-government" was "lost or greatly impaired". Cleckley (1964) listed sixteen features of psychopathy which can be put into three broad categories: inadequately motivated antisocial behaviour, the absence of a conscience and sense of responsibility to others, and emotional poverty.

Although psychopathy has not been specifically described in either the DSM-IV (1992, 1994, 2004), or the International Statistical Classification of Disease and Related Health Problems, Tenth Revision (ICD-10; World Health Organisation, 1992), this condition clearly shows some overlap with ASPD (Coid & Ullrich, 2010; Durand & Barlow, 2000). Psychopathy (as operationalised by the Psychopathy Checklist, Hare, 1991, 2003) represents a constellation of personality traits that also include affective deficiency (e.g. lack of empathy) and interpersonal characteristics (e.g. glibness and superficial charm), seen to an extent beyond that typical of ASPD in the absence of comorbid psychopathy. However, notably both psychopathy and ASPD are characterized by a disinhibited lifestyle and a tendency to transgress social norms and legal rules. Over recent years, there has been extensive research on features of psychopathy, and researchers have formally proposed to consider the inclusion of the diagnosis of psychopathy in the forthcoming DSM-V (Widiger & Lowe, 2008).

1.4.3.2 Psychopathy and inhibitory dysfunctions

Consistent with the pattern of affective, interpersonal and behavioural symptoms in psychopaths, empirical studies have reported that they are also characterized by anomalies in attentional functioning and learning deficits (Cleckley, 1964; Kosson & Newman, 1986; Lykken, 1957; Newman et al., 1987). In the 1950s, the first laboratory learning task was conducted among psychopaths, neurotic criminals, and controls. Participants were required to make a judgement which aimed to avoid punishment (Lykken, 1957). The learning task was described as a "mental maze", and involved a series of 20 choice points and the participants were told to choose and press one of four levers for each choice. At a given choice, only one lever was the correct one and participants had to learn to

press the correct one. The task was given for 20 trials to let participants learn the maze, committing as few errors as possible. According to the different levels of errors, participants were given two types of punishments. If participants made an incorrect choice, one punishment was simply being told "wrong", another was being given an electric shock. The study found that compared with controls, psychopaths made the most errors that led to physical punishment. This suggested that psychopaths showed a learning deficit in avoiding the aversive consequences of their behaviour.

Gorenstein and Newman (1980) proposed an explanation for psychopaths' failure to inhibit punished responses: it is because they are prone to response perseveration. Later, Newman, Patterson & Kosson (1987) studied and compared the behavioural performances among 36 psychopaths and 36 controls in a computerized version of the WCST (Newman & Howland, 1986). The experiment involved monetary rewards and punishments, which revealed unambiguous evidence of response perseveration in psychopaths even using tangible punishments such as the loss of money. This learned inhibition of behaviour in order to avoid punishment is called passive avoidance learning. Many previous studies have supported the hypothesis that psychopaths show deficits in passive avoidance learning (Kosson, Smith & Newman, 1990; Newman & Kosson, 1986; Newman & Schmitt, 1998; Schmauk, 1970; Thornquist & Zuckerman, 1995; Vitale & Newman, 2001). Newman (1987) suggested that the poor passive avoidance learning and impulsive behaviour are the characteristics of disinhibition (loss of inhibition or insensitivity to aversive events).

To date, learning differences and attentional anomalies have been most extensively investigated in relation to psychopathy rather than ASPD and BPD as defined by DSM-IV criteria. These studies have also tended to use aversively motivated learning tasks, consistent with the fact that a defining feature of impulsivity is heedless action despite negative consequences (Cleckley, 1964; Flor, Birbaumer, Hermann, Ziegler & Patrick, 2002; Gorenstein & Newman, 1980; Kosson & Newman, 1986; Kosson et al., 1990; Lykken, 1957; Newman, 1987; Newman & Kosson, 1986; Newman et al., 1987; Newman & Schmitt, 1998; Schmauk, 1970; Thornquist & Zuckerman, 1995; Vitale & Newman, 2001). However, as discussed above, psychopathy has been argued to be on a continuum with ASPD (Coid & Ullrich, 2010; Durand & Barlow, 2000). Notably both psychopathy and ASPD are characterized by a disinhibited lifestyle and a tendency to transgress social norms and legal rules. If an effective learning task is thought to involve inhibition of stimuli-stimuli (S-S) associations, it may find a deficit in CI in these clinical groups. Thus the present study expected an impaired CI would be found in these patients.

1.4.4 Summary

To sum up, although the symptoms and conditions of schizophrenia, personality disorders and psychopathy differ in many respects, there are some overlapping neurocognitive dysfunctions and behavioural features present in all these disorders, such as frontal lobe deficits, impulsivity, disorganized and poorly planned thought and behaviour (Cleckley, 1964; DSM-IV-TR, 2004; Eronen, Angermeyer & Schulze, 1998; Kraepelin, 1919; Moeller et al., 2001).

Various lines of research suggest that the cognitive fragmentation in schizophrenic disorders, personality disorders and psychopathy may be due

– at least in part – to inhibitory dysfunctions. Inhibitory learning is a useful model for examining the cognitive dysfunctions because previous studies suggested disinhibition and poor impulse control are common factors across these disorders (Baruch et al., 1988; Bolino et al., 1994; Braff et al., 1978, 1992, 1999; Cleckley, 1964; Gray et al., 1992; Grootens et al., 2008; Kathmann et al., 2000; Kosson & Newman, 1986; Kumari et al., 2000; Lykken, 1957; Newman et al., 1987; Nigg, et al., 2005; Vitale & Newman, 2001; Weike et al., 2000).

Previously inhibitory learning has been measured by laboratory behavioural learning tasks, and the learning performance was examined thought to involve inhibition of S-R association (e.g. using variants of the Go/NoGo and Stop-signal tasks, as described above), which explored the participants' ability to inhibit pre-potent motor responses. However, as a construct, inhibition encompasses a diverse range of processes and should not be too narrowly identified with any one paradigm. For example, in the chain of cause and effect that ultimately results in unwanted actions, environmental cues which trigger associated thoughts and emotions through stimulus-stimulus (S-S) associations can be primary. Inhibition of these S-S associations might therefore play a critical role in suppressing unwanted behaviours in normal subjects. Thus, as it cannot be assumed that the same psychological mechanisms inhibit S-S and S-R associations (Nigg, 2000); the inhibition of such stimulus-stimulus associations - formally 'conditioned inhibition' – should also be examined.

1.5 Measures and designs of conditioned inhibition

1.5.1 Measures of conditioned inhibition

Since Pavlov first demonstrated classical conditioning, many models of associative learning have been proposed during the past five decades. The

most influential theory is the Rescorla-Wagner Model (Rescorla & Wagner, 1972; Wagner & Rescorla, 1972). This model is built on the idea that learning occurs only if the US is "surprising". That is to say, when subjects are presented with CSs paired with US on any one trial, according to the degree of surprisingness of the US, subjects will gain a positive associative strength with a US. If any stimulus possesses a negative associative strength with a US (the CS signal an omission of a US), this stimulus will be a conditioned inhibitor, which has ability to counteract stimuli with positive associative strength. The model argued that a conditioned inhibitor is a CS with a negative associative strength value. For example, a CS (bell) is presented to a subject and is associated with a US (food). After several trials, the associative strength between the CS and the US grows, until the subject learns that bell means food. In the next phase, the reinforced trials continue to occur [CS (bell) indicated US (food)]. At the same phase, the CS (bell) is compounded with another CS (light) and this compound is presented without the US (food). The value of associative strength between CS (bell) and US will decrease from zero to negative, and after a number of trials, the subject can learn that light means no food. The CS (light) becomes a conditioned inhibitor (CI).

Rescorla (1969) suggested that two critical methods should be used to measure conditioned inhibition: the summation test and the retardation-of-acquisition test. In a summation test, subjects will show less response to the inhibitor and conditioned excitor (a different excitor from training one) compound than a conditioned excitor presented alone. During a retardation-of-acquisition test, if a conditioned inhibitor is paired with a US, then the responding to the CS will develop very slowly compared with a neutral CS. Rescorla (1969) has argued that the summation test combined

with a retardation test offers the possibility of the most conclusive evidence of learned conditioned inhibition. Rescorla noted that if CI is only measured by the summation test, the measurement may be confounded by attention argument – the conditioned inhibitor distracts attention; if CI is only measured by the retardation test, the CS may be slow to acquire excitatory strength when reinforced, because attention to it has been reduced. If CI is measured by both summation and retardation tests, then the attention argument can be ruled out.

Since Rescorla's (1969) review of procedures for identifying Pavlovian conditioned inhibition, most animal studies followed Rescorla in using both summation and retardation tests for measuring CI (e. g., Cotton, Goodall & Mackintosh, 1982; Schachtman et al., 1987). Williams, Overmier and LoLordo (1992, p. 287) argued that although perhaps it is not always "necessary" to use both tests if the experiment is well controlled, because "they rule out rival hypotheses", it would be better do both together to provide compelling evidence of inhibition. To date, there has been no published research successfully demonstrated a retardation task in humans.

1.5.2 Conditioned inhibition in humans

There are many studies measuring conditioned inhibition in animals (e.g. Holland, 1984; Holyoak, Koh & Nisbett, 1989; Nicholson & Freeman, 2002; Rescorla & Holland, 1977), but few conditioned inhibition experiments have been conducted on human participants (Grings, Carey & Schell, 1974; Migo et al., 2006; Neumann, Lipp & Siddle, 1997; Wilkinson, Lovibond, Siddle & Bond, 1989). Since the 1970s, research started to explore conditioned inhibition in humans, and these studies measured inhibition by a summation test. For example, Grings et al. (1974) used six different visual

CSs (A, B, C, D, E, and P) and a US (shock) to measure Pavlovian conditioned inhibition (A+ and AP –) and inhibition produced by differential conditioning (C+ and E –). It was the first paper investigating conditioned inhibition in humans. The CSs were produced by different combinations of colours (red, green, blue, or yellow) and geometric shapes (triangle, horizontal or vertical dots, or horizontal lines). During the training phase, participants were given A+, B+, BP –, and E –, and the test was A, B, AC, BD, AP, and BE. Thus the original excitatory CSs were A and B, the inhibitory transfer compounds were AP (conditioned inhibition compound) and BE (differential inhibition compound), and the neutral control compounds were AC and BD. The study recorded the participants' electrodermal responses and self-reported US expectancy, and expected that participants would give significantly lower scores on AP and BE than those of AC and BD. The experiment found that conditioned inhibition was shown in US expectancy, but not in electrodermal responses. Grings et al. suggested that the novelty of the CSs (C and D) during the test stage caused orienting which produced an enhancement of electrodermal responses to inhibitory transfer compounds rather than diminished responses as predicted after inhibitory training.

Neumann and his colleagues modified Grings' experiment design and conducted a similar study to investigate conditioned inhibition processes in humans by a summation test (Neumann et al., 1997). The study used four geometric shapes, a square, a circle, a triangle, and a diamond (A, B, C and D) as CSs and electric shocks as USs. The training stage included A+, C+, AB–, AC+, and B–, and the test was C, CB, and CD. If the participants' responses to CB were significantly lower than their responses to C and CD, this would constitute evidence of inhibition. This is because B as the inhibitor suppresses excitation to the test excitor (C). According to

Rescorla's recommendations, it was a well controlled experimental design, in which D was a novel stimulus, because the novel stimulus could produce an enhancement of orienting behaviour which might interfere with the US omission responding. The study recorded participants' self-reported US expectancy and electrodermal responses. The results showed evidence for conditioned inhibition in US expectancy: the ratings of CB were significantly lower than those of C and CD. The results also found CI effects by second interval electrodermal responses: the response magnitude during CB was significantly lower than those of C and CD. The study provided a suitable CI learning procedure (measured by a summation test) for future studies in human.

1.5.3 Conditioned inhibition in relation to individual differences

Up to date, there has been one study which examined CI learning procedures in relation to individual differences in schizotypy – Migo et al. (2006). The study explored the correlation between the levels of conditioned inhibitory learning (using a summation test) and individual differences (measured by BIS/BAS, STA, and STB). In the study, conditioned inhibition was measured by presenting a CI with a CS, and this CS had never been presented with the CI before. The training phase included A+, B+, T+, AP−, and BP−, the test phase was A+, B+, T+, N+, AP−, BP−, TP−, and NP−, in which P was the inhibitor, T was a trained test excitor, and N was the novel "test excitor". The participants had to rate the likelihood of the presentation of US from 1 to 9. The measure of inhibition was indicated by a CI ratio (the average expectancy scores for all non-reinforced trials divided by the average expectancy scores for all reinforced trials). The study found that the level of conditioned inhibition was negatively correlated with the degree of schizotypy. The results suggested that conditioned inhibition processes may contribute to the symptoms of

schizophrenia. Migo and her colleagues' experiment (2006) is the only study which showed some evidence that there was a relationship between conditioned inhibition processes and a measure of personality differences. Nevertheless, no study so far has explored inhibition thought S-S association (CI learning tasks) in clinical groups. Therefore the present study will focus on the conditioned inhibition phenomenon in individual differences and schizophrenia and PD patients.

1.6 Aims of the thesis

The aims of the present doctoral research were to develop a suitable and robust CI procedure to test human participants, and to explore Pavlovian excitatory learning and CI learning performance in relation to individual differences in general populations. The study also aimed to investigate CI learning deficits in clinical groups (eg. schizophrenia, PD and psychopathy). Individual differences were measured by a set of questionnaires (see table 1.2). Combined with the questionnaires, a computer-based conditioned inhibitory learning task (see details in Chapter II) was designed and developed to assess CI learning performance in normal populations and disorders.

Table 1.2 The questionnaires which were used in the present study

Questionnaire	Measures
Behavioural inhibition system and the behavioural activation system (BIS/BAS, Carver & White, 1994)	Two general motivational systems that underlie behaviour and affect, in which the level of BIS activation should reflect to anxiety, and the BAS functioning is related to impulsive or antisocial tendencies.
The Urgency, Premeditation, Perseverance, and Sensation Seeking Impulsive Behaviour Scale (UPPS, Whiteside & Lynam, 2001).	Impulsiveness, which included four subscales: urgency, (lack of) premeditation, (lack of) perseverance, and sensation seeking.
Eysenck Personality Questionnaire Revised short scale (EPQ-RS, Eysenck, Eysenck & Barrett; 1985).	The dimensions of personality, which includes 4 factors, extraversion (E), psychoticism (P), neuroticism (N), and response distortion scale (Lie).
Oxford–Liverpool Inventory of Feelings and Experiences short scale (O-LIFE short, Mason, Linney & Claridge, 2005),	Schizotypal levels in normal people, e. g., unusual experiences, cognitive disorganization, introverted anhedonia, and impulsive non-conformity.

Questionnaire	Measures
Schizotypal Traits: traits B (STB, Rawlings, Claridge & Freeman; 2001).	Borderline personality in general populations, e.g. self-harm, destructive and impulsive behaviours.

1.7 Hypotheses of the thesis

This thesis tests the general hypothesis that individual differences (measured by BIS/BAS, UPPS, EPQ-R, O-LIFE and STB scales) in normal populations should predict differences in conditioned inhibition learning performance. The alternative specific hypotheses that can be justified with reference to the literature are summarised below. There are a number of hypotheses across a variety of individual difference measures, and the underlying mechanisms whereby CI may be reduced in relation to different aspects of personality and temperament are likely to be different.

1. Although there was lack of significant correlation between BIS scores and CI learning performance in Migo et al.'s study (2006), wider research and theory suggests that people with higher BIS score are vulnerable to anxiety and other negative affective states (Fowles, 1980, 1993; Gray 1985). Both theoretically and empirically evidence suggested an abnormal associative learning processes on aetiology and maintenance of anxiety (Barlow, 2000; Grillon, 2002). Therefore the hypothesis that individuals with higher BIS scores should show reduced CI.
2. The high BAS sensitivity reflects high impulsivity; furthermore, in extreme cases, heightened BAS sensitivity may contribute to the sociopathic personality (Fowles, 1980; Gray, 1985). According to Migo et al. (2006)'s study, individuals with high BAS Reward Responsiveness scores showed less evidence of CI learning. Based on theories, it is hypothesised that individuals with higher BAS scores will perform worse on the CI learning task.

3. Besides, the UPPS scale has been widely used to measure impulsivity (Billieux et al., 2007; Gay et al., 2008; Magid & Colder, 2007; Ray et al., 2009), and some research suggests that individuals with high level of impulsiveness show worse performance in tests of inhibition (Gay et al., 2008; Horn et al., 2003). Thus, it can be hypothesised that individuals with higher UPPS scores should perform worse on the CI learning task.
4. With respect to the EPQ (revised scale), individuals with high neuroticism scores are more likely to experience anxiety (Eysenck, 1957; 1967). Moreover, Helmers et al. (1997) suggested that extraverts show high level of impulsivity and related this aspect of temperament to increased errors of commission in the Go/Nogo task. On this basis it is predicted that individuals with higher neuroticism and extraversion scores might perform worse on the CI learning task. However, to date, no research has explored the relationship between EPQ scores and inhibitory learning of the kind measured in the present thesis.
5. According to Migo et al. (2006)'s study, individuals with higher schizotypy levels (in this case measured by the earlier STA scale) showed less evidence of CI. Therefore, it is predicted that individuals with higher schizotypy levels (to be measured by O-LIFE in present study) will show reduced CI.
6. The STB scale measures borderline personality in general populations and these scores could relate to the symptoms of BPD (e.g. impulsivity, Rawlings et al., 2001). No correlation was found between STB scores and CI learning performance in Migo's study (2006) but this may have been underpowered. Therefore the hypothesis was that those normal participants with higher STB scores will perform worse on the CI task in the present thesis.

With respect to clinical groups, although the underlying psychopathology is very different, both schizophrenic patients, and individuals with certain types of personality disorder and/or psychopathy have shown various types of cognitive dysfunctions consistent with anomalies in inhibitory processes, and specifically worse performance in a range of inhibitory tasks (Braff et al., 1978, 1992, 1999; Cleckley, 1964; Grootens et al., 2008; Kumari et al., 2000; Lykken, 1957; Newman et al., 1987; Nigg, et al., 2005; Vitale & Newman, 2001; Weike et al., 2000). Accordingly, although, as for the personality measure predictions, the underlying mechanisms are likely to be different, it is hypothesised that schizophrenic patients and individuals with PD who recruited from a forensic population, will perform worse on the CI learning task. Moreover, stronger effects (CI abolition rather than attenuation) are anticipated in these clinical groups compared with normal populations with higher measures of anxiety, impulsivity, or schizotypal personality trials.

Chapter II: Conditioned inhibition (CI) in normal populations (E1-5)

2.1 Introduction

This chapter reported a pilot experiment and 5 CI experiments. The pilot experiment selected 10 neutral and 10 positive pictures from the International Affective Picture System (IAPS) as appetitive USs using in the later CI experiments. For the CI experiments, 188 students at the University of Nottingham took part in the experiments. The CI learning procedures were designed and refined in the 5 CI experiments. The main different features between all the CI experiments are listed in appendix 6. The aim of these experiments was to design and develop a better controlled CI learning procedure than previous studies (e.g. Migo et al., 2006). In order to explore the relationship between CI learning performance and disorder in the future, the experiments also aim to find a robust CI effect in human participants.

2.1.1 The general experimental design for present study

The design can be expressed as CS+/[CI, CS]–, where 'CS' is the conditioned stimulus, 'CI' is the conditioned inhibitor, '+' is a reinforced US (a positive picture) and '–'is non-reinforced US (a neutral picture). All the US stimuli were from the International Affective Picture System (IAPS, selected by pilot study). The CI experiment included 3 basic stages, pre-test stage, training stage and test stage (see table 2.1). The pre-test stage was identical to the test stage. The purpose of the pre-test stage was to examine whether there were any pre-existing biases in responding to the critical test compounds and also the training compounds before the experiment. During the training stage, the simplest design should only include A+ and AP- (P as a putative inhibitor). However, this may lead to participants have learned that compounds were non-reinforced and elements were reinforced. Therefore, AZ+ was presented during this stage, so the AZ compound signalled reinforcement (AZ+), whereas the AP

compound signalled no reinforcement (AP-). In the training stage, it is expected that participants would give a high rating for AZ, which indicated the occurrence of US, and low rating for AP which indicated the occurrence of no US. However, it also could be argued that rating AZ higher than AP does not necessarily mean that P is a conditioned inhibitor, for several reasons. One reason was that participants gave a lower rating score for AP compound, because they could regard AP as a new unique cue stimulus, but do not regard AP compound as A stimulus plus P stimulus. Another reason was that participants might give a lower rating for AP compound, because P was a new stimulus which could be a distractor and draw attention from A.

In order to rule out these alternative explanations, two more training compounds were introduced: one is a control compound BX–, and another is a test excitor compound CY+. C provided an excitatory test stimulus against which the inhibitory effects of P could be evaluated, whereas X was a control stimulus that was presented the same number of times as P, but in the absence of any specific inhibitory training. However, the stimulus with which X was presented was novel so that X, unlike P, did not signal the absence of reinforcement during this training stage, and so should not have acquired any inhibitory properties.

Table 2.1 The general design of a summation test for CI experiment.

	Phase	
Pre-test	**Training**	**Test**
CSs	**CSs and US outcome**	**CSs**
AZ	AZ +	AZ
AP	AP –	AP
BX	BX –	BX
CY	CY +	CY
CP		CP
YP		YP
CX		CX
YX		YX

Note: A, B, P, X C, Z and Y were conditioned stimuli. With respect to US presentations, '+' represents positive pictures and '–' represents neutral IAPS pictures (selected by a pilot study).

The test stage compared the ratings given to the trained compounds that had signalled reinforcement (AZ, CY) and non-reinforcement (AP, BX). It was expected that participants would give a significantly higher rating score for AZ and CY than for AP and BX. If the significant differences were found, then participants learned the main discrimination. The test stage also compared the critical comparison between CP/YP and CX/YX. In these four test compounds, there are equal number of excitors (C or Y) and non-reinforced stimuli (P or X). C and Y were excitatory stimuli, and were predicted to elicit high ratings indicating expectation of reinforcement. P was the putative conditioned inhibitor, whereas X was a control stimulus that had received no inhibitory training, but had otherwise been treated identically to P (i.e. presented in a non-reinforced compound on an equal number of occasions). Thus if P was a conditioned inhibitor it should reduce this high rating to C, whereas the comparison stimulus, X, should not. Therefore, it was expected that there would be significant differences between CP/YP and CX/YX, which means the rating scores for CP/YP should be significantly lower than the rating scores for CX/YX. If these significant differences were found, then P could be viewed as a conditioned inhibitor. The identities of the stimuli used as P and X were counterbalanced across the participants, as were A and B.

2.1.2 The general analysis for CI experiments

During the experiments, participants were asked to guess or predict what kind of picture would follow presentation of the CS pictures (domino blocks or Lego blocks) using a rating scale from 1 (neutral) to 9 (positive), with the rating 5 to reflect uncertainty. For data analysis, the dependent variable was the mean rating given for each particular trial type, which was assessed at each stage of the experiment. Statistical analyses were by a within-subjects analysis of variance (ANOVA), with discrimination (e.g. AZ

or AP v. CY or BX), reinforcement (reinforced or not) and trial block as factors. Significant interactions were further examined by simple main effects analysis using the pooled error term.

2.2 Pilot experiment

2.2.1 Introduction

The International Affective Picture System (IAPS) has been developed to provide a set of normative emotional stimuli (colour photograph pictures) for academic research on emotion and attention (Lang, Bradley & Cuthbert, 2005). The pictures from IAPS have a wide range of semantic categories, which include animals, people (baby and family), mutilation, erotic pictures, plants, violent settings, sports settings and natural world. The rating of IAPS' pictures was conducted in college students in Gainesvile, FL. USA, but the stimuli have been frequently used for experimental investigations of emotion, attention and learning at School of Psychology, the University of Nottingham. It is likely that the rating scores of the pictures in IAPS do not transfer perfectly from the United States of America to the United Kingdom. Indeed researchers in the school observed that participants have different views of these pre-rated pictures based on their race, culture, and experience. The aim of the pilot experiment is to select a set of normative emotional stimuli (divided by three types: negative, neutral and positive) from IAPS. Therefore these pictures could be used as experimental stimuli for the further experiments, and all the experiments which would be conducted in Nottingham, UK.

2.2.2 Methods

2.2.2.1 Participants

An opportunity sample of 28 students and academic staff (13 male, 15 female) from the University of Nottingham volunteered to participate in the

pilot experiment. The mean age was 22.3 years, with a range of 19–43 years. All experimental procedures in the chapter conformed to the requirements of the Ethics Committee at the School of Psychology, The University of Nottingham.

2.2.2.2 Stimuli and materials

All pictures in IAPS have two primary dimensions – affective valence (ranging from pleasant to unpleasant) and arousal (ranging from calm to excite). These pictures have rated from 1 to 9, 1 representing a low rating on each dimension and 9 representing a high rating on each dimension (i.e. 1 as low pleasure, and low arousal). Compared with other categories (e.g. animals, people, plants and natural world), the valence rating scores for erotic pictures shows male and female had different views on these pictures. For examples, the mean valence of the erotic picture no. 4142 was 5.45 (neutral picture), however, the male's rating score was 7.55 (positive picture) and the female rating score was 3.49 (negative picture). The mean valence of the erotic picture no.4210 was 5.72, but the male's rating score was 8.25, and the female rating score was 3.13. That is to say, without considering gender difference, some erotic pictures were neutral; however, for male those were positive, and for female those were negative. In general, the difference between male and female on mean rating scores of the dimensions of valence for erotic pictures were 0.72, but for animals were 0.19, for people were 0.11, for plants were 0.21, and for natural world were 0.03. Considering male and female have significantly different views about erotic pictures, the erotic category was excluded from the pilot experiment.

75 pictures were chosen from IAPS which covered all but one (erotic) of the picture categories and represented 3 types (negative, neutral, and

positive) of picture groups and each group included 25 pictures (see appendix 1). The main criteria for choosing pictures from IAPS were according to the mean and standard deviation of the dimensions of valence ratings (see table 2.2). Appendix 1 shows the slide numbers of these 75 pictures.

Table 2.2 Criteria for choosing pictures from IAPS.

Images	Mean valence (SD; range)	Mean arousal (SD; range)
25 negative	1.85 (0.23; 1.40–2.19)	6.22 (0.68; 4.53–7.29)
25 neutral	5.01 (0.13; 4.85–5.21)	3.59 (1.33; 1.72–6.97)
25 positive	7.75 (0.26; 7.49–8.28)	5.12 (0.86; 3.08–6.73)

The computer program was written in E-studio and used E-prime (Psychology Software Tools Inc., Pittsburgh, US). The experiment was conducted on a personal computer with a standard 17-in. monitor. The 75 pictures were individually shown on the centre of screen, and each picture was approximately 25×18.5cm. The nine rating buttons were shown at the bottom of the screen, and each rating button was approximately 3×3 cm. The gap between each rating button was minimized to avoid missing data, which was caused by participants accidentally clicking in those gaps (figure 2.1 shows screenshot of a rating trial in the pilot experiment).

Figure 2.1 Screenshot showing a rating trial during the pilot experiment. Participants used the rating buttons to indicate how pleasant they thought the picture was.

2.2.2.3 Procedure

Each participant read an information sheet and signed a consent form before the pilot study. All participants were instructed to evaluate emotional pictures by rating of how pleasant they thought the picture was. All participants were also informed that they might be asked to rate some unpleasant pictures. On the consent form (see appendix 2), there was a statement which informed participants they had the right to withdraw at any time during the experiment.

The 75 pictures were randomly individually presented on the computer screen and participants were asked to give a rating of how pleasant they thought the pictures were. The participants received the following instructions on screen:

> "You will see 75 pictures. Please click the mouse on one number button to rate the pictures from number 1 to 9. 1 as negative pictures, 5 as neutral pictures, 9 as positive pictures."

There was no time limit for participants' reaction. After they clicked a rating button, the next picture followed immediately. The procedure was completed in approximately 10 minutes, and all participants had opportunities to ask questions before and after the pilot experiment.

2.2.3 Analysis

The mean and standard deviation of the rating scores were calculated. Thirty pictures were chosen to represent the 3 types of pictures (10 for each type). The criteria for negative pictures, $1 \leq mean < 1.54$, $SD < 1$; neutral pictures, $4 < mean < 6$, $SD < 1$; and positive pictures, $mean \geq 7$,

SD<1.29. Appendix 1 indicates the slide numbers of the 30 pictures chosen from IAPS.

2.3 Experiment 1: CI experiment measured by a summation test

2.3.1 Methods

2.3.1.1 Participants

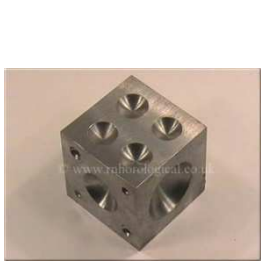
Experiment 1 was conducted on an opportunity sample of 16 students at the University of Nottingham (14 males, and 2 females), with a mean age of 21.31, range from 19 to 28 years. All participants were paid £3 as their inconvenience allowance.

2.3.1.2 Stimuli and materials

2.3.1.2.1 CSs and USs

The CSs presented are shown in figure 2.2 and the USs were 10 positive pictures and 10 neutral pictures chosen from the pilot study. All negative pictures were excluded from the experiments, in case these pictures would upset schizophrenic patients or excite patients with psychopathy at Rampton Hospital in future clinical studies.

The CSs, USs and rating buttons were shown on screen and the size of these images were approximately 14×12cm, 25×18.5cm and 3×3 cm respectively.



I

II

III

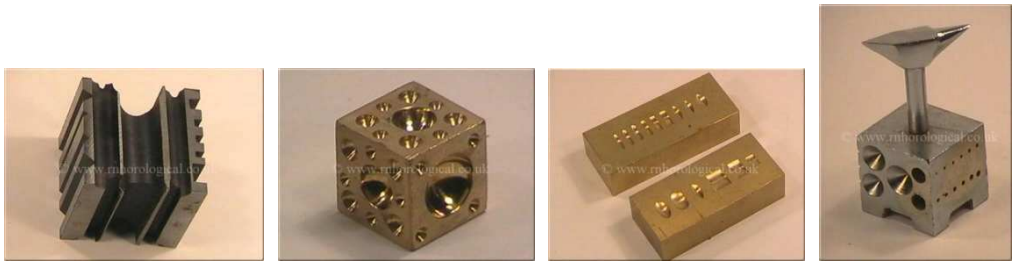


Figure 2.2 The conditioned stimuli pictures in experiment 1 (see table 2.3 for experimental design).

2.3.1.2.2 Questionnaires

Four questionnaires (BIS/BAS, EPQ–RS, O–LIFE short scale, and STB scale) were given to all participants.

Behavioural inhibition system and the behavioural activation system (BIS/BAS) questionnaire consists of a list of 20 items in which participants use a 4-point response scale to express whether the statement is true or false for them (Carver & White, 1994). The questionnaire divides in four sub-scales: BIS, BAS drive, BAS fun seeking, and BAS reward responsiveness. Examples of statements from the sub-scales are "I worry about making mistakes"; "I go out of my way to get things I want"; "I often act on the spur of the moment"; "It would excite me to win a contest" respectively. Gray (1981, 1982) suggested that there are two general motivational systems that underlie behaviour and affect, which are the behavioural inhibition system (BIS) and the behavioural activation system (BAS). According to Gray (Gray 1972, 1977, 1978, 1982, 1990), the BIS measures aversive motives (move away from something unpleasant), which is sensitive to signals of punishment, non-reward, and novelty. Thus, BIS activation leads to behavioural inhibition of movement toward goals, and should be reflected in greater proneness to anxiety. The BAS measures appetitive motives (move toward something desired), and BAS functioning is related to impulsive or antisocial tendencies. The BIS

scale had an alpha coefficient of 0.74; for BAS drive α =0.76; for BAS fun seeking α =0.66, and for BAS reward responsiveness α =0.73 (Carver & White, 1994).

The Eysenck Personality Questionnaire Revised short scale (EPQ–RS) is a 48–item yes/no questionnaire for the age range 16 to 70–years–old (Eysenck, Pearson, Easting & Allsopp, 1985). It is used to assess dimensions of personality, which includes 4 factors, extraversion (E), psychoticism (P), neuroticism (N), and response distortion scale (Lie). There are 12 items for each personality factor, The examples of the items in the factor contains: "Are you a talkative person?"; "Would you like other people to be afraid of you?"; "Does your mood often go up and down?"; "Are all your habits good and desirable ones?". Reliabilities (*a*-coefficients) of E, P, N, and L are between .73 and .90 in both male and female subjects.

The Oxford–Liverpool Inventory of Feelings and Experiences (O-LIFE) short scale is a 43-item yes/no scale, which aims to measure schizotypal levels in non-clinical individuals (Mason et al., 2005). The short scale has four sub-scales: unusual experiences ("Does a passing thought ever seem so real it frightens you?"), cognitive disorganization ("Do you frequently have difficulty in starting to do things?"), introverted anhedonia ("Do you often feel uncomfortable when your friends touch you?"), and impulsive non-conformity ("Do you often overindulge in alcohol or food?"). Psychometric evaluation of the O-LIFE has shown it to have good test-retest reliability (coefficient alpha =0.80), as well as acceptable internal reliability (coefficient alpha =0.70).

The Schizotypal Traits Questionnaires includes schizotypal traits A (STA) and schizotypal traits B (STB) questionnaires (Rawlings, Claridge, & Freeman, 2001). STA has been extensively used in many research contexts for measuring schizotypal personality in a normal population. The purpose of developing the STB scale is to measure borderline personality; for example it measures self–harm, destructive and impulsive behaviours. In the present study, we used O–LIFE short scales for assessing schizotypal levels, and STB for measuring the borderline personality in general population. STB is a yes/no scale and includes 18 items and two sub–scales (hopelessness and impulsiveness). The examples of the questions in the first sub–scale (hopelessness) include "Does life seem entirely hopeless?" and "Do you ever have suicidal thoughts?" In second subscale (impulsiveness) includes "Do you frequently gamble money?" and "Do you often have the urge to hit someone?". The first sub-scale questions had an alpha coefficient of 0.72; the second sub-scale questions had one of 0.66, and the full STB one of 0.80.

2.3.1.3 Design

Table 2.3 shows the details of the design of experiment 1. Participants were equally divided into 4 counterbalanced groups during experiment 1. For half the participants, when the CS stimulus A was picture I, B was picture II; for the other half of the participants, CS stimulus A was picture II, B was picture I. For half of each of these subgroups, when CS stimulus P was picture IV, X was picture V; for the other half P was picture V, and X was picture IV. All groups used picture III as CS stimulus C, picture VI as CS stimulus Y and picture VII as CS stimulus Z.

Table 2.3 The design of experiment 1.

Phase					
Pre-test		**Training**		**Test**	
CSs	No. trials	CSs and US outcome	No. trials	CSs	No. trials
AZ	2	AZ +	8	AZ	2
AP	2	AP –	8	AP	2
BX	2	BX –	8	BX	2
CY	2	CY +	8	CY	2
CP	2			CP	2
YP	2			YP	2
CX	2			CX	2
YX	2			YX	2

Note: The conditioned stimuli pictures were as shown in figure 2.2. A was picture I or II; B was II or I; P was IV or V; X was V or IV; C was III; Y was VI, and Z was VII. With respect to US presentations, '+' represents positive pictures and '–' represents neutral IAPS pictures (selected by pilot study).

2.3.1.4 Procedure

2.3.1.4.1 Before the experiment

Participants were invited to take part in a research study on learning which involved two parts: a computer-based learning task and a set of questionnaires. Before the learning task, each participant read the information sheet and signed a consent form (see appendix 2 and 3). The task instructions were that a cat 'Mogwai' would bring participants either a nice picture or a neutral, boring picture, depending on what kind of Domino blocks she found in her basket. Participants were asked to guess or predict what kind of picture would follow presentation of the blocks using a rating scale from 1 (neutral) to 9 (nice), with rating 5 to reflect uncertainty. Reminder instructions were presented on–screen at each stage of the procedure.

The computer-based learning experiment lasted about 15 minutes and comprised three stages.

2.3.1.4.2 Pre-test stage

During the first stage (pre-test stage), participants were told to guess the valence of a US after a CS compound. Participants should use a mouse to

click a number button, which was shown on the bottom of computer screen (see figure 2.3). The following instructions appeared on the screen:

> "You will see two blocks. According to the two blocks, please guess how likely the cat will give you a nice picture or a neutral picture. You will NOT see any pictures in this phase. Please use mouse to click a number button from 1 to 9. Number 1 as neutral picture, 5 as not sure, 9 as nice picture. Click any button on the mouse to continue."

A screenshot of an example of one of the CS compounds at the pre-test stage is provided in figure 2.3. After participants clicked on a number button, the next CS compound was immediately shown on the screen. There were 8 types of trials: AZ, AP, BX, CY, CP, YP, CX, YX. On the screen, the side of presentation of each element of each compound was counterbalanced (ie, figure 2.3 shows AP compound in which CS picture I was on the left and picture IV was on the right, then another AP compound would be shown in which picture I was on the right and picture IV was on the left). Therefore, each type of trial was shown on the screen twice, so there were 16 trials in total during this stage. The order of CS presentation was randomized by the computer. No USs occurred in the pre-test stage.

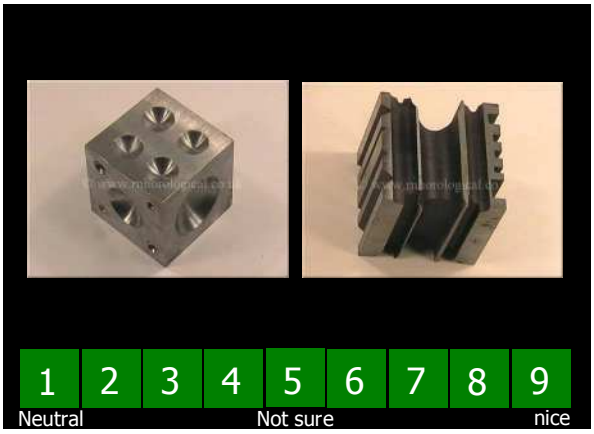


Figure 2.3 Screenshots showing conditioned stimuli presentations with the rating scales used to guess or predict what valence of a US (a nice or a neutral picture) Mogwai (figure 2.4) would bring.

2.3.1.4.3 Training stage

After the pre-test stage, the following instructions appeared on the screen.

> "Thank you for your guessing. Now it is time to predict what type of picture Mogwai will bring. Again you will be shown two blocks. According to the two blocks, please predict what type of picture will follow. Depending on the blocks she finds, the cat will give you a nice picture or a neutral picture. Please use mouse to click a number from 1 to 9. Number 1 as neutral picture, 5 as not sure, 9 as nice picture. Click any button on the mouse to continue."

The second stage (training stage) comprised 4 trial blocks in total. Each trial block contained 4 types of trials (AZ+, AP–, BX– and CY+ compound), and each trial was shown on the screen twice (the position of elements on the screen was counterbalanced as in the pre-test stage). After participants clicked a number button to predict the valence of the US to follow, a US, randomly selected from the pool of positive or neutral USs as appropriate, was shown on the screen for 1s, followed by a 1s gap before the next trial started. During the 1 sec. gap, there was a picture of the cat ("Mogwai", around 6×6 cm) in the middle of a screen with a white background (see figure 2.4). It was anticipated that participants would learn to predict what type of US would occur according to the CSs were presented. There were 8 presentations of the reinforced training compounds (AZ and CY) and 8 of the non-reinforced training compounds (AP and BX), analysed in four blocks of training trials.

Figure 2.4 The picture of "Mogwai" – the cat as presented prior to the USs in the training stages.

2.3.1.4.4 Test stage

After the training stage, the following instructions showed on the screen:

> "Now it is your turn to make judgments about the blocks. Again you will be shown two blocks, and you will be asked to judge what type of picture the cat would bring if she found them in her basket. You will not see any pictures in this phase. Please use mouse to click a number from 1 to 9. Number 1 as neutral picture, 5 as not sure, 9 as nice picture. Click any button on the mouse to continue."

The test stage was exactly the same as the pre-test stage. According to the CS compound on the screen, participants used their previous knowledge to predict the US. No US was presented in the test stage.

2.3.2 Results

2.3.2.1 Pre-test stage

Figure 2.5 shows rating scores during the pre-test stage. The rating scores for all the compounds were around 4 to 5. Comparing the two critical

compounds CP/YP and CX/YX, the rating scores of CP/YP were higher than the rating scores of CX/YX, which may suggest some pre-existing biases occurred before the training stage.

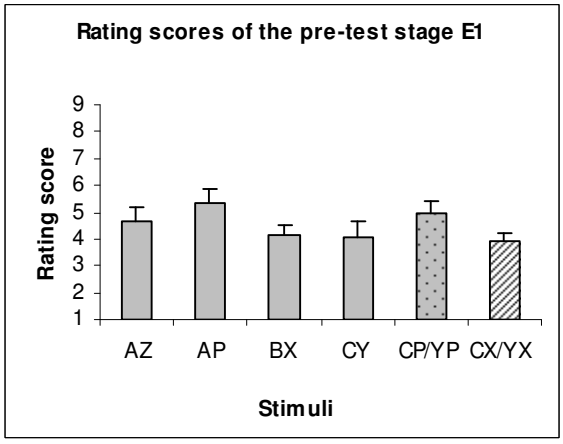


Figure 2.5 Rating scores for AZ, AP, BX, CY, CP/YP and CX/YX at the pre-test stage during experiment 1. A rating of 9 reflected expectation of a nice picture, 1 of a neutral picture and 5 indicated uncertainty.

The rating scores of the training compounds (AZ, AP CY and BX) were analyzed using a two–way repeated measures analysis of variance with discrimination and reinforcement as factors. The analysis aimed to test the differences between the rating scores of the stimulus compounds to be discriminated in the training stage (AZ+ v. AP– and CY+ v. BX–); the factor reinforcement referred to whether the compound would be reinforced or non-reinforced in the subsequent training stage, and the factor discrimination to the AZ/AP or CY/BX compound pairs. The ANOVA revealed no main effect of either reinforcement $F(1,15)=1.22$, $p=0.29$, or interaction between these two factors $F<1$. However, there was a significant effect of discrimination (AZ, AP v. CY, BX), $F(1,15)=5.47$, $p=0.03$ showing some pre-existing biases before the training stage. It can be seen from figure 2.5, the ratings of AZ and AP were higher than those of BX and CY. Although this was unexpected, it should not have affected subsequent discrimination performance, as there was no biases between the to-be-discriminated stimuli – the main effect of reinforcement was not significant, and did not interact with any other factor.

Comparing the two critical rating scores CP/YP and CX/YX, the ANOVA revealed a significant difference between the two scores $F(1,15)=3.03$, $p=0.008$. The analysis during the pre-test stage suggested that there were pre-existing biases before the training stage. During the pre-test stage, the rating of CP/YP was significantly higher than the rating of CX/YX which would work against establishing P as an inhibitor, because I expected CP/YP would be significantly lower than CX/YX after training. Therefore, these pre-existing biases would not make P look like a conditioned inhibitor when it wasn't one. However, the pre-existing biases might make the experiment difficult to demonstrate CI effects.

2.3.2.2 Training stage

During the training stage, ratings of AZ steadily increased, while those to AP fell slightly. This suggests that the participants had learnt the critical discrimination. A rating difference also developed between the control compounds, the reinforced CY and non-reinforced BX, although this was less pronounced (see figure 2.6). These differences were maintained in the test stage.

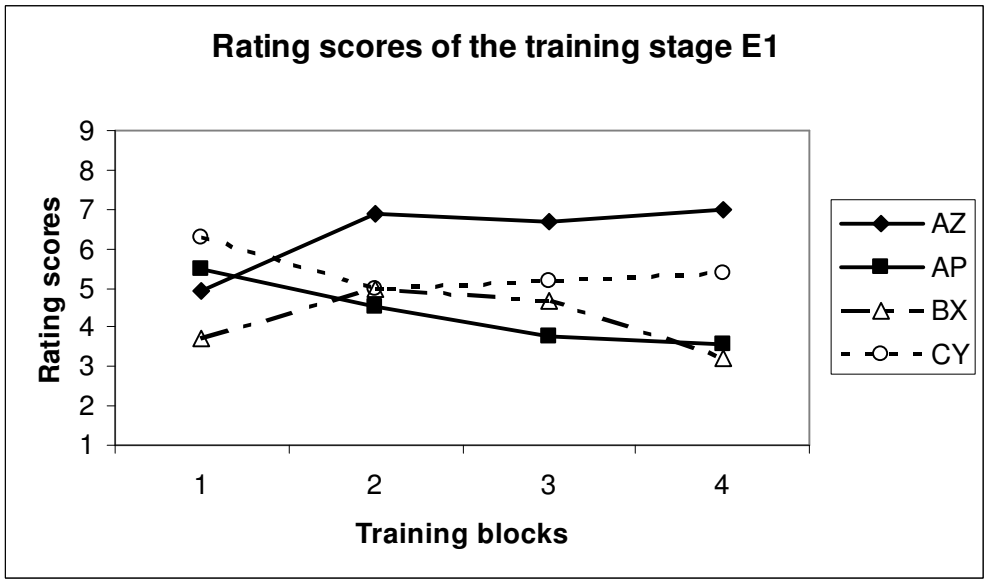


Figure 2.6 Rating scores for AZ+, AP–, BX– and CY+ at the training stage during experiment 1. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

During the training stage, the significance of these differences was evaluated by performing an ANOVA with discrimination (AZ or AP v. CY or BX), reinforcement and training block (1–4) as factors. This revealed no main effect of either discrimination $F(1,15)=1.70$, $p=0.21$, or training block, $F<1$. However, the main effect of reinforcement was significant, $F(1,15)=11.07$, $p=0.005$. The interaction between reinforcement and training block was significant $F(3,45)=3.55$, $p=0.022$.

Furthermore, there was a three-way significant interaction $F(3,45)=10.62$, $p<0.001$. To further analyse the three-way interaction, ANOVAs with reinforcement and training block analysed BX v. CY and AZ v. AP discriminations separately. For BX v. CY discrimination type, the ANOVA revealed no main effect of either reinforcement $F(1,15)=3.62$, $p=0.08$, or training block, $F<1$. However, the interaction between two factors was significant, $F(3,45)=5.17$, $p=0.004$. For AZ v. AP discrimination type, the ANOVA revealed no main effect of the training block, $F<1$. However, reinforcement was significant, $F(1,15)=12.53$, $p=0.003$, the interaction between two factors was significant, $F(3,45)=8.21$, $p<0.001$. These analyses suggested the discriminations were learned effectively.

2.3.2.3 Test stage

Figure 2.7 shows the rating scores during the test stage. It can be seen that the ratings of reinforced trials AZ and CY were higher than the ratings of non-reinforced trials AP and BX at this stage. An analysis of variance with discrimination and reinforcement as factors, revealed no main effect of either discrimination or interaction between of these two factors. However, there was a significant effect of reinforcement, $F(1,15)=10.94$, $p=0.005$, suggesting participants gave significantly different ratings to reinforced and non-reinforced stimuli.

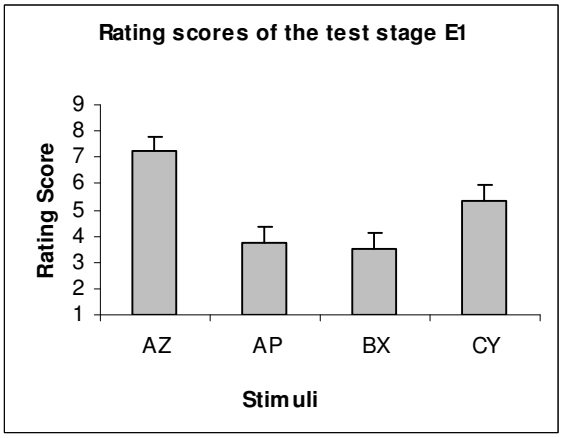


Figure 2.7 Rating scores for AZ+, AP–, BX– and CY+ at the test stage during experiment 1. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

Figure 2.8 shows the rating scores of the two critical stimuli CP and CX at the pre-test and the test stages. It is clear that, while during the pre-test stage ratings of CP/YP were higher than these of CX/YX, during the test stage CP/YP were lower than CX/YX. An ANOVA with stage (pre-test and test) and stimulus (CP/YP v. CX/YX) as factors, revealed no main effect of either stage, or stimulus, $Fs<1$. However, the interaction between these two factors was significant $F(1,15)=8.50$, $p=0.01$. To further analyse this interaction, the simple main effects revealed that nothing was significant, the largest $F(1,15)=3.21$, $p=0.09$. Clearly, there was no significant evidence that P had become a conditioned inhibitor relative to strong control of differential inhibition in experiment 1, but numerically the difference between CP/YP and CX/YX was in the correct direction.

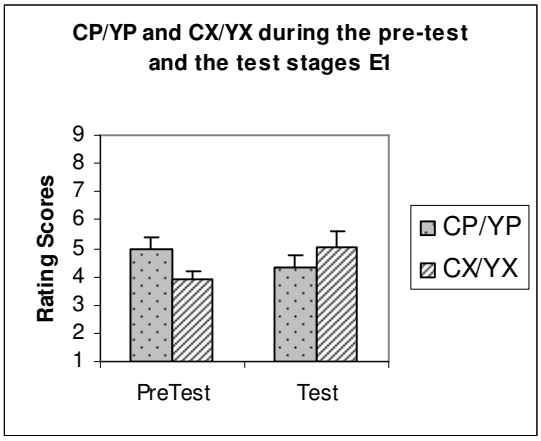


Figure 2.8 Rating scores for the key comparison stimuli CP/YP and CX/YX at the pre-test and the test stages during experiment 1. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty. The pre-test ratings showed some pre-existing biases for the stimuli: CP/YP rated higher than CX/YX. The test ratings confirmed week effects of conditioned inhibition, which was shown as higher ratings to CX/YX than CP/YP.

2.3.3 Discussion

The experiment 1 tried to provide a demonstration of conditioned inhibition using summation test in humans. Compared with the ratings before and after training, the results showed CP/YP was lower than CX/YX; however, this difference was not significant. The results suggested a weak CI effect, although the experiment did not successfully find evidence that P was a conditioned inhibitor. There are several reasons that may explain these results.

First, at the pre-test stage, in the responses to the test compounds the rating scores of CP and YP were significantly higher than the rating scores of CX and YX. The reasons for the pre-existing biases were unknown (the pictures of CSs, P and X were counterbalanced), and biases would not affect the study's aim – establish P as a conditioned inhibitor (it is expected the ratings of CP & YP should significantly lower than the ratings of CX & YX). It is possible that the pre-existing biases may lead to difficulty in demonstrating P as CI in the experiment, because the rating score of these critical compounds were in a different direction. Despite starting off the wrong way, the ratings of CP/YP v. CX/YX were numerically in the right

direction at the test stage, so it was a promising start for developing a CI summation test procedures in humans.

Second, another possible reason why the experiment did not successfully find the evidence that the putative inhibitor (P) became a conditioned inhibitor was because the test excitors C and Y were not strong excitors in experiment 1. At the pre-test stage, the rating of CY was quite low at around 4. During the training stage, the score of CY was around 5, suggesting C and Y had not become strong excitors during the experimental procedures. At the test stage, the score of CY was just above 5, which again showed that test excitors C and Y were not strong enough during experiment 1. According to Rescorla–Wagner Model (Rescorla & Wagner, 1972; Wagner & Rescorla, 1972), an inhibitor should suppress excitation during the experiment, and if the test excitor had no excitation, then the inhibition could be hard to measure.

Besides, these results were unable to conclude whether A was a strong excitor or not. It is because AZ+ and AP– discrimination was rather different from the normal A+ and AB–, where B must acquire inhibition (B signals the absence of the US). According to strict Rescorla Wagner rules (1972), the current experimental design (AZ+) was different from the case in which stimulus A was reinforced when presented alone (A+). In a CI experiment, if only presented A+ trial, A always predicted the US and was never presented without it, so A was a strong excitor. However, if the experiment's training stage included AZ+ and AP-, it would be expected that Z could become an excitor, P as an inhibitor, and A as a neutral stimulus. If A does not become a strong excitor, then it will take longer to produce an inhibitor with the AZ+ and AP- version than the A+ and AB- version. However, if an experiment uses the A+ and AB– version, the

excitor and non-reinforced stimuli were not balanced, and B also could be viewed as a distracter or an inhibitor. Therefore, the next experiment should still use the AZ+ and AP- version, but clearly it may need to increase the strength of the excitor.

2.4 Experiment 2: CI experiment measured by summation test (coloured pictures were used as CSs)

2.4.1 Introduction

A number of changes were made during experiment 2, which included experimental stimuli, design, and procedures.

2.4.1.1 Experimental stimuli

During the experiment 2, all CSs pictures were changed to coloured Lego blocks (see figure 2.9). Lego blocks are colourful with more different shapes, which may help participants remember the CSs. Besides, Lego blocks are easy to obtain, so the experiment would be easy to replicate in the future. One US picture was excluded because it confused participants. The neutral picture no. 7010 (See figure 2.10) in IAPS was replaced with no. 2512. The reason for replacing picture no. 7010 was because as a basket it should be regarded as a neutral picture in the experiment. However, on the experimental information sheet, "basket" was used as the cat's home, so some participants were confused whether the basket picture should be rated as a neutral or as a positive picture during the previous experiment.

2.4.1.2 Experimental design

The results for experiment 1 revealed that the training and test excitors were not strong enough to establish and detect CI effects. In experiment 2, the design was revised and improved. First, a pre-training stage was added

before the training stage, which included 4 types of training trials: A+, C+, U– and V–. According to the Rescorla–Wagner Model (Rescorla & Wagner, 1972; Wagner & Rescorla, 1972), a strong training excitor (A in current experiment) would produce a stronger inhibitor, and a strong test excitor (C in current experiment) would be able to show inhibition at test. If the training and test excitors had no excitation, then the inhibition could be hard to be established with the training excitor and to be measured with the test excitor. It is because during inhibitory training, the inhibitor cancels the expectation produced by the excitor (A) – so the stronger expectation, the stronger the inhibitor (P). Furthermore, two new stimuli U– and V– were added during the pre-training stage, so both reinforced and non-reinforced trials were included which ensured participants paid attention during this stage.

Another change of experimental design was that two compounds (YP and YX) were deleted during the pre-test and test stages. According to the Rescorla–Wagner Theory (Rescorla & Wagner, 1972; Wagner & Rescorla, 1972), if a subject is first trained with C+, then CY+, C will block conditioning to Y. Because of the experimental procedure, the pre-training stage (A+ and C+) was followed by a training stage (AZ+ and CY+), then A and C could block conditioning to Z and Y, so A and C could retain their strength more effectively. The purpose of this change attempted to ensure that the A became a stronger excitor, and C became a stronger test excitor in the experiment. If A is strong, then P can become a strong inhibitor; if C is strong then it is easier to detect that inhibition.

The pre-training stage also provided a measure of participants' excitatory associative learning; therefore the score of C+ and V– would be compared. It is clear that if participants cannot learn the excitatory associative

learning task, they will have difficulties learning the conditioned inhibitory learning task. For this reason, there was an a priori exclusion criterion based on the pre-training performance: the participants who failed this stage would be excluded from the CI learning measure. That is to say, participants who failed to learn the simple discrimination between C and V (i.e. rating scores (C–V)=<0) were excluded from the CI analysis (the C/V discrimination was fully counterbalanced for stimulus identity for this purpose).

2.4.1.3 Experimental procedures

During the experiment 1, some of participants were confused by the learning task although all the instructions were clearly shown on the computer screen. For example, some participants thought the rating score from 1 to 9 was the measurement of the valence of the CSs (blocks), but not the valence of the following USs. Other participants were confused about the types of USs. Especially if a US picture was a person without a happy facial expression, then the participants were not sure whether this picture should be regarded as a neutral picture or a nice picture. Consequently before experiment 2, the experimental procedures were explained in more detail to the participants.

2.4.2 Methods

All details not mentioned were identical to those of experiment 1.

2.4.2.1 Participants

Experiment 2 was conducted on an opportunity sample of 40 students at the University of Nottingham (19 males, and 21 females), with a mean age of 21.73, range from 18 to 39 years. There were three participants excluded from the experiment because of failing the pre-training stage.

2.4.2.2 Stimuli

Figure 2.9 shows CS pictures for experiment 2. Figure 2.10 shows one US picture that excluded from experiment 2 (appendix 1 listed the details of USs' ID from IAPS)

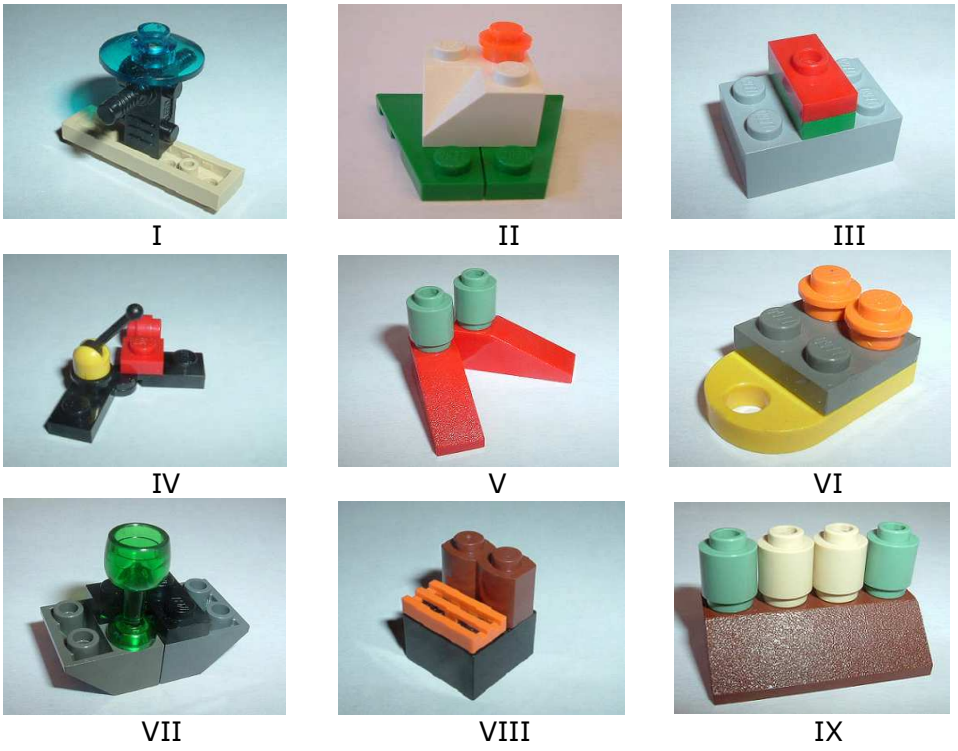


Figure 2.9 The conditioned stimuli pictures for experiment 2 (see table 2.4 for experimental design).

Figure 2.10 Picture No. 7010 in IAPS. The picture was excluded from experimental CS due to cause some confusion to participants.

2.4.2.3 Design

Table 2.4 shows the experimental design, compared with experiment 1, the number of CP and CX trials increased from 2 to 4 at the test stage in

experiment 2. The rating of CP and CX was important measure of CI effects, so increasing the number of trials would collect a better sample of responding to these compounds. If the results showed the score of CP to be significantly lower than the score of CX at the test stage, this would suggest that P was a conditioned inhibitor.

Table 2.4 The design of experiment 2.

Phase							
Pre-test		**Pre-training**		**Training**		**Test**	
CSs	No. trials	CS & US outcome	No. trials	CSs & US outcome	No. trials	CSs	No. trials
A	2	A +	12	AZ +	8	A	2
C	2	U –	12	AP –	8	C	2
AZ	2	V –	12	BX –	8	AZ	2
AP	2	C +	12	CY +	8	AP	2
BX	2					BX	2
CY	2					CY	2
CP	2					CP	4
CX	2					CX	4

Note: The conditioned stimuli pictures were as shown in figure 2.9. A was picture I or II; B was II or I; P was IV or V; X was V or IV; C was III; Z was VII; V was IX; and U was VIII. With respect to US presentations, '+' represents positive pictures and '–' represents neutral IAPS pictures (selected by pilot study).

The experimental counterbalancing was identical to experiment 1 except for the addition of C and V; for half of each of the 4 counterbalanced subgroups C was picture II, V was picture IX and half of each of these subgroups was opposite (see table 2.5).

Table 2.5 The counterbalanced groups of experiment 2, 3, 4, 5a and 5b.

Counterbalanced Groups	**Conditioned stimuli and name of Lego pictures (see figure 2.9)**								
	A	**B**	**C**	**P**	**X**	**Y**	**Z**	**U**	**V**
1	I	II	III	IV	V	VI	VII	VIII	IX
2	I	II	III	V	IV	VI	VII	VIII	IX
3	II	I	III	IV	V	VI	VII	VIII	IX
4	II	I	III	V	IV	VI	VII	VIII	IX
5	I	II	IX	IV	V	VI	VII	VIII	III
6	I	II	IX	V	IV	VI	VII	VIII	III
7	II	I	IX	IV	V	VI	VII	VIII	III
8	II	I	IX	V	IV	VI	VII	VIII	III

Note: The pictures of CSs were counterbalanced in 8 groups. Subgroups 1 to 4 were identical to experiment 1. Subgroups 5 to 8 counterbalanced additionally C and V. The participants were equally divided into 8 counterbalanced groups.

2.4.2.4 Procedure

2.4.2.4.1 Before the experiment

Before the experiment, participants were shown some example pictures of CSs and USs to explain the computer–based task. All these sample pictures were individually colour printed on a 4.5×6 cm card (see figure 2.11, 2.12 and 2.13), but not subsequently used as stimuli during the experiment. Participants were told that the whole computer experimental session would last about 15 minutes and comprise three stages. At the same time, they were shown an example of a rating trial (figure 2.14) and were told that during the experiment they would click a number button to guess or predict the valence of a US (a positive or a neutral picture) according to the different Lego blocks that occurred.

Figure 2.11 Example CS pictures which showed participants before the experiment.

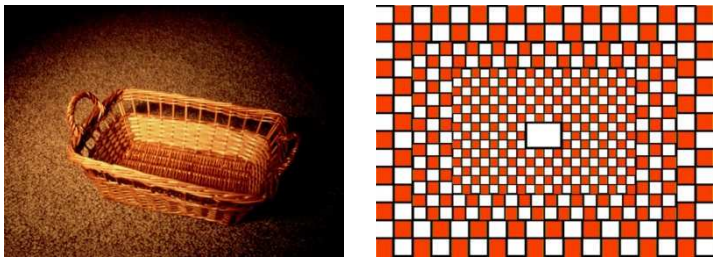


Figure 2.12 Example US neutral pictures which showed participants before the experiment.

Figure 2.13 Example US positive pictures which showed participants before the experiment.

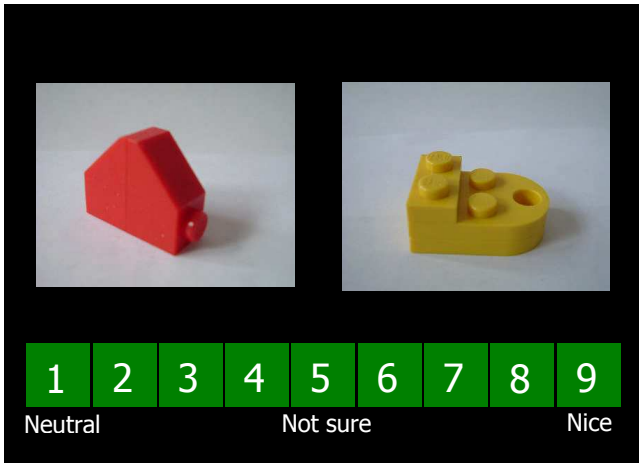


Figure 2.14 An example of a rating trial which was shown to participants before the experiment. The screenshots showing conditioned stimuli presentations with the rating scales used to guess or predict what valence of unconditioned stimuli (USs: nice or neutral pictures) Mogwai would bring.

The three stages of the computer experimental session occurred as follows:

2.4.2.4.2 Pre-test stage

There were a total of 16 presentations, two of each stimulus or stimulus combination presented in the pre-test stage (these being A, C, AZ, AP, BX, CY, CP and CX).

2.4.2.4.3 Pre-training and training stages

After the pre-test stage, pre-training and training stages followed. Compared with experiment 1, the instructions were slightly changed in that the phrase "two blocks" was changed to "ONE or TWO Lego blocks".

The pre-training stage comprised 6 pre-training blocks in total. Each block contained 4 types of trials (A+, U–, V– and C+), and each stimulus was shown on the screen twice (the position of stimulus on the screen was counterbalanced as in the pre-test stage). After participants clicked a number button to predict the valence of the US to follow, a US, randomly selected from the pool of positive or neutral USs as appropriate, was shown on the screen for 1s, followed by a 1s gap before the next trial started. The order of CSs and USs presentations was randomised by computer. After the pre-training stage, the training stage followed directly, this stage was same as in the experiment 1.

2.4.2.4.4 Test stage

The instructions of the test stage were identical to experiment 1 except for the fact that the phrase "blocks" was changed to "Lego blocks". There was a total of 20 presentations, two of each stimulus or stimulus combination presented (A, C, AZ, AP, BX, and CY), except for CP and CX, which were presented 4 times during this stage.

2.4.3 Results

2.4.3.1 Pre-test stage

Figure 2.15 shows the rating scores during the pre-test stage. Comparing the two critical compounds CP and CX, the rating scores of CP were lower than the rating scores of CX, which may suggest some pre-existing biases occurred before the training.

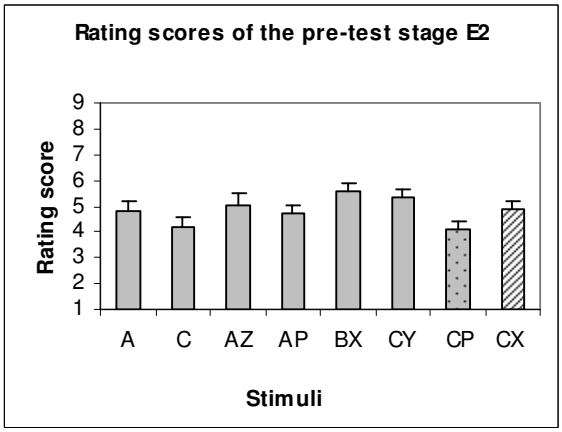


Figure 2.15 Rating scores for A, C, AZ, AP, BX, CY, CP and CX at the pre-test stage during experiment 2. A rating of 9 reflected expectation of a nice picture, 1 of a neutral picture and 5 indicated uncertainty.

An ANOVA with discrimination (AZ v AP and CY v BX) and reinforcement as factors, revealed no significant effects or interactions for training compounds, the largest $F(1,39)=1.51$, $p=0.23$. Comparing the two critical rating scores CP and CX, the ANOVA revealed no significant difference, $F(1,39)=1.94$, $p=0.06$. However this difference was close to statistical significance and drew our attention to the fact that a pre-existing bias for CSs may exist during this stage: the rating scores of CP were lower than those of CX before the training stages. The exact reason for the difference in ratings between CP and CX was not clear. The CS stimuli of C, P and X (pictures III, IX, IV and V) were counterbalanced and the order of presenting CP and CX was randomly selected by the computer during the experiment. However, after we compared CS pictures carefully, we noted that pictures III, IV and V had some portion of red (see figure 2.9). It has been suggested that different cultures have different strong views on red (Gage, 1999). The stimuli containing red could occasionally be very extreme, this might produce a bias during this pre-test stage despite the fact that identities of CP and CX were counterbalanced.

2.4.3.2 Pre- training stage

During the pre-training stage, the ratings of A and C steadily increased, while those to U and V stimuli fell gradually. This suggests that the participants had learned the critical discrimination (see figure 2.16).

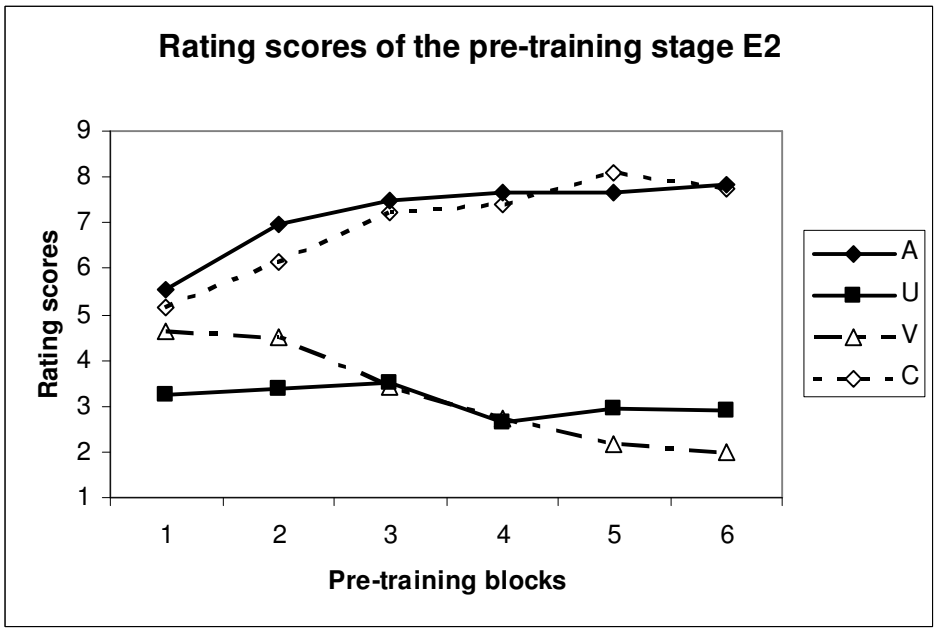


Figure 2.16 Rating scores for A+, U–, V– and C+ at the pre-training stage during experiment 2. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

During the pre-training stage, the significances of the difference were evaluated by performing an analysis of variance with discrimination (A or U v. C or V), reinforcement and pre-training block (1–6) as factors. This revealed no main effect of discrimination F <1; however, the main effects of pre-training block and reinforcement were significant $F(5,195)=4.22$, $p<0.001$; $F(1, 39)=127.60$, $p<0.001$ respectively. The interaction between these two factors was also significant $F(5,195)=25.73$, $p<0.001$, suggesting the difference between reinforced and non-reinforced trials developed over pre-training.

There was also significant effect of the three–way interaction $F(5,195)=5.54$, $p<0.001$. To further analyze the three-way interaction, ANOVAs with reinforcement and training block analysed A v. U and C v. V

discriminations separately. For A v. U discrimination type, the ANOVA revealed main effect of reinforcement $F(1,39)=86.72$, $p<0.001$, and training block, $F(5,195)=4.11$, $p=0.001$. Furthermore, the interaction between two factors was significant, $F(5,195)=7.17$, $p<0.001$. For C v. V discrimination type, the ANOVA revealed no main effect of training block, $F(1,39)=1.25$, $p=0.29$. However, reinforcement was significant, $F(1,39)=103.64$, $p<0.001$, the interaction between two factors was significant, $F(5,195)=25.08$, $p<0.001$. These analyses suggested that participants learnt both A v. U and C v. V discrimination types. No other two–way interactions were significant, the largest $F(5,195)=1.45$, $p=0.21$.

2.4.3.3 Training stage

During the training stage, the ratings of AZ steadily increased, while those to AP fell gradually. This suggests that participants had learned the critical discrimination. A discrimination also developed between control compounds, CY and BX (see figure 2.17). These differences were maintained in the test stage.

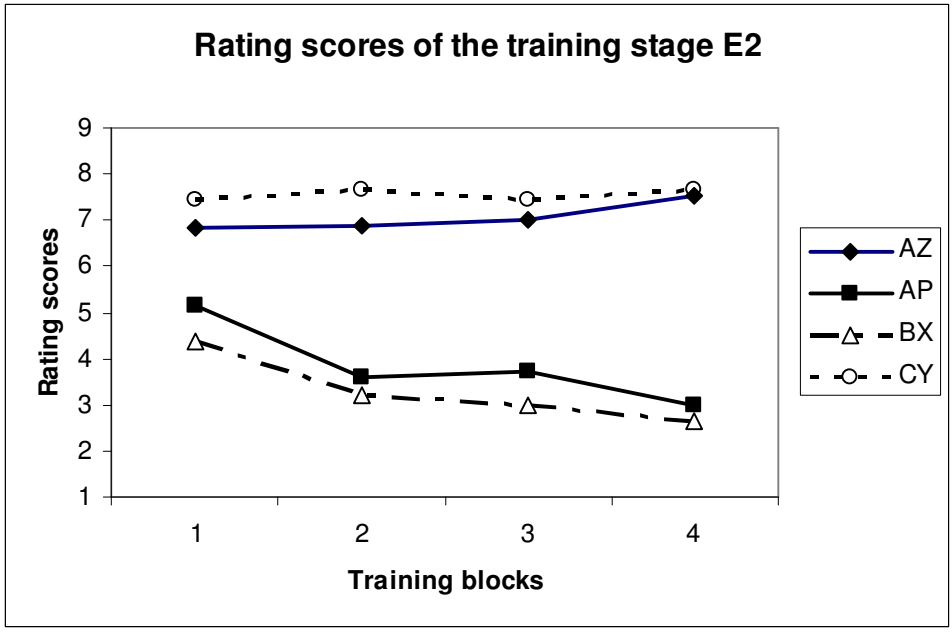


Figure 2.17 Rating scores for AZ+, AP–, BX– and CY+ at the training stage during experiment 2. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

During the training stage, ANOVA with discrimination [(AZ or AP) versus (CY or BX)], reinforcement and training block (1–4) as factors, revealed no main effect of discrimination $F<1$; however, the main effects of training block and reinforcement were significant $F(3,117)=8.98$, $p<0.001$; $F(1,39)=75.94$, $p<0.001$ respectively. The interaction between these two factors was also significant $F(3,117)=12.99$, $p<0.001$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. To further analyze the interaction between reinforcement and training block, we performed simple main effects analysis which revealed that there was an effect of blocks on non-reinforced trials $F(3,117)=27.06$, $p<0.001$, but not on reinforced trials $F(3,117)=1.65$, $p=0.18$. The simple main effects also found that the differences between reinforced and non-reinforced trials were significant on all training trials, the smallest $F(1,39)=7.64$, $p=0.009$.

The interaction between the discrimination and reinforcement factors was also significant $F(1,39)=6.10$, $p=0.02$; it can be seen from figure 2.17, the discrimination between AZ and AP was not as large as the discrimination between BX and CY. However, the simple main effects revealed no main effect of AZ v. CY, $F(1,39)=1.58$, $p=0.22$; or AP v. BX, $F(1,39)=2.11$, $p=0.15$, but that the differences between reinforced and non-reinforced trials were significant on both discrimination types, $F(1,39)=28.08$, $p<0.001$; $F(1,39)=49.35$, $p<0.001$, suggesting both discriminations were learnt effectively during the training stage.

No other two–way and three–way interactions were significant, $Fs<1$.

2.4.3.4 Test stage

Figure 2.18 shows the rating scores during the test stage. The ratings of A and C remained high, and the AZ v. AP and BX v. CY discriminations were maintained. The latter observation was confirmed by the results of an ANOVA with discrimination (AZ or AP v. CY or BX) and reinforcement as factors, which revealed no main effect of discrimination $F<1$, but a significant effect of reinforcement $F(1,39)=63.38$, $p<0.001$. The interaction between discrimination and reinforcement was significant $F(1,39)=8.46$, $p=0.006$. The simple main effects revealed that no difference between AZ and CY, $F<1$; or between AP and BX, $F(1,39)=2.68$, $p=0.11$. However, the simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant on both discrimination types, $F(1,39)=21.48$, $p<0.001$; $F(1,39)=43.88$, $p<0.001$, suggesting both reinforced and non-reinforced trials were learnt effectively and maintained in the test stage.

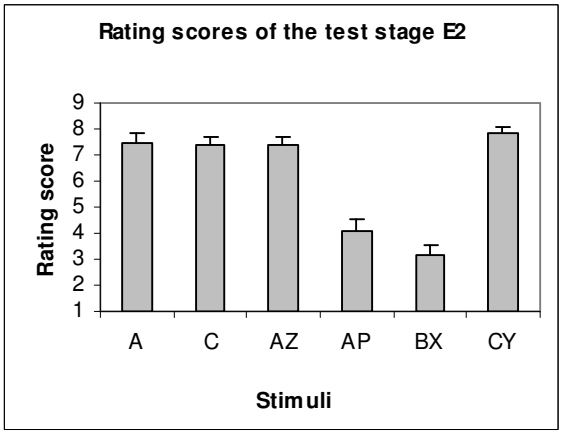


Figure 2.18 Rating scores for A+, C+, AZ+, AP–, BX– and CY+ at the test stage during experiment 2. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

Comparing the two critical compounds CP and CX before and after training, it can be seen from figure 2.19 that these two rating scores during the two stages were quite similar. An analysis of variance performed with stage (pre-test and test), and stimulus (CP v. CX) as factors, revealed no main effect of stage $F<1$, but a significant effect of stimulus $F(1,39)=7.38$,

p=0.01. Furthermore, there was no significant interaction of these factors, F<1. The results suggested there was no evidence that P had become a conditioned inhibitor in experiment 2, even though the ratings of CP were lower than the ratings of CX at test stage. These ratings were in the same direction even before the training, and in that case it may suggest some pre-existing biases during the experiment.

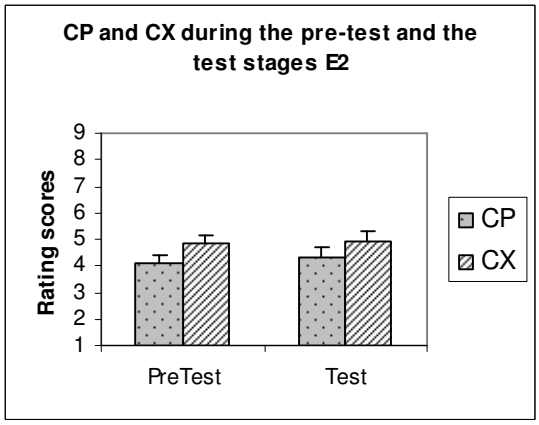


Figure 2.19 Rating scores for the key comparison stimuli CP and CX at the pre-test and the test stages during experiment 2. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty. The pre-test ratings showed some pre-existing biases for the stimuli: CP rated lower than CX, which was hard to confirm the CI effects after the trading stages, although CX rated lower than CP at the test stage.

2.4.4 Discussion

Experiment 2 had a better controlled experimental procedure and design than experiment 1. During the experiment, no participants misunderstood the learning task, which involved guessing and predicting the valence of a US according to previously presented CSs. During the training, the pre-training stage not only measured excitatory associative learning performance, but also strengthened excitors A and C. If A was a strong excitor, then P could become a strong inhibitor; if C was a strong excitor, then it was easier to detect that inhibition. The results also revealed high ratings of all reinforced trials – A, C, AZ, and CY during the training stages and these ratings was maintained in the test stage.

Despite some promising results being found, the experiment encountered a new problem – pre-existing biases. The data suggested participants may have colour biases before the training. The next experiment aimed to solve this problem.

2.5 Experiment 3: CI experiment measured by summation test (black and white pictures were used as CSs)

2.5.1 Introduction

It was noticed that there were pre-existing biases, despite the fact that all pictures of CS were counterbalanced. After inspecting the data carefully, we hypothesised that some participants may have had a strong reaction to red colour (picture V and III), and this might have created biases in the pre-test ratings. To solve this problem all CS pictures were changed into black and white pictures in experiment 3.

2.5.2 Methods

All details not mentioned were identical to those of experiment 2.

2.5.2.1 Participants

Experiment 3 was conducted on an opportunity sample of 16 students at the University of Nottingham (9 males, and 7 females), with a mean age of 21.56, range from 18 to 28 years. There were three participants excluded from the experiment because of failing the pre-training stage.

2.5.2.2 Stimuli and materials

CS Lego block pictures in experiment 3 were changed from coloured pictures to black and white pictures (see figure 2.20).

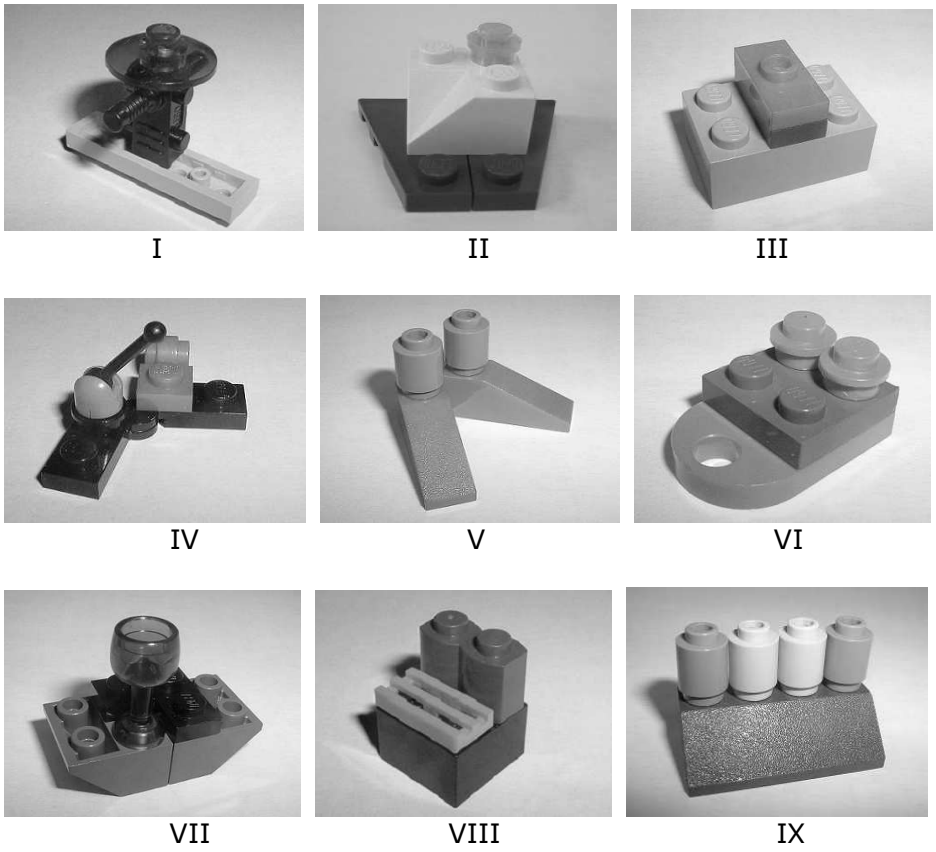


Figure 2.20 The conditioned stimuli pictures for experiment 3 (see table 2.4 for experimental design).

2.5.3 Results

2.5.3.1 Pre-test stage

Figure 2.21 shows the rating scores during the pre-test stage. It can be seen that the rating scores of CP and CX during this stage were very similar, which may suggest the problem of the pre-existing biases was solved when using the black and white CS pictures. An ANOVA with discrimination (AZ or AP v. CY or BX) and reinforcement as factors revealed no significant effects or interactions, the largest $F(1,15)=2.32$, $p=0.15$. Most importantly, there was no significant difference in responding to the test compounds (CP v. CX), $F<1$. The analysis during the pre-test stage suggested that our attempt to eliminate the pre-existing bias was successful – no pre-existing biases in responding to the stimuli.

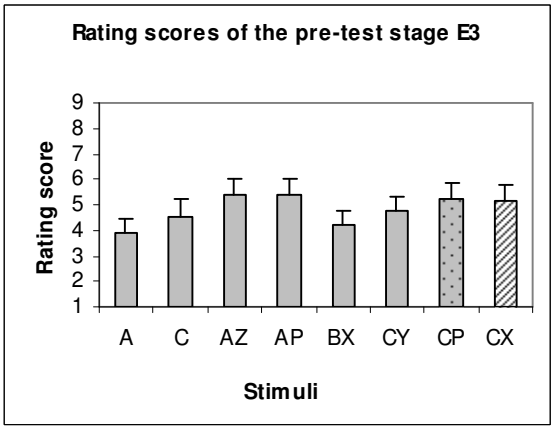


Figure 2.21 Rating scores for A, C, AZ, AP, BX, CY, CP and CX at the pre-test stage during experiment 3. A rating of 9 reflected expectation of a nice picture, 1 of a neutral picture and 5 indicated uncertainty.

2.5.3.2 Pre- training stage

During the pre-training stage, the ratings of A and C steadily increased, while those to U and V fell gradually (see figure 2.22). Participants appeared again to learn the discrimination in this phase, an ANOVA with discrimination (A or U v. C or V), reinforcement and pre-training block (1–6) as factors, revealed no main effect of either pre-training block $F(5,75)=1.84$, $p=0.12$; or discrimination $F(5,75)=1.76$, $p=0.20$. However, the main effect of reinforcement was significant $F(1,15)=35.53$, $p<0.001$. The interaction between pre-training block and reinforcement was also significant $F(5,75)=7.60$, $p<0.001$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. The simple main effects revealed that there was an effect of block on both reinforced and non-reinforced trials, $F(5,75)=10.20$, $p<0.001$; $F(5,75)=6.79$, $p<0.001$ respectively. The simple main effects also found that the differences between reinforced and non-reinforced trials were significant from third to sixth pre-training trials, the smallest $F(1,15)=7.24$, but not on first and second pre-training blocks, the largest $F(1,15)=2.87$, $p=0.11$. It is clear that participants learnt the Pavlovian discriminations.

No other two–way and three–way interactions were significant, the largest $F(5,75)=1.29$, $p=0.28$.

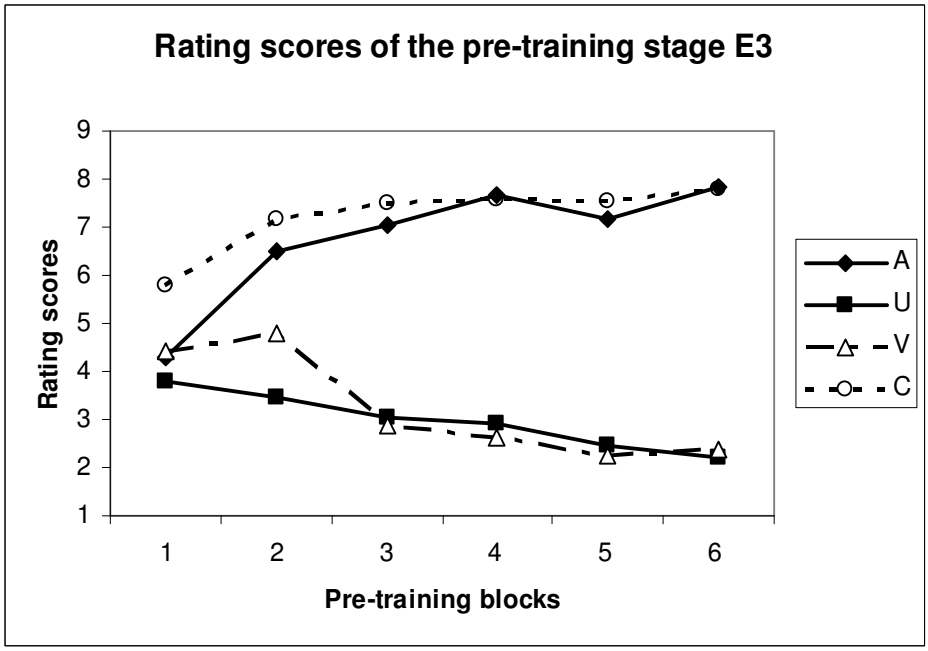


Figure 2.22 Rating scores for A+, U–, V– and C+ at the pre-training stage during experiment 3. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

2.5.3.3 Training stage

During the training stage, participants again learned the discrimination between CY and BX. At the same time, the ratings of AZ increased and remained steady at around 7, but the ratings of AP did not drop as much as those of during experiment 2 (see figure 2.17 and figure 2.23).

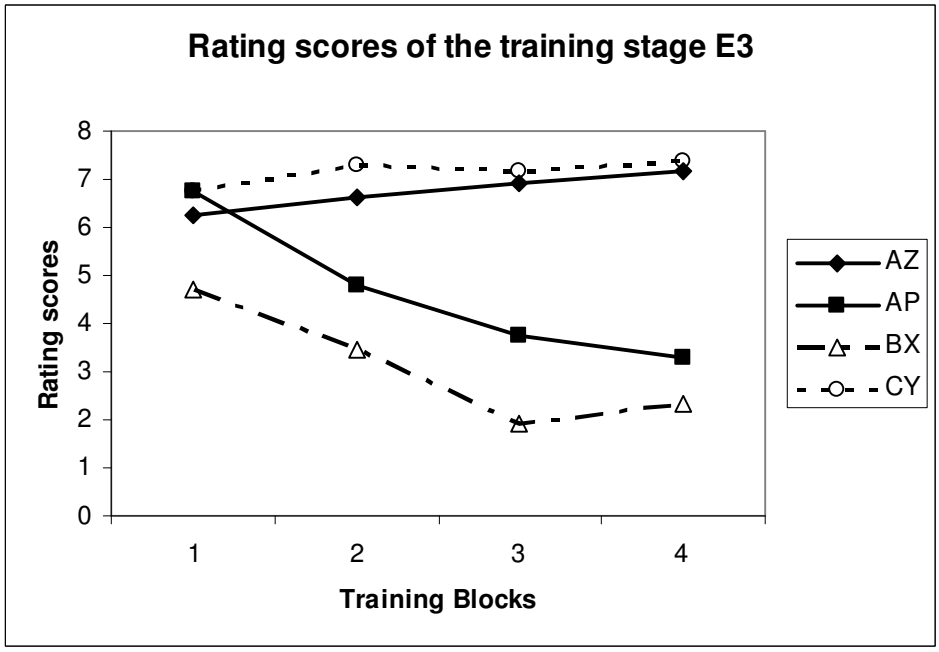


Figure 2.23 Rating scores for AZ+, AP–, BX– and CY+ at the training stage during experiment 3. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

During the training stage, an ANOVA with discrimination (AZ or AP v. CY or BX), reinforcement and training block (1–4) as factors, revealed no main effect of discrimination $F(1,15)=2.78$, $p=0.12$; but the main effects of training block and reinforcement were significant, $F(3,45)=4.90$, $p=0.005$; $F(1,15)=27.16$, $p<0.001$ respectively. Furthermore the interaction between training block and reinforcement was also significant $F(3,45)=12.50$, $p<0.001$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. The simple main effects revealed that there was an effect of block on non-reinforced trials $F(3,45)=15.84$, $p<0.001$, but not on reinforced trials $F<1$. The simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant from second to fourth training blocks, the smallest $F(1,15)=5.79$, $p=0.03$; but not on first block, $F<1$.

The interaction between the discrimination and reinforcement factors was also significant $F(1,15)=7.03$, $p=0.02$. The simple main effects revealed that the ratings differed between the non-reinforced compounds AP and

BX, $F(1,15)=10.39$, $p=0.006$; but not between AZ and CY, reinforced trials $F<1$. The simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant on both discrimination types, $F(1,15)=6.30$, $p=0.02$; $F(1,15)=23.62$, $p<0.001$, suggesting both discriminations were learnt during the training stage. However, it can be seen from figure 2.23, the discrimination between AZ and AP was not as large as the discrimination between BX and CY. No other two–way and three–way interactions were significant, $Fs<1$.

2.5.3.4 Test stage

Figure 2.24 shows the rating scores during the test stage. It can be seen that the ratings of A and C remained high, and AZ v. AP and BX v. CY discriminations were maintained. The latter observation was confirmed by the results of an ANOVA with discrimination (AZ or AP v. CY or BX), plus reinforcement as factors, which revealed a significant effect of reinforcement $F(1,15)=15.49$, $p<0.001$, suggesting participants gave significantly different ratings to reinforced and non-reinforced stimuli. However, there was no main effect on discrimination $F(1,15)=3.74$, $p=0.07$, and the interaction between these two factors was not significant $F<1$.

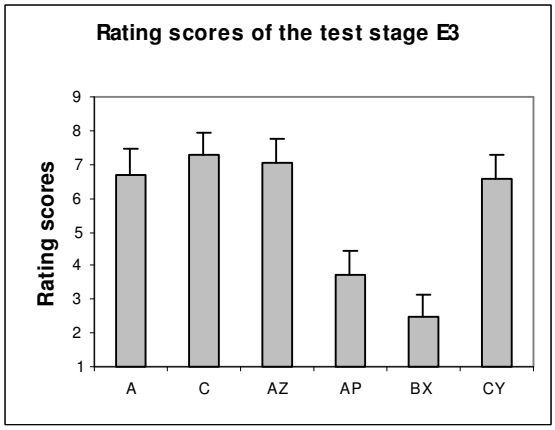


Figure 2.24 Rating scores for A+, C+, AZ+, AP–, BX– and CY+ at the test stage during experiment 3. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

Figure 2.25 shows the rating scores of the two critical stimuli CP and CX at the pre-test and the test stages. It is clear that, while during the pre-test stage ratings of the two stimuli were quite similar. However, during the test stage, CP was rated lower than CX. An ANOVA with stage (pre-test and test) and stimulus (CP v. CX) as factors, revealed only stimulus was significant $F(1,15)=8.75$, $p=0.01$. At the same time, the interaction between these two factors were no significant, $F<1$; $F(1,15)=2.06$, $p=0.17$. The results suggested that there was no evidence that P had become a conditioned inhibitor in experiment 3, but numerically the difference between CP and CX was in the correct direction.

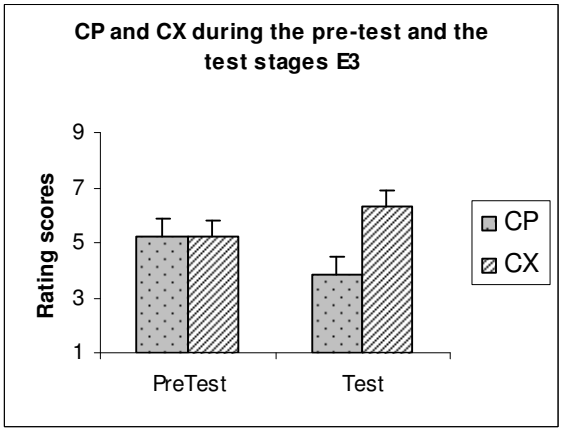


Figure 2.25 Rating scores for the key comparison stimuli CP and CX at the pre-test and the test stages during experiment 3. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty. The pre-test ratings showed that the stimuli elicited similar ratings prior to conditioning. The test ratings confirmed the presence of conditioned inhibition, which was shown as higher ratings to CX than CP.

2.5.4 Discussion

The data analysis only suggested a weak inhibition effect in experiment 3, although the experiment solved the problem of pre-existing biases. According to the Rescorla–Wagner Theory (Rescorla & Wagner, 1972; Wagner & Rescorla, 1972), the difference between AZ and AP was the most important discrimination in this conditioned inhibition learning experiment, which was trying to demonstrate that P was a conditioned inhibitor. However, figure 2.23 showed that the rating of AP did not drop quickly and

sharply during the training. The results suggested that participants did not learn the critical AZ v. AP discrimination well enough. Considering the CI learning procedures would be examined in clinical groups in future, it aimed produce a robust CI effect. In order to enhance the CI effect, the proportion of non-reinforced trials usually is greater than the proportion of reinforced trials in many CI learning tasks using animal subjects (Nicholson & Freeman, 2002; Rhodes & Killcross, 2007; Tobler, Dickinson & Schultz, 2003). These previous studies suggested that the proportion of non-reinforced trials (AP and BX) should be increased during the training stage for the next experiment.

2.6 Experiment 4: CI experiment measured by summation test (non-reinforced training trials were increased)

2.6.1 Introduction

The experimental design was refined in experiment 4 – the proportion of non-reinforced trials was increased during the training. It aimed to enhance AZ v. AP discrimination; theoretically it could help to produce the strong CI effect.

2.6.2 Methods

All details not mentioned were identical to those of experiment 3.

2.6.2.1 Participants

Experiment 4 was conducted on an opportunity sample of 24 students at the University of Nottingham (11 males, and 13 females), with a mean age of 21.08, range from 18 to 33 years. There were two participants excluded from the experiment because of failing the pre-training stage.

2.6.2.2 Design

In experiment 4, the proportion of non-reinforced trials (AP–, BX–) was increased compared to that employed in the previous experiments (see table 2.6).

Table 2.6 The design of experiment 4.

Phase							
Pre-test		**Pre-training**		**Training**		**Test**	
CSs	No. trials	CS & US outcome	No. trials	CSs & US outcome	No. trials	CSs	No. trials
A	2	A +	12	AZ +	8	A	2
C	2	U –	12	AP –	12	C	2
AZ	2	V –	12	BX –	12	AZ	2
AP	2	C +	12	CY +	8	AP	2
BX	2					BX	2
CY	2					CY	2
CP	2					CP	4
CX	2					CX	4

Note: The conditioned stimuli pictures were as shown in figure 2.20. A was picture I or II; B was II or I; P was IV or V; X was V or IV; C was III or IX; Z was VII; V was III or IX; and U was VIII. With respect to US presentations, '+' represents positive pictures and '–' represents neutral IAPS pictures (selected by pilot study).

2.6.2.3 Procedure

During the training stage, there were 8 reinforced training compounds (AZ and CY) and 12 non-reinforced training compounds (AP and BX), analysed in two blocks of 4 and 6 respectively.

The data was collected before the Christmas Holidays 2007 at the University of Nottingham.

2.6.3 Results

2.6.3.1 Pre-test stage

Figure 2.26 shows the rating scores during the pre-test stage. There was not much difference on the rating score of all stimuli which were around 5, except the score of A was 4.28 which was slightly lower than the others. Comparing the rating scores of CP and CX, it can be seen that the score of CP was slightly higher than the score of CX. An ANOVA with discrimination

(AZ or AP v. CY or BX) and reinforcement as factors, revealed nothing was significant, the largest $F(1,23)=2.78$, $p=0.11$. There was no significant difference in responding to the two critical test compounds (CP v. CX), $F(1,23)=1.24$, $p=0.23$. The analysis during the pre-test stage suggested no pre-existing biases in responding to the stimuli.

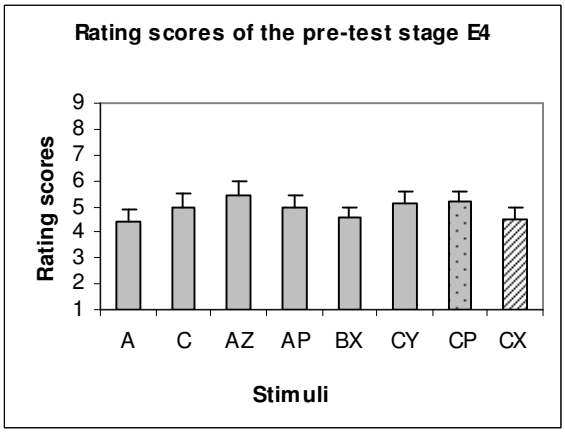


Figure 2.26 Rating scores for A, C, AZ, AP, BX, CY, CP and CX at the pre-test stage during experiment 4. A rating of 9 reflected expectation of a nice picture, 1 of a neutral picture and 5 indicated uncertainty.

2.6.3.2 The pre-training stage

During the pre-training stage, the ratings of A and C steadily increased, while those to the U and V stimuli fell gradually. Participants appeared again to learn the discrimination in this phase (see figure 2.27). An ANOVA with discrimination (A or U v. C or V), reinforcement and pre-training block (1–6) as factors, revealed no main effect of discrimination $F<1$. However, the main effect of pre-training block and reinforcement was significant, $F(5,115)=2.26$ $p=0.05$; $F(1,23)=53.13$, $p<0.001$ respectively. The interaction of these two factors was also significant $F(5,115)=17.61$, $p<0.001$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. To further analyze the interaction, simple main effects analysis was conducted; this revealed that there was an effect of block on both reinforced and non-reinforced trials, $F(5,115)=18.94$, $p<0.001$; $F(5,115)=6.95$, $p<0.001$ respectively. The simple main effects also revealed that the differences between reinforced

and non-reinforced trials were significant from second to sixth pre-training blocks, the smallest $F(1,23)=5.35$, $p=0.03$, but not on the first block $F<1$. It is clear that participants learnt the Pavlovian discriminations.

No other two–way and three–way interactions were significant, $Fs<1$.

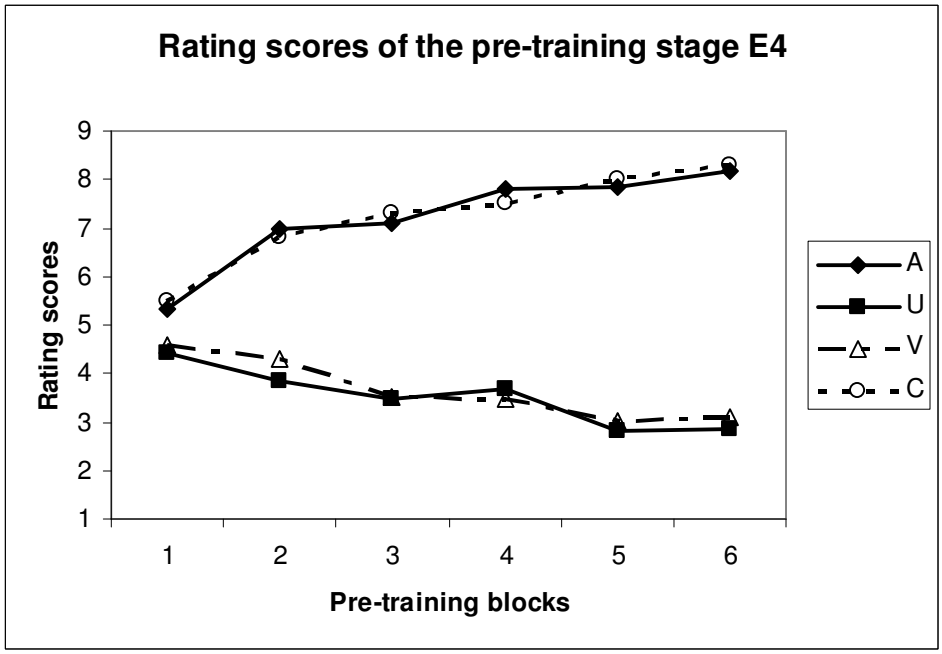


Figure 2.27 Rating scores for A+, U–, V– and C+ at the pre-training stage during experiment 4. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

2.6.3.3 Training stage

During the training stage, the ratings of AZ and CY steadily increased, while those of AP and BX fell gradually (see figure 2.28), which suggested that participants had learned the critical discrimination. It also can be seen that the ratings of AP were lower compared with those in experiment 3. An ANOVA with discrimination (AZ or AP v. CY or BX), reinforcement and training block (1–2) as factors, revealed no main effect of discrimination $F(1,23)=2.41$, $p=0.13$. However, the main effect of training block and reinforcement was significant, $F(1,23)=12.70$, $p=0.002$; $F(1,23)=137.69$, $p<0.001$ respectively.

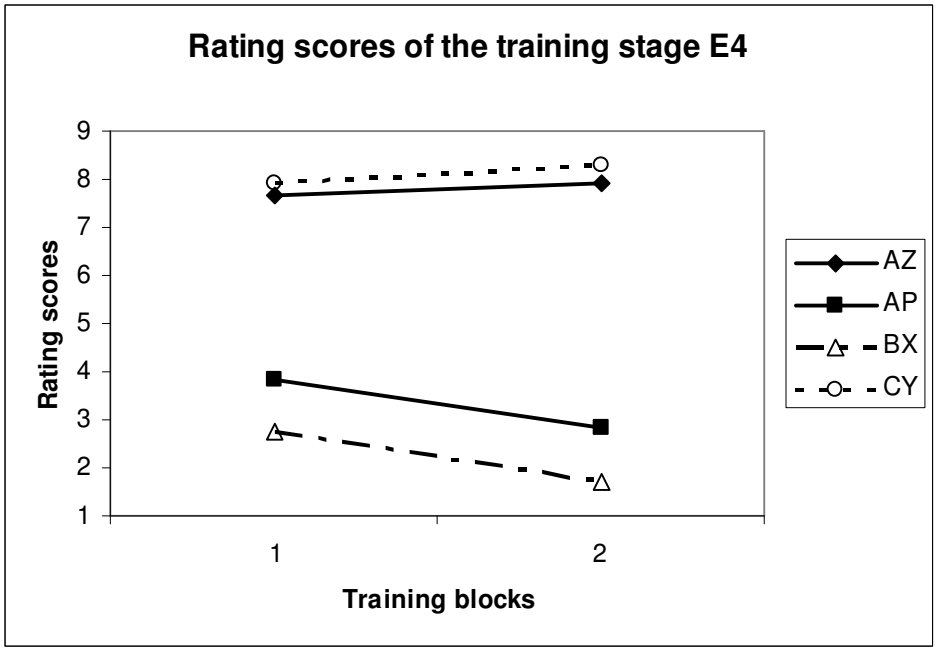


Figure 2.28 Rating scores for AZ+, AP–, BX– and CY+ at the training stage during experiment 4. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

The interaction between training block and reinforcement was also significant $F(1,23)=26.28$, $p<0.001$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. The simple main effects revealed that there was an effect of block on both reinforced and non-reinforced trials, $F(1,23)=5.40$, $p=0.03$, $F(1,23)=54.20$, $p<0.001$ respectively. The simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant on both training blocks, $F(1,23)=52.31$, $p<0.001$; $F(1,23)=87.65$, $p<0.001$ respectively.

A significant interaction was also found between discrimination and reinforcement, $F(1,23)=6.32$, $p=0.02$. The simple main effects revealed that the ratings differed between AP and BX, $F(1,23)=10.14$, $p=0.004$, but not between CY and AZ, $F<1$, suggesting a key difference in the processing of P and X at this stage. The simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant on

both discrimination types, $F(1,23)=51.11$, $p<0.001$, and $F(1,23)=89.22$, $p<0.001$. This suggested that both sets of stimuli were sufficiently distinctive to support the learning of the discrimination.

There were no other significant differences for two–way and three–way interactions, $Fs<1$.

2.6.3.4 Test stage

Figure 2.29 shows the rating scores during the test stage. Again, the ratings of A and C remained high, and the AZ v. AP and BX v. CY discriminations were maintained; the latter observation was confirmed by the results of an ANOVA with discrimination (AZ or AP v. CY or BX) and reinforcement as factors, which revealed no main effect of discrimination $F(1,23)=1.96$, $p=0.18$. However, the effect of reinforcement was significant $F(1,23)=135.00$, $p<0.001$. The interaction between discrimination and reinforcement was also significant $F(1,23)=6.65$, $p=0.02$. The simple main effects revealed a main effect of AZ v. CY, $F(1,23)=4.47$, $p=0.045$; and a main effect of AP v. BX, $F(1,23)=16.75$, $p<0.001$. Furthermore, the simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant on both discrimination types, $F(1,23)=47.83$, $p<0.001$; $F(1,23)=90.56$, $p<0.001$, suggesting both discrimination and reinforcement were learned effectively and maintained in the test stage.

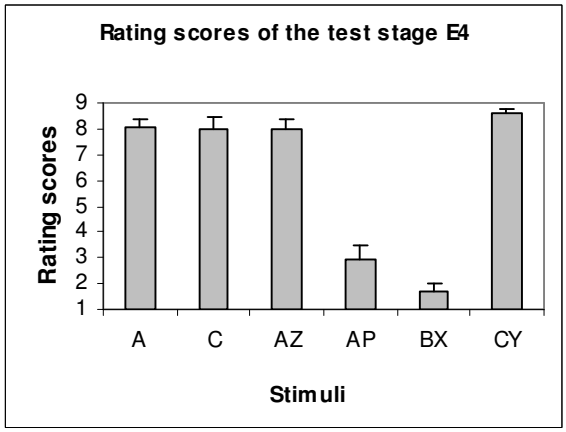


Figure 2.29 Rating scores for A+, C+, AZ+, AP–, BX– and CY+ at the test stage during experiment 4. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

Comparing the two critical stimuli CP and CX during the pre-test and the test stages, it can be seen from figure 2.30, the rating of CP was noticeably lower than CX during the test stages. The difference was confirmed by statistical analysis: an ANOVA with stage (pre-test and test), and stimulus (CP v. CX) as factors, revealed no main effect of either stage $F<1$, or stimulus $F(1,23)=1.60$, $p=0.22$. However, the interaction between the two factors was significant $F(1,23)=10.96$, $p=0.003$. The simple main effects revealed that participants gave significantly lower rating scores to CP than to CX during the test stage $F(1,23)=7.25$, $p=0.01$, but not at the pre-test stage $F<1$. The results suggest that P had become a conditioned inhibitor in experiment 4.

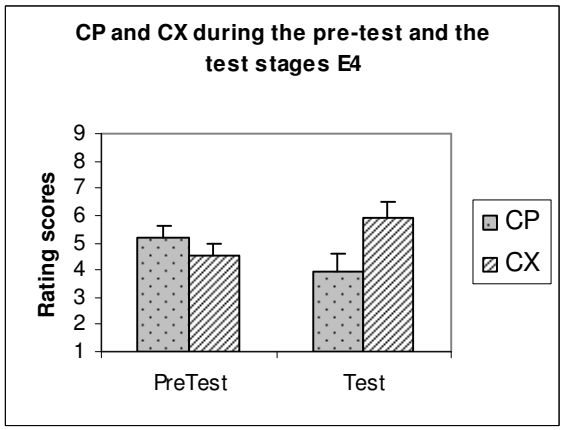


Figure 2.30 Rating scores for the key comparison stimuli CP and CX at the pre-test and the test stages during experiment 4. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty. The pre-test ratings showed that the stimuli

elicited similar ratings prior to conditioning. The test ratings confirmed the presence of conditioned inhibition, which was shown as higher ratings to CX than CP.

2.6.4 Discussion

To sum up, the previous experiments have gradually developed a suitable procedure to measure conditioned inhibitory learning phenomena using a summation test. Experiment 1 compared the rating scores of CP/YP (P as a putative conditioned inhibitor) and CX/YX (X as a control stimulus) before and after training. The results did not find a significant difference between the ratings of CP/YP and CX/YX at the test stage, although numerically they were in the correct direction.

Compared with experiment 1, the main differences of experiment 2 were the new pictures of CS and the new pre-training stage. In experiment 2, 9 coloured Lego block pictures were used instead of the 7 domino block pictures as CSs; and at the same time, a pre-training stage was added before the training stage. The aim of the pre-training stage was not only to ensure the production of stronger excitors (A and C), but also to measure Pavlovian excitatory associative learning phenomena. It was presumed that if participants could not learn Pavlovian excitatory association very well, they may have difficulties to learn conditioned inhibition. The pre-training stage contained 4 CSs, each CS followed a reinforced or non-reinforced US, which examined participants' simple associative learning performance. This stage became a new criterion for analysing the CI learning performance. If participants failed the pre-training stage, they would be excluded from the measuring of the CI task. However, some pre-existing biases were found at the pre-test stage which made the experiment hard to demonstrate the CI learning performance.

With the purpose of solving the problem of the pre-existing biases, all coloured Lego block pictures were changed to black and white pictures as CSs in experiment 3. The results did not show any pre-existing biases, nevertheless, the data analysis only revealed weak inhibitory effects in experiment 3. The results of experiment 1, 2 and 3 demonstrated that there was no evidence that P had become a conditioned inhibitor relative to the strong control of differential inhibition, although numerically the difference between CP and CX was in the correct direction in all the experiments.

In order to enhance CI learning performance, experiment 4 increased the proportion of non-reinforced trials during the training stage which was consistent with CI learning tasks in animal subjects (Nicholson & Freeman, 2002; Rhodes & Killcross, 2007; Tobler et al., 2003). The experiment successfully demonstrated a better controlled conditioned inhibitory learning procedure in human participants. First, the experimental design tried to rule out several alternative explanations (e.g. attention) when P acted as a conditioned inhibitor. The two training compounds (BX– and CY+) not only helped to minimize distraction, but also balance the excitors and non-reinforced stimuli. Second, the experiment not only examined pre-existing biases (pre-test stage), but also measured Pavlovian excitatory associative learning phenomena (pre-training stage) and conditioned inhibitory learning performance (training stage) in the same experimental procedure. The experiment demonstrated robust conditioned inhibitory effects in humans using a summation test.

2.7 Experiment 5: CI experiment measured by both summation and retardation tests

2.7.1 Introduction

Rescorla (1969) suggested two critical methods should be used to measure conditioned inhibition. One method is the summation test, in which subjects should show less responding to an inhibitor and a conditioned excitor compound than a conditioned excitor presented alone. For example, in a test of C v. CP, with P as a putative inhibitor and C as a test excitor, subjects will show less responding to CP than C. Another method is the retardation–of–acquisition test; if a conditioned inhibitor is paired with a US, then the responding to the CS will develop very slowly compared with learning about a neutral CS. For example, comparing stimulus X versus stimulus P, where X is a neutral CS and P is a putative inhibitor, when P and X are separately paired with a US, subjects will show slower acquisition of responding when P is paired with US than when X is paired with US.

Rescorla (1969) has recommended that summation test combined with retardation test offers the possibility of the most conclusive evidence of learned conditioned inhibition. He pointed if conditioned inhibition is only measured by a summation test, it may be confounded by generalization decrement (makes test excitor seems a different stimulus) and/or attentional distraction (the putative inhibitor acts as a distractor, which attract attention from the excitor). If CI learning performance is only measured by the retardation test, the CS may be slow to acquire excitatory strength when reinforced, because attention to it has been reduced. Therefore, if the result from both summation and retardation tests support CI learning phenomena, then the attention and generalization decrement

arguments can be ruled out. However, Williams et al. (1992, p. 287) stated their opinion of those two tests, saying that perhaps it is not always be "necessary" to use both tests if the experimental design is well controlled and rules out other alternative views.

The present summation test tried to rule out the alternative explanations, which tested a putative inhibitor (P) to become a conditioned inhibitor. During the experiment, two training compounds (BX– and CY+) not only helped to minimize distraction, but also balance the comparison of excitors and distracters. However, the experiment comparing two critical compounds CP and CX, it relies on the attention and generalisation decrement commanded by the experimental control stimulus and the putative inhibitor to be the same. One solution for this uncertainty is to run a retardation test after the summation test. In the retardation test, it will compare the rating scores between P and X, and examine the stimuli P and X to act alone. If participants show slower acquisition of responding to P+ than X+, it should be confirmed P as a conditioned inhibitor. Therefore, both attention and generalisation decrement arguments can be clearly ruled out, but up to now, no successful retardation test has been reported in humans.

Applying Rescorla's theory (1969) to the present study, if P is the putative inhibitor, then if P paired with a US (a positive picture), the responding to P would develop slowly compared with the neutral stimulus X paired with a US. The reason for choosing X as the neutral stimulus was equating the amount of exposure given to the two test stimuli. It is important to control the amount of exposure because pre-exposure alone can retard conditioning, for example, during the latent inhibition procedure (Lubow, 1965).

Experiment 5 was conducted to measure CI learning by the summation test and a retardation test. The experimental design for the summation task was identical to experiment 4, but the design for the retardation test was newly added. During experiment 5, P and X were partially reinforced. The design was intended to prevent participants learning too quickly, which might obscure any retardation effects. If the whole procedure of retardation task only included P and X, the training would be too simple and the participants might reduce attention during the experiment because most of trials were reinforced. In order to ensure participants' attention, two new non-reinforced CSs (E– and F–) were added during the task.

During the data collection for this experiment period, I was informed that my potential clinical participants – PD patients had been completed the Urgency, Premeditation, Perseverance, and Sensation Seeking Impulsive Behaviour Scale (UPPS Scale; Whiteside & Lynam, 2001) for the assessment of impulsivity. It would be important to compare the UPPS scores between the clinical populations and normal participants. Therefore the UPPS questionnaire was used during the experiment.

The data of experiment 5 were collected in two different periods. First, it was during the university final examination period 2008 at the University of Nottingham (experiment 5a). Second, was during the university summer holidays (experiment 5b).

2.7.2 Experiment 5a: methods

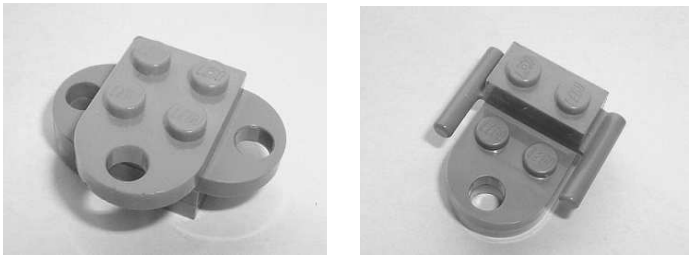
All details not mentioned were identical to those of experiment 4.

2.7.2.1 Participants

Experiment 5a was conducted on an opportunity sample of 32 students at the University of Nottingham (16 males, and 16 females), with a mean age of 21.97, range from 18 to 33 years. There were four participants excluded from the experiment due to failing the pre-training stage.

2.7.2.2 Stimuli and material

Two new CSs were added during the retardation task (see figure 2.31).



X XI

Figure 2.31 Two added conditioned stimuli pictures for experiment 5a retardation task (see table 2.6 for experimental design).

In order to further measure the impulsiveness among the participants, the UPPS questionnaire was added to the previous questionnaire package during experiment 5. It is a 45–item self–response scale that features four subscales: urgency, premeditation, perseverance, and sensation seeking. The scale ranges from one "not true of me" to five "very true of me." The urgency subscale (α=.86) measures the degree to which individuals act rashly in the face of negative affect; e.g. "I have trouble controlling my impulses". The Premeditation subscale (α=.88) measures the degree to which individuals act without first considering the potential consequences of their actions; e.g. "I have a reserved and cautious attitude toward life". The perseverance subscale (α=.82) measures the degree to which individuals find it difficult to persist in activities that are or become difficult or boring; e.g. "I generally like to see things through to the end". The sensation Seeking subscale (α=.81) measures the degree to which

individuals seek out activities that involve a sense of risk or thrill; e.g. "I quite enjoy taking risks".

2.7.2.3 Design

Table 2.7 shows the detail of the retardation task design in experiment 5a.

Table 2.7 The design of retardation test procedure in experiment 5a.

Phase			
Training		**Test**	
CS & US outcome	No. trials	CS	No. trials
P +	8	P	2
X +	8	X	2
P –	4	E	2
X –	4	F	2
E –	12		
F –	12		

Note: CS stimuli were used in experiment 5a are shown in figure 2.20 and figure 2.31. For US stimuli, + are positive pictures, – are Neutral pictures from IAPS (selected by pilot study).

2.7.2.4 Procedure

During the retardation test, participants needed to click a number button to predict the valence of US after a CS was shown on the screen. The following instructions appeared on the screen:

> "Please PREDICT again! What type of picture Mogwai will bring. You will be shown ONE Lego block. According to the block you are shown, please guess what type of picture will follow either a nice picture or a neutral picture.
>
> Please use the mouse to click on a number from 1 to 9. Number 1 means a neutral picture, 5 means not sure, 9 means a nice picture.
>
> *Click any button on the mouse to start observation*"

The training stage in the retardation task contained 6 types of trials: P+, X+, P–, X–, E– and F–. There were 8 trials of P+ and X+, 4 trials of P– and X–, and 12 trials of E– and F– (the position of CS on the screen (left or right) was counterbalanced). The order of presenting CSs on the screen was randomly selected by the computer. The right/left position of stimulus on the screen was counterbalanced as in the previous experiments. After participants clicked a number button to predict the US, the US was shown on the screen for 1 sec., and followed by a 1–sec gap before the next trial started. During the 1–sec gap, there was a picture of cat in the middle of the screen with a white background (same as in experiment 1). It was anticipated that participants would learn to predict what type of US would occur according to the CS stimulus presented.

2.7.2.5 Test stage in retardation task

A retardation test followed immediately after the retardation training stage, which comprised four CSs (P, X, E and F). After participants clicked on a number button on the rating scale, the next CS was immediately shown on the screen. Again, the order of the presentation was randomly selected by computer, and the right/left position of stimulus on the screen was counterbalanced as in the previous experiments. There were a total of 8 presentations, and each CS was presented twice. No USs occurred in the retardation task test stage.

2.7.3 Results

2.7.3.1 Pre-test stage

Figure 2.32 shows the rating scores during the pre-test stage. It can be seen that most of rating scores were very similar, which were around 5. The scores of A, AZ and BX were lower than others, which were around 4. An ANOVA with discrimination (AZ or AP v. CY or BX), and reinforcement as

factors, revealed no main effect of either discrimination $F<1$, or reinforcement $F(1,31)=1.88$, $p=0.18$. There was no significant interaction between discrimination and reinforcement $F(1,31)=2.97$, $p=0.10$. Furthermore, there was no significant difference in responding to the test compounds (CP v. CX), $F<1$.

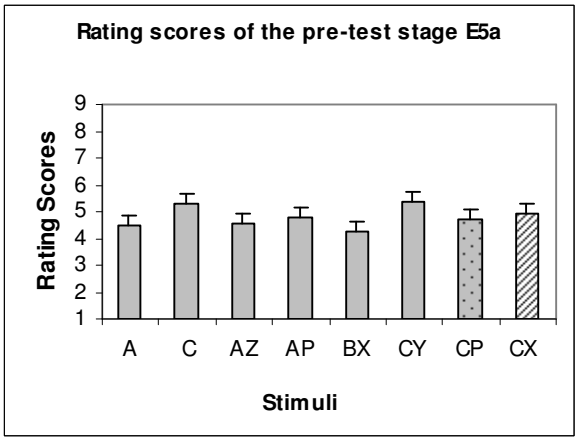


Figure 2.32 Rating scores for A, C, AZ, AP, BX, CY, CP and CX at the pre-test stage during experiment 5a. A rating of 9 reflected expectation of a nice picture, 1 of a neutral picture and 5 indicated uncertainty.

2.7.3.2 Pre-training stage

During the pre-training stage, ratings of the A and C steadily increased, while those to the U and V fell gradually (see figure 2.33). Participants appeared again to learn the discrimination in this phase, and an ANOVA with discrimination (A or U v. C or V), reinforcement and pre-training block (1–6) as factors revealed no main effect of either pre-training block, or discrimination $Fs<1$. However, the main effect of reinforcement was significant $F(1,31)=46.21$, $p<0.001$. The interaction between reinforcement and pre-training block was significant $F(5,155)=24.59$, $p<0.001$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. The simple main effects revealed that there was an effect of blocks on both reinforced and non-reinforced trials, $F(5,155)=22.75$, $p<0.001$; $F(5,155)=16.37$, $p<0.001$ respectively. The simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant from third to sixth pre-training

blocks, the smallest $F(1,31)=9.63$, $p=0.004$, but not on the first and second pre-training blocks, the largest $F(1,31)=1.56$, $p=0.22$.

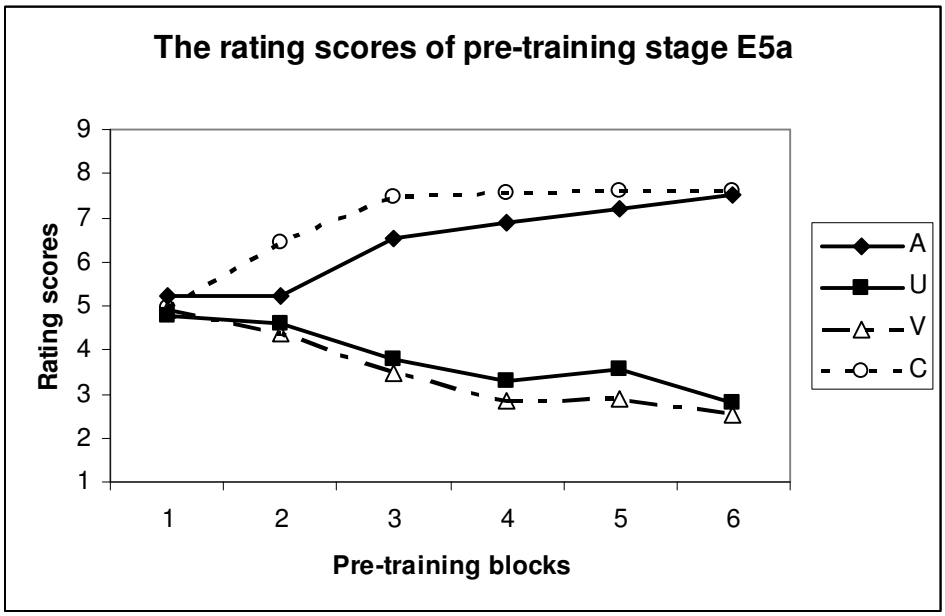


Figure 2.33 Rating scores for A+, U–, V– and C+ at the pre-training stage during experiment 5a. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

The interaction between reinforcement and discrimination was also significant $F(1,31)=4.70$, $p=0.04$. The simple main effects revealed that the ratings between the reinforcement in the two discriminations (A or U v. C or V) were not significant, $F(1,31)=3.71$, $p=0.06$; $F(1,31)=1.24$, $p=0.27$ respectively. The simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant on both discrimination types, $F(1,31)=17.31$, $p<0.001$; $F(1,31)=29.74$, $p<0.001$, suggesting that both discriminations were learned effectively. However, it can be seen from figure 2.33, the discrimination between A and U was not as large as the discrimination between C and V.

There was no other significant differences for two–way and three–way interactions, the largest $F(5,155)=1.10$, $p=0.36$.

2.7.3.3 Training stage

During the training stage, the ratings of AZ and CY steadily increased, while the ratings of AP and BX fell gradually (see figure 2.34), suggesting participants had learnt the differences between the reinforced (AZ and CY) and non-reinforced (AP and BX) trials.

Figure 2.34 Rating scores for AZ+, AP–, BX– and CY+ at the training stage during experiment 5a. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

During the training stage, an ANOVA with discrimination (AZ or AP v. CY or BX), reinforcement and training block (1–2) as factors, revealed no main effect of training block $F(1,31)=1.82$, $p=0.19$; however, the main effects of discrimination and reinforcement were significant $F(1,31)=5.40$, $p=0.03$; $F(1,31)=63.70$, $p<0.001$ respectively. The interaction between reinforcement and training block was significant $F(1,31)=8.27$, $p=0.007$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. The simple main effects revealed that there was an effect of block on non-reinforced trials $F(1,31)=14.93$, $p<0.001$, but not on reinforced trials $F(1,31)=3.83$, $p=0.06$. The simple main effects also revealed that the differences between reinforced and non-reinforced trials

were significant on both training blocks, $F(1,31)=21.81$, $p<0.001$; $F(1, 31)=43.78$, $p<0.001$ respectively.

The interaction between reinforcement and discrimination was also significant $F(1,31)=8.88$, $p=0.006$. The simple main effects revealed that the ratings differed between AZ and CY, $F(1,31)=18.47$, $p<0.001$, but not between AP and BX, $F(1,31)=1.02$, $p=0.32$. The simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant on both discrimination types, $F(1,31)=20.04$, $p<0.001$, and $F(1,31)=46.38$, $p<0.001$. This suggested that both sets of stimuli were sufficiently distinctive to support the learning of the discrimination. However, it can be seen from figure 2.34, the discrimination between AZ and AP was not as large as the discrimination between BX and CY.

No other two–way and three–way interactions were significant, Fs<1.

2.7.3.4 Test stage

Figure 2.35 shows the rating scores during the test stage. Again, ratings of A and C remained high, and the discriminations were maintained. The latter observation was confirmed by the results of an ANOVA with discrimination (AZ or AP v. CY or BX) and reinforcement as factors, which revealed no main effect of discrimination $F(1,31)=1.22$, $p=0.28$. However, the effect of reinforcement was significant, $F(1,31)=103.96$, $p<0.001$, suggesting participants gave significantly different ratings to reinforced and non-reinforced stimuli. There were no significant interactions between these two factors, $F(1,31)=2.45$, $p=0.13$.

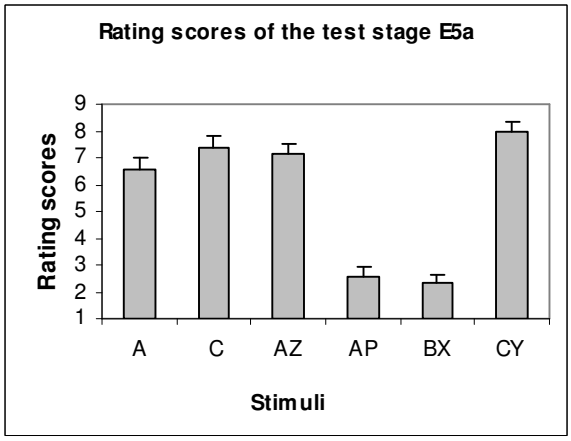


Figure 2.35 Rating scores for A, C, AZ+, AP–, BX– and CY+ at the test stage during experiment 5a. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

Comparing two critical stimuli CP and CX, an ANOVA with stage (pre-test and test) and stimulus (CP v. CX) as factors revealed no significant effects or interactions, the largest $F(1,31)=2.19$, $p=0.15$, suggesting no evidence that putative inhibitor P had become a conditioned inhibitor in the summation test.

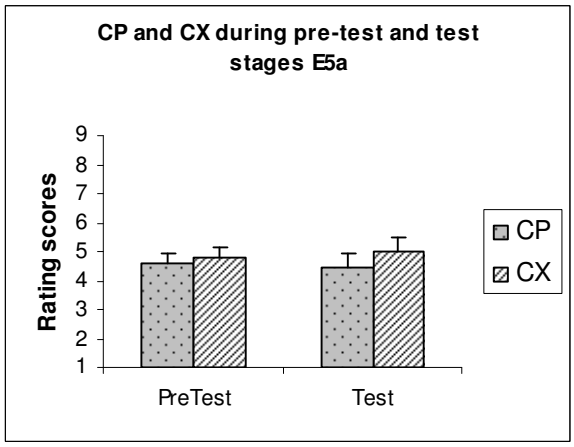


Figure 2.36 Rating scores for the key comparison stimuli CP and CX at the pre-test and the test stages during experiment 5a. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty. The pre-test ratings showed that the stimuli elicited similar ratings prior to conditioning. The test ratings confirmed week effects of conditioned inhibition, which was shown as higher ratings to CX than CP.

2.7.3.5 Retardation test

Figure 2.37 shows the rating scores during the retardation task. It can be seen, the ratings of E and F were very similar during the whole task; and both ratings steadily decreased. However, these ratings were not what was theoretically important, so they were not considered further. The ratings of

P were lower than the ratings of X at the first training block, but both ratings became quite similar during the second and third training blocks and test stage. An ANOVA with stimulus (P v. X) and training block (1–3) as factors, revealed a main effect of training block $F(2,62)=9.96$, $p<0.001$; but no main effect of stimulus $F<1$. The interaction between training block and stimulus was not significant $F(2,62)=2.88$, $p=0.06$. Clearly, there was no evidence that putative inhibitor P had become a conditioned inhibitor in experiment 5a in either the summation or the retardation test.

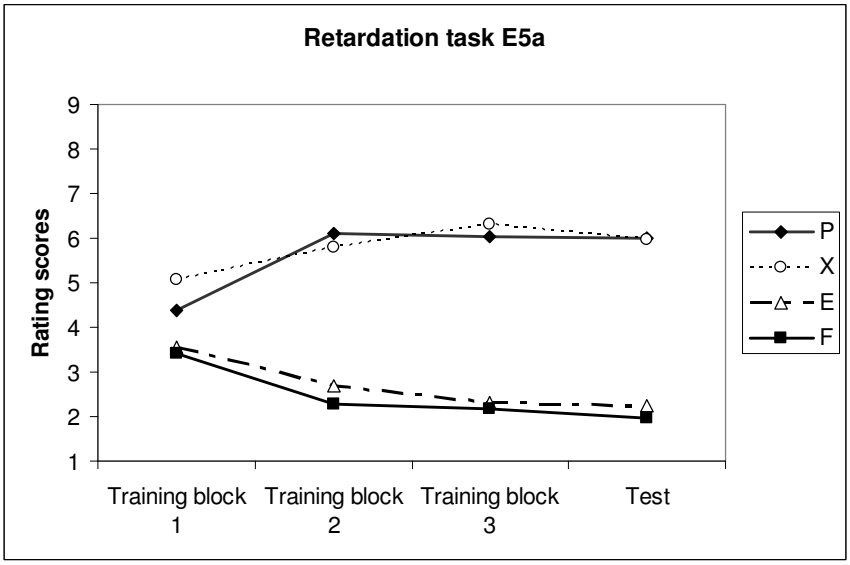


Figure 2.37 Rating scores for P+/–, X+/–, E– and F– during the retardation task. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

2.7.4 Discussion

It was unexpected that experiment 5a failed to replicate the previous findings in the summation test, at the same time the experiment did not find the CI effect in the retardation test. However, it was noticeable that all the data were collected during the students' final examination period at the university in experiment 5a. Some participants said that they were under stress for preparing exams after they took part in the experiment. It can be hypothesised that the stress and anxiety may affect students' conditioned inhibition learning performance, so the next experiment (experiment 5b) conducted during the university's summer holidays. Therefore the CI

learning performance and the measures of individual difference can be compared before and after the examination, which can possibly find some evidence to support the hypothesis.

2.7.5 Experiment 5b

Experiment 5b replicated experiment 5a, but the data was collected during the university summer holidays. I expected that the CI learning performance would be different among the university students in two different periods (examination period v. holidays).

2.7.6 Methods

All details not mentioned were identical to those of experiment 5a.

2.7.6.1 Participants

Experiment 5b was conducted on an opportunity sample of 32 students and staff at the University of Nottingham (12 males, and 20 females), with a mean age of 25.88, range from 19 to 47 years. There were two participants excluded from the experiment because of failing the pre-training stage.

2.7.6.2 Procedures

The data were collected during the university summer holidays 2008 at the University of Nottingham.

2.7.7 Results

2.7.7.1 Pre-test stage

Figure 2.38 shows rating scores during the pre-test stage. Most ratings were around 5, except for the rating of AP which was slightly lower than others. Comparing the ratings of CP and CX, it can be seen CP was a bit

higher than CX. An ANOVA with discrimination (AZ or AP v. CY or BX) and reinforcement as factors revealed no significant effects or interactions, the $F(1,31)=3.77$, $p=0.06$ for discrimination factor. There was no significant difference in responding to the test compounds (CP v. CX), $F<1$.

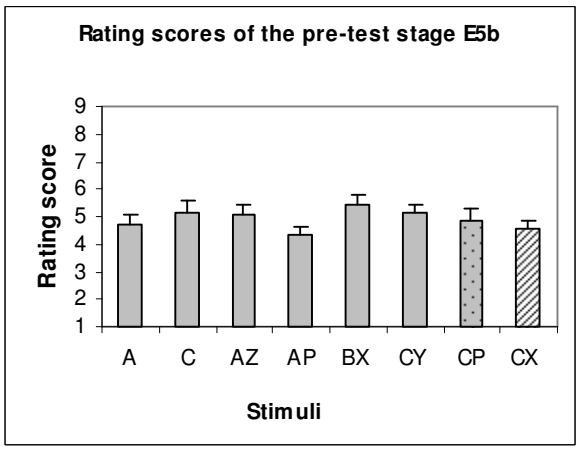


Figure 2.38 Rating scores for A, C, AZ, AP, BX, CY, CP and CX at the pre-test stage during experiment 5b. A rating of 9 reflected expectation of a nice picture, 1 of a neutral picture and 5 indicated uncertainty.

2.7.7.2 Pre-training stage

During the pre-training stage, ratings of A and C steadily increased, while those to U and V fell gradually (see figure 2.39). Participants appeared again to learn the discrimination in this phase. An ANOVA with discrimination (A or U v. C or V), reinforcement and pre-training block (1–6) as factors, revealed no main effect of either discrimination $F<1$, or pre-training block $F(5,155)=1.87$, $p=0.10$; however, the main effect of reinforcement was significant $F(1,31)=83.05$, $p<0.001$. The interaction between reinforcement and block was significant $F(5,155)=20.90$, $p<0.001$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. Nothing else was significant, the largest $F(5,155)=1.84$, $p=0.11$. To further analysis the interaction between reinforcement and block, the simple main effects revealed that there was an effect of block on both reinforced and non-reinforced trials, $F(5,115)=16.06$, $p<0.001$; $F(5,115)=17.91$, $p<0.001$ respectively. The

simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant from the second to sixth pre-training blocks, the smallest $F(1,31)=10.72$, $p=0.003$, but not significant on the first block, $F<1$.

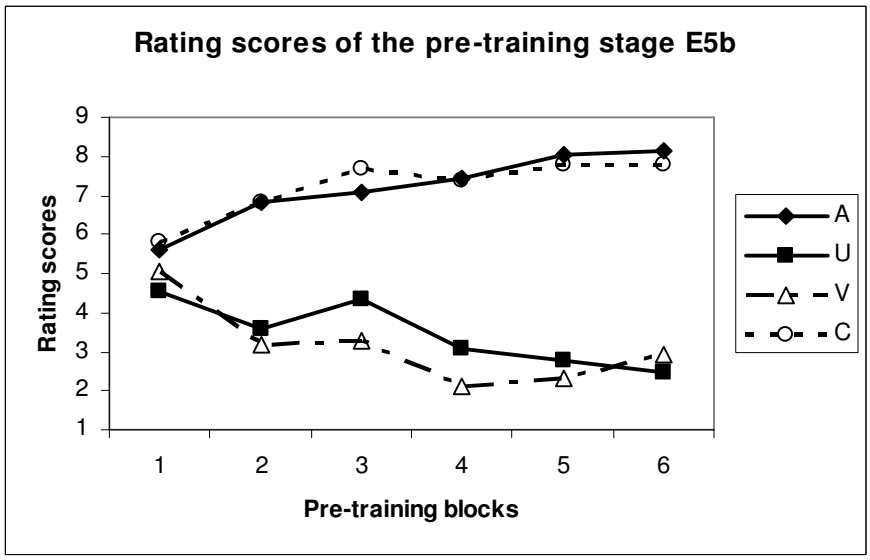


Figure 2.39 Rating scores for A+, U−, V− and C+ at the pre-training stage during experiment 5b. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

No other two-way and three-way interactions were significant, the largest $F(5,115)=1.84$, $p=0.11$.

2.7.7.3 Training stage

During the training stage, ratings of AZ and CY steadily increased, while those to AP and BX fell gradually (see figure 2.40), which suggested that participants had learned the critical discrimination. An ANOVA with discrimination (AZ or AP v. CY or BX), reinforcement and training block (1–2) as factors, revealed no main effect of discrimination $F<1$; however, the main effects of training block and reinforcement were significant, $F(1,31)=7.61$, $p=0.01$; $F(1,31)=98.43$, $p<0.001$ respectively. The interaction between training block and reinforcement was also significant $F(1,31)=20.59$, $p<0.001$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. To further analyze the

interaction, the simple main effects revealed that there was an effect of block on both reinforced and non-reinforced trials: $F(1,31)=4.46$, $p=0.04$; $F(1,31)=36.16$, $p<0.001$ respectively. The simple main effects also found that the differences between reinforced and non-reinforced trials were significant on both training blocks, $F(1,31)=33.58$, $p<0.001$; $F(1,31)=67.83$, $p<0.001$ respectively.

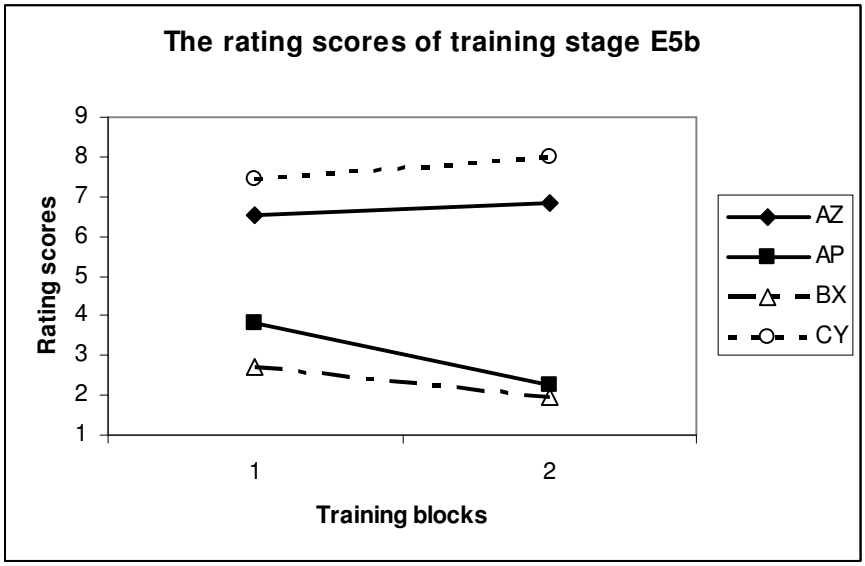


Figure 2.40 Rating scores for AZ+, AP–, BX– and CY+ at the training stage during experiment 5b. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

The interaction between discrimination and reinforcement was also significant $F(1,31)=17.40$, $p<0.001$. The simple main effects revealed that the ratings differed between the reinforced stimuli in the two discriminations, and also the two non-reinforced stimuli (AZ v. CY and AP v. BX), $F(1,31)=10.87$, $p=0.003$; $F(1,31)=5.05$, $p=0.03$ respectively. The simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant on both discrimination types, $F(1,31)=31.82$, $p<0.001$, and $F(1,31)=70.40$, $p<0.001$. This suggested that both sets of stimuli were sufficiently distinctive to support the learning of the discrimination. However, it can be seen from figure 2.40, the discrimination between AZ and AP was not as large as the discrimination between BX and CY.

Nothing else was significant, the largest $F(1,31)=3.83$, $p=0.06$.

2.7.7.4 Test stage

Figure 2.41 shows the rating scores during the test stage. Again, ratings of A and C remained high, and the discriminations (AZ or AP v. BX or CY) were maintained; the latter observation was confirmed by the results of an ANOVA with discrimination, and reinforcement as factors, revealed no main effect of discrimination $F(1,31)=1.19$, $p=0.28$; however, the main effect of reinforcement was significant $F(1,31)=148.93$, $p<0.001$, suggesting participants gave significantly different ratings to reinforced and non-reinforced stimuli. The interaction between the two factors was not significant $F<1$.

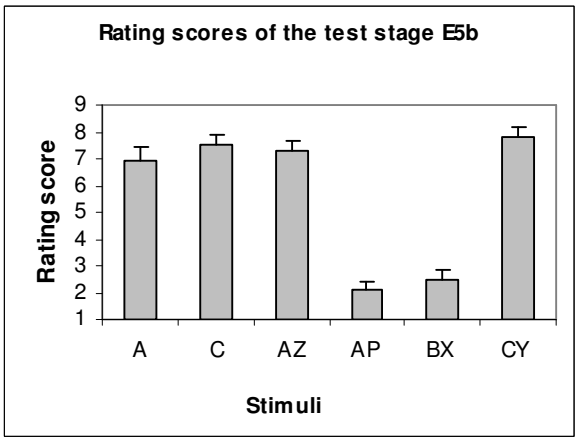


Figure 2.41 Rating scores for A+, C+, AZ+, AP–, BX– and CY+ at the test stage during experiment 5b. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

Comparing two critical stimuli CP and CX, figure 2.42 shows that the rating score of CP was lower than the rating score of CX, which was our expectation. An ANOVA with stage (pre-test and test), and stimulus (CP v. CX) as factors, revealed no main effects of either stages, or stimulus, the largest $F(1,31)=3.64$, $p=0.07$. However, the two–way interaction between these two factors was significant $F(1,31) =6.59$, $p=0.02$. To further analyze the interaction between stages and stimulus, the simple main

effects revealed that although the ratings of CP and CX did not differ at the pre-experimental stage $F(1,31)=0.50$, $p=0.48$; they differed significantly at the test stage $F(1,31)=11.62$, $p=0.002$. The results suggest that P had become a conditioned inhibitor relative to strong control of pseudo inhibitor in experiment 5b in summation task.

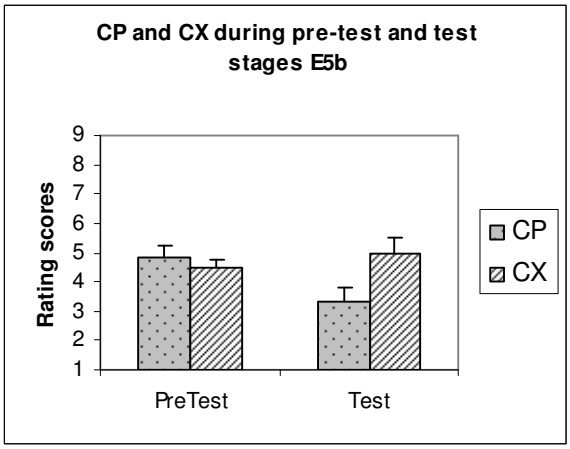


Figure 2.42 Rating scores for the key comparison stimuli CP and CX at the pre-test and the test stages during experiment 5b. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty. The pre-test ratings showed that the stimuli elicited similar ratings prior to conditioning. The test ratings confirmed the presence of conditioned inhibition, which was shown as higher ratings to CX than CP.

2.7.7.5 Retardation test

Figure 2.43 shows the rating scores during the retardation task. Again, it can be seen, the ratings of E and F were very similar during the whole task, and both ratings steadily decreased. However, these ratings were not theoretically important, so were not considered further. The ratings of P were lower than the ratings of X in the first training block, but subjects rated P slightly higher than X during the second and third training blocks and test stage, although these differences were small. ANOVA with stimulus (P v. X) and training block (1–3) as factors, revealed no main effect of stimulus $F<1$, but one of retardation training block $F(2,62)=4.28$, $p=0.02$. There was no significant interaction between training block and stimulus $F(2,62)=2.74$, $p=0.07$. The results suggested that there was no evidence that P was a conditioned inhibitor in the retardation task.

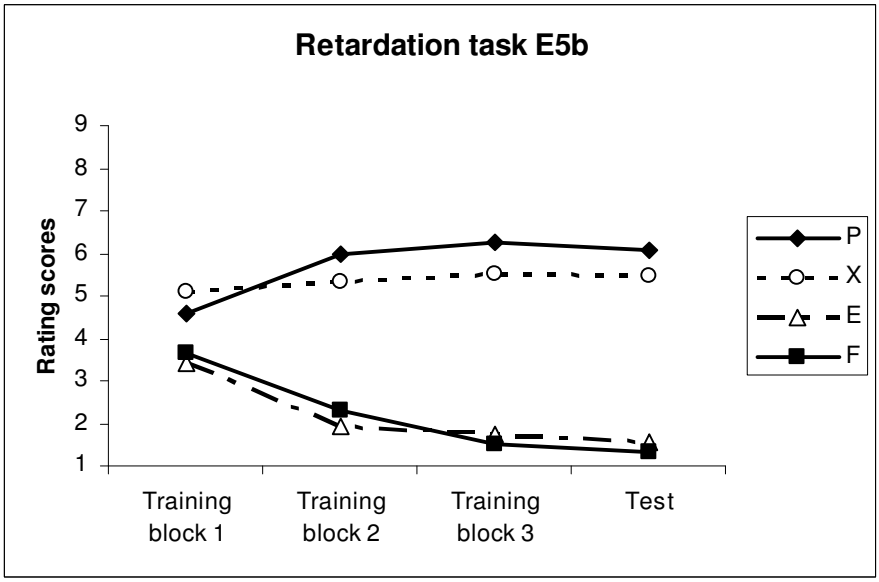


Figure 2.43 Rating scores for P+/–, X+/–, E– and F– during the retardation task. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

Comparing experiment 5a and 5b, experiment 5a did not find the evidence that P had become a conditioned inhibitor in either summation or retardation tasks, but experiment 5b did find evidence that P had become a conditioned inhibitor in summation task. The experimental design and procedures were identical in the two experiments, and the only difference was the data collection time: the data of experiment 5a were collected during the university final examination period, and the data of experiment 5b were collected during the university summer holiday. The results suggested that stress during examination period among the participants affected their CI learning performance.

An independent t–test revealed that the BIS scores were significantly different during and after the undergraduates' examination period, $t(62)=2.01$, $p=0.05$. The BIS scores were significantly higher during the examination period (M=33.72, SD=31.36), than during the summer holidays (M=22.50, SD=3.43). Previous research suggested that people with a higher BIS score were vulnerable to states of anxiety and other negative affects (Fowles, 1980, 1993; Gray 1985). The present

experiments found that people with higher BIS score (high anxiety level) performed worse in the CI learning summation task, but not in the excitatory learning task. The results may suggest that higher anxiety level would negatively correlate to CI learning.

2.8 Discussion

The CI learning procedures were designed and refined in the 5 CI experiments. The learning of CI was confirmed by the results of the summation tests, specifically by the transfer of inhibition to an excitatory CS not previously presented with the conditioned inhibitor during training (stimulus C in the present study). Importantly the training history of the critical test stimuli X and P was identically matched in all respects apart from the fact that P was only trained as an inhibitor – both were previously non-reinforced in the compound stimulus presentations on an equivalent number of trials. The only difference was that during the training stage P but not X was presented with a stimulus (A) that was reinforced during the pre-training stage, so that P uniquely specified that an otherwise expected reinforcement would not now occur. Moreover, P and X were fully counterbalanced, and the critical comparison stimuli (CP and CX) were overall well-matched, in that there were no pre-existing differences in the ratings. In the present study this CI effect was clearly demonstrated in the summation task.

It was unexpected that the results did not confirm the CI effects in the retardation test. However, the lack of CI evidence in the retardation task would not negatively impact on exploring the CI effects in relation to individual differences and disorder. It was because the experimental design of the summation task was well controlled. The non-significant results from the retardation task may be due to participants learning too fast in the

task, and the differences between the two stimuli were evidenced by - a "ceiling" effect. The maximum positive rating on the scale was 9, but for the simple associative learning task (the pre-training stage) the maximum positive rating was around 8 in the summation procedures. However, P and X was partially reinforced during the retardation training, the maximum positive rating was around 6. Participants started to rate P and X between 4 or 5, and the ratings quickly reached to the maximum positive score – 6 at the second training block, so it is hard to see the evidence of CI effect in the task. For example, in figure 2.37 and 2.43, it can be seen that the rating of conditioned inhibitor (P) was lower than that of pseudo inhibitor (X) in the first retardation training block. Nevertheless, the two learning curves soon reached a similar level, and even the rating of P was slightly higher than those of X in experiment 5b. Up to date, there are no published studies which have reported CI effects evidenced in both summation and retardation procedures in humans. Presumably, researchers have not found a good way to demonstrate the CI effects in humans by a retardation procedure.

The results in experiment 5 may suggest that higher anxiety levels would negatively correlate to CI learning. The negative correlation between BIS scores and CI learning could be relevant to our understanding of a wide range of disorders including, conduct disorder, anxiety or depressive disorder, OCD, ADHD, as well as schizophrenia. Further experiments will test the association between inhibitory learning and clinical groups, including people with schizophrenia, personality disorders and psychopaths.

Chapter III: Evaluative Conditioning (EC) (E6-8)

3.1 Introduction

Conditioned inhibition is a type of classical conditioning (CC) – a procedure in which an initially neutral stimulus (conditioned stimulus or CS) is repeatedly paired with an unconditioned stimulus (US). Subjects can learn that the CS is a signal for the US (Pavlov, 1927). Sometimes a CS not only signals the US, but can substitute for the US, so if a CS can substitute for the affective properties of the US, then it becomes pleasant or unpleasant itself - and that is evaluative conditioning (EC). Evaluative conditioning is usually conceived as a variety of classical conditioning, which refers to the phenomenon when a neutral stimulus is paired with a stimulus that has strong affective properties; these properties often appear to be transferred to the neutral stimulus (Levey & Martin, 1975).

Both classical conditioning and conditioned inhibition are forms of associative learning, which is learning about the association or relationship between events that occur together. The procedures of evaluative conditioning and classical conditioning obviously share similarities, therefore, many scientists believe that evaluative conditioning is an important variant of classical conditioning, and that they should be viewed as a similar learning phenomena (for a overview, see De Houwer, Thomas & Baeyens, 2001). However, Levey and Martin (1987) argued that the process and representational structure underlying evaluative conditioning are completely different from those involved in classical conditioning, and they suggested a different theory: The subject's evaluative reaction evoked by the US is transferred to the CS, then the CS itself becomes liked or disliked. One of the reasons Martin and Levey can sustain their claim is because EC seems to have different characteristics from CC. For example, other researchers suggested that the basic associative phenomena like extinction are not evident in EC, so CC and EC are different learning

phenomena (e.g. Baeyens, Crombez, van den Bergh & Eelen, 1988; De Houwer, et al., 2001;).

According to Rescorla-Wagner's model (1972), an associative learning equation can be described as follows:

$$\Delta V = \alpha\left(\lambda - \sum V\right)$$

ΔV = the change in the strength of association during a trial.

α = the salience of the CS (bounded by 0 and 1, where 0 indicates that the CS attracts no attention and 1 indicates that it attracts maximum attention.)

λ = the maximum conditioning possible for the US

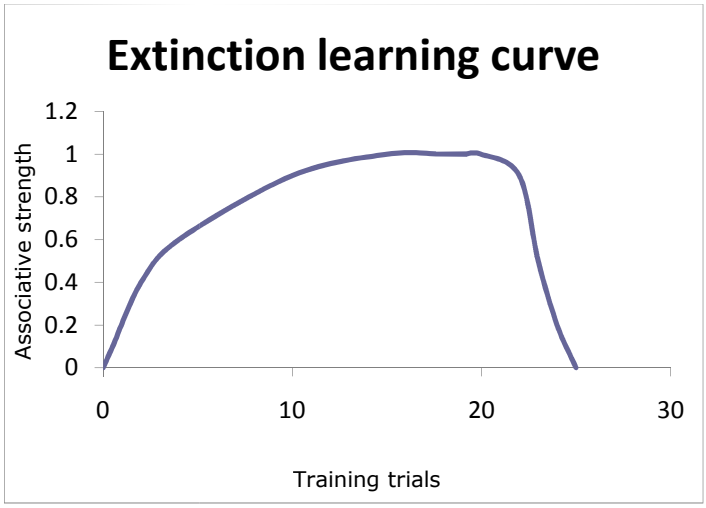
$\sum v$ = the current associative strength of all the CSs that are present

From the equation, if subjects are training A+ during the extinction, then A reaches asymptote. However, learning stops when $(\lambda-\Sigma v)=0$, therefore conditioning stops when A has a strength of λ (as US is present). Then subjects are given A- training trials, so its associative strength drops. Learning stops when $(\lambda-\Sigma v)=0$; as $\lambda=0$ on extinction trials (because nothing happens), then learning stops when Σv (i.e. associative strength of A, because only A is present) is 0.

During the CI learning task, if subjects are training A+, again A reaches asymptote; learning stops when $(\lambda-\Sigma v)=0$; so conditioning stops when A has a strength of λ (as US is present). This is just like the first part of extinction. Then if subjects are training AB- as well as A+; learning on AB trials again stops when $(\lambda-\Sigma v)=0$, and here Σv refers to BOTH A and B. But

A started off at λ; so learning stops when the sum of λ and the strength of B=0, so that leaves B with -λ strength.

According to Rescorla-Wagner's theory (1976), extinction is a type of inhibitory learning - acquisition of negative associative strength. If extinction does exist in EC learning, then both EC and CI learning tasks should involve learning the negative associative strength. Figure 3.1 illustrates an example of extinction and CI learning curves, for extinction ΔV should equal 0, but for CI learning, ΔV equals -1. Therefore, if CI effect is found in an EC rating task, we can conclude extinction in EC.



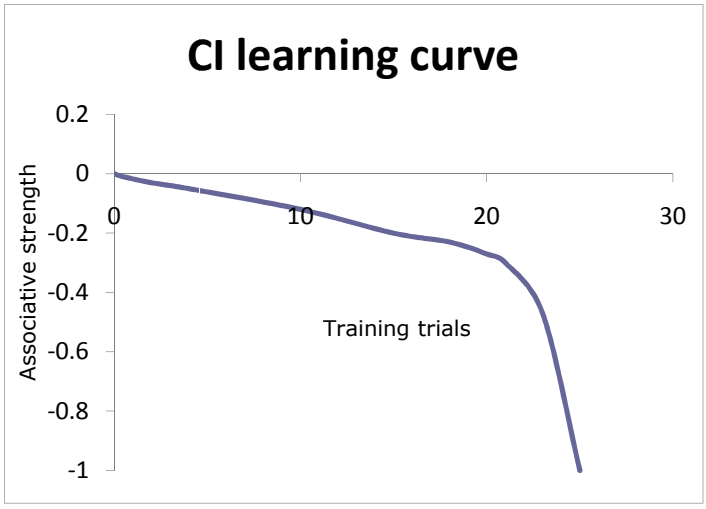


Figure 3.1 Example of extinction and CI learning curves.

Experiment 4 provided a demonstration of CI effects in humans using a summation test. If the same results can be found in EC experimental procedures, then it not only implies that the extinction exists in the EC experiment, but also suggests that both CI and EC are a similar type of associative learning phenomenon. The study of evaluative conditioning does not closely relate to my PhD research area. However, I had to wait for a research ethic permission for my CI study in clinical participants from the NHS Research Ethics Committee; at the same time, in the light of examining the scientific debate and exploring classical conditioning and evaluative conditioning learning phenomena, experiments 6, 7 and 8 were conducted.

Compared with CI experiments, EC experiments used similar rating trials. For these rating trials, participants gave a rating score which indicated whether they liked or disliked CSs, rather than guessing or predicting the valence of USs. The rating scale was slightly changed compared with the CI experiments – a rating of 9 meant the participant liked the CSs, 5 meant neither liked nor disliked the CSs, 1 meant they disliked them. The EC experimental design was based on the previous CI experiment 4.

3.2 Experiment 6: EC experiment (CSs and USs were presented sequentially)

3.2.1 Methods

All details not mentioned were identical to those of experiment 4.

3.2.1.1 Participants

Experiment 6 was conducted on an opportunity sample of 16 students at the University of Nottingham (7 males, and 9 females), with a mean age of 24.25, range from 19 to 35 years. All participants were paid £2 as their

inconvenience allowance. All experimental procedures in the chapter conformed to the requirements of the Ethics Committee at the School of Psychology, The University of Nottingham.

3.2.1.2 Stimuli and materials

There were no questionnaires for participants.

3.2.1.3 Procedure

The participants only took the computer learning task during the experiment. The information sheet was slightly changed (see appendix 4). Participants were informed that "Mogwai" would bring various images, and their task was to pay close attention to the images on the screen and then answer any questions about them.

The instructions were changed in the experiment, instead of asking participants to guess or predict the valence of a US, the present experiment required participants to choose a number which represented their liking of the CSs. Figure 3.2 shows the rating trial for experiment 6.

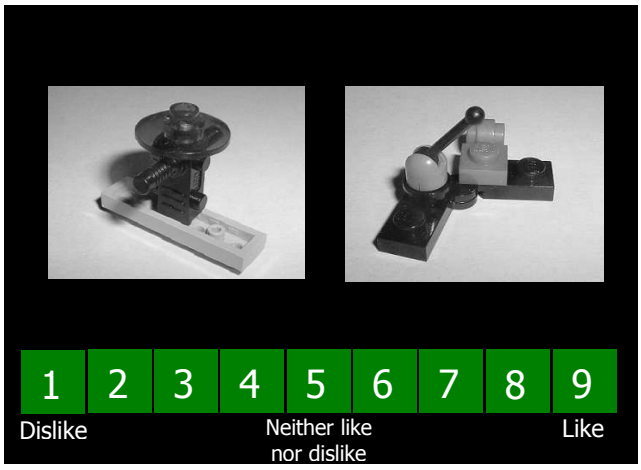


Figure 3.2 The example of a rating trial which was shown to participants. According to the two Lego blocks, participants needed to chose a number which represented whether they liked the two Lego blocks or did not like them.

At the pre-test stage, participants received the following instructions on the screen:

> "Here is the magical cat, Mogwai. She will show you a series of images. Please pay close attention to what you see. You will be asked occasionally to judge how much you like or dislike some of these images. Please answer as quickly and accurately as possible.
>
> Please use the mouse to click on a number from 1 to 9. Number 9 means you like the image(s), 5 means neither like nor dislike, 1 means you dislike the image(s).
>
> *Click any button on the mouse to continue*"

At pre-training and training stages, participants received the following instructions on the screen:

> "Now Mogwai will show you another series of images. Please pay close attention to what you see. You will be asked occasionally to judge how much you like or dislike some of these images. Please answer as quickly and accurately as possible.
>
> Please use the mouse to click on a number from 1 to 9. Number 9 means you like the image(s), 5 means neither like nor dislike, 1 means you dislike the image(s).
>
> *Click any button on the mouse to start observation*"

At test stage, participants received the following instructions on the screen:

> "Mogwai will now show you a final series of images. Please pay close attention to what you see. You will be asked occasionally to

judge how much you like or dislike some of these images. Please answer as quickly and accurately as possible.

Please use the mouse to click on a number from 1 to 9. Number 9 means you like the image(s), 5 means neither like nor dislike, 1 means you dislike the image(s).

Click any button on the mouse to continue"

3.2.2 Results

3.2.2.1 Pre-test stage

Figure 3.3 shows the rating scores during the pre-test stage. There was not much difference between the ratings of stimuli, and most of them were around 5. An ANOVA with discrimination (AZ or AP v. CY or BX) and reinforcement as factors, revealed no significant effects or interactions, the largest $F(1,15)=2.37$, $p=0.15$. The ratings of CP were slightly higher than those of CX, but there was no significant difference in responding to these test compounds $F(1,15)=1.95$, $p=0.07$, suggesting no pre-existing biases for the CSs.

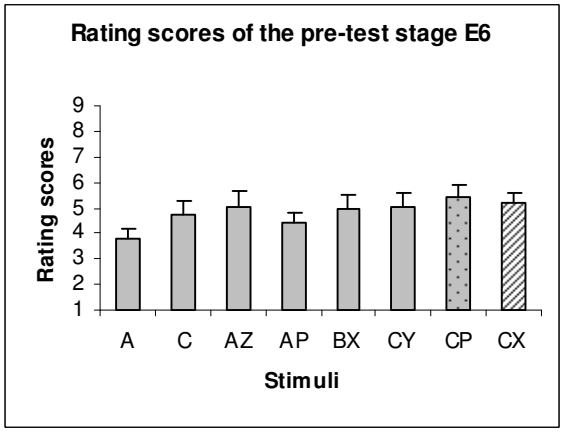


Figure 3.3 Rating scores for A, C, AZ, AP, BX, CY, CP and CX at the pre-test stage during experiment 6. A rating of 9 reflected that participants liked the CSs' picture(s), 1 indicated that participants disliked the CSs' picture(s), and 5 suggested that they neither like nor dislike the CSs' picture(s).

3.2.2.2 Pre-training stage

During the pre-training stage, ratings of all stimuli remained at a similar level, between 4 and 5 (see figure 3.4). An ANOVA with discrimination (A or U v. C or V), reinforcement and pre-training block (1-6) as factors, revealed nothing was significant, the largest $F(1,15) = 1.96$, $p = 0.18$. It is suggested that participants did not learn the discrimination during the pre-training stage. Clearly if participants did not learn the simple associative learning task, they would not learn more advanced associative learning task – CI learning task during the training stage, therefore, the analysis of training stage and test stage are not reported further.

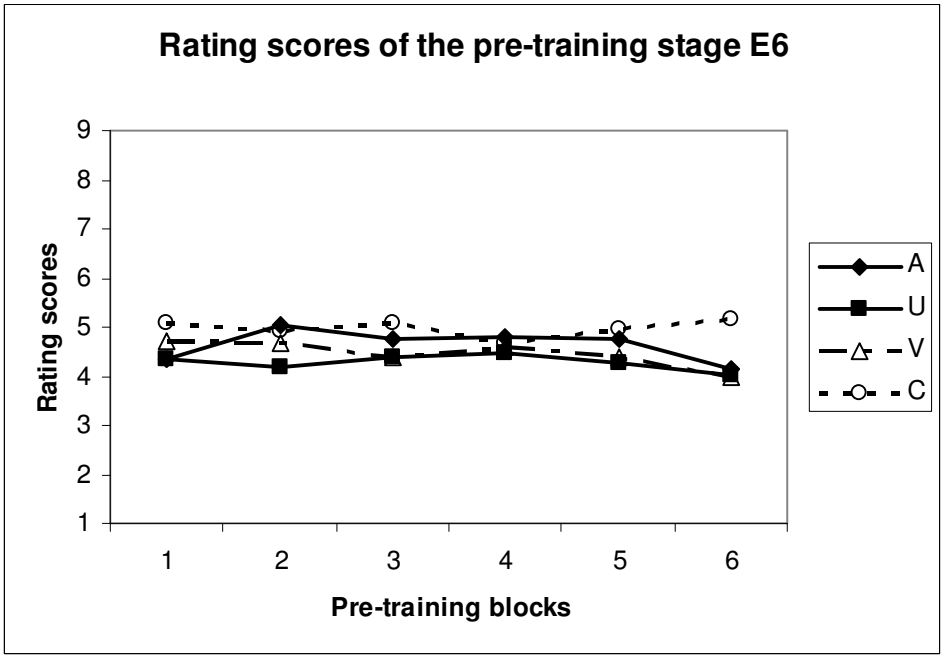


Figure 3.4 Rating scores for A+, U–, V– and C+ at the pre-training stage during experiment 6. A rating of 9 reflected that participants liked the CSs' picture(s), 1 indicated that participants disliked the CSs' picture(s), and 5 suggested that they neither like nor dislike the CSs' picture(s).

3.2.3 Discussion

Interestingly the experiment failed to show basic discrimination between the reinforced and the non-reinforced trials in the pre-training stage. This might have been due to the different tasks (questions) in the CI and EC experimental procedures. Despite CS and US being presented sequentially in both experimental procedures, the question for the participants was

different in the experiments. During the CI experiments, participants gave rating scores to guess or predict the valence of a following US, and the number button was presented underneath the CSs' pictures. In experiment 6 (EC experiment), participants gave the ratings to indicate whether they liked or disliked the CSs, and then a US was presented immediately after the CSs. It can be seen clearly that in the CI experiment, participants were asked about what was going to follow the CS - drawing attention to what follows; whereas in the EC experiment, participants were asked a question about the CS - so in a way distracting them from what follows. This could be the possible reason for why experiment 6 failed to demonstrate the basic discrimination in the first training stage. During the next experiment, the CSs and the USs were presented simultaneously, in the hope that participants could be aware of the link between the CSs and the USs, therefore learning of the basic discrimination could be improved.

3.3 Experiment 7: EC experiment (CSs and USs were presented simultaneously)

3.3.1 Introduction

Experiment 7 presented the CS and US pictures simultaneously, participants still gave a rating score to indicate their affections towards CS pictures. In order to present CSs and USs simultaneously on the screen, the original rating trials were slightly changed – all rating buttons were presented on right hand side of the screen and the pictures of CSs were on the left (see figure 3.5). A new type of trial – training trial was added. For the training trials, the position of CSs were same as the rating trials, but a US was presented on the right hand side of the screen (see figure 3.6). If only one CS was presented, the position of the CSs was counterbalanced (either at left top corner or at left bottom corner on the screen).

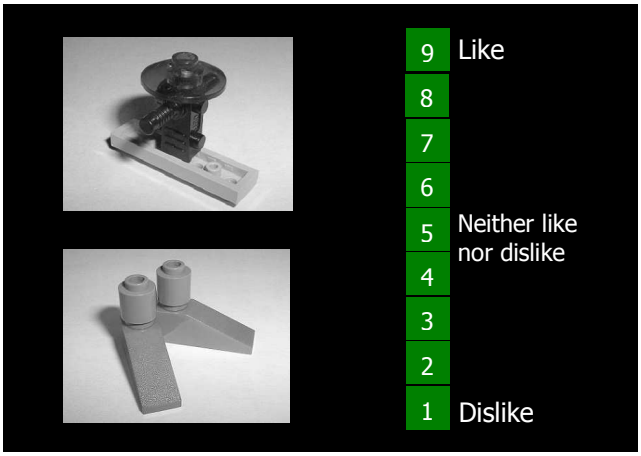


Figure 3.5 The example of a rating trial which was shown to participants. According to the two Lego blocks, participants needed to chose a number which represented if they liked the two Lego blocks or they do not like them.

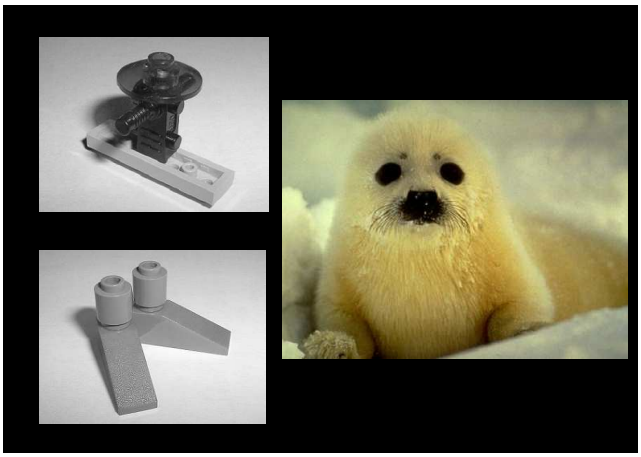


Figure 3.6 The example of a training trial. Participants were told that they should pay close attention to what they saw.

3.3.2 Methods

All details not mentioned were identical to those of experiment 6.

3.3.2.1 Participants

Experiment 7 was conducted on an opportunity sample of 16 students at the University of Nottingham (9 males, and 7 females), with a mean age of 22.56, range from 18 to 36 years.

3.3.2.2 Procedure

To avoid affective biases (if a rating trial was immediately followed by a training trial, participants might give a rating score that was just based on the affection of the preceding US), experiment 7 presented a number of training trials followed by a number of rating trials during two training stages.

The pre-training stage still comprised 6 pre-training blocks; however, each block contained 8 training trials and 8 rating trials (A+, U-, V-. and C+, two trials for each). Each training trial was shown for two seconds on the screen (no gap between the trials). During one pre-training block, after participants observed 8 training trials, rating trials followed. Participants should click on a numbered button of the rating trial, and the next one was immediately shown on the screen.

Training stage comprised of 8 training blocks. At first, 4 blocks, each block contained 6 training trials and 6 rating trials (1×AZ+, 2×AP–, 1×CY+, 2×BX–); in the last 4 blocks, each block contained 4 training trials and 4 rating trials (1×AZ+, 1×AP–, 1×CY+, and 1×BX). Therefore the total number of training trials was the same as experiment 4, 5 and 6. During a training block, after the participants has observed 6 or 4 training trials, the rating trials followed. Again, they needed to click on a numbered button of the rating trial, and the next rating trial was immediately shown on the screen.

The instructions for experiment 7 were same to those of experiment 6.

3.3.3 Results

3.3.3.1 Pre-test stage

Figure 3.7 shows the rating scores during the pre-test stage, which were quite similar for all stimuli, and were all around 4 or 5. An analysis of variance with discrimination (AZ or AP v. CY or BX) and reinforcement as factors revealed no significant effects or interactions, the largest $F(1,15)=2.71$, $p=0.12$. There was no significant difference in responding to the test compounds (CP v. CX), $F<1$.

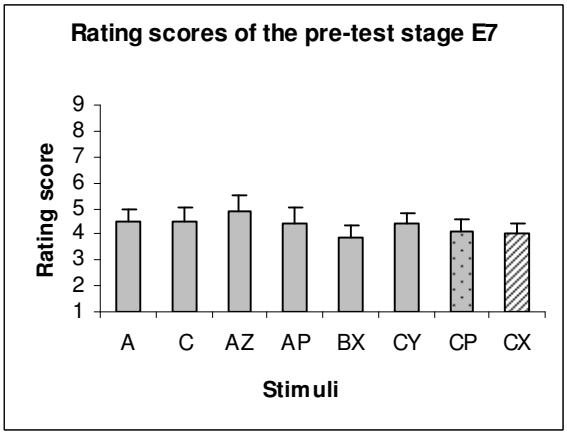


Figure 3.7 Rating scores for A, C, AZ, AP, BX, CY, CP and CX at the pre-test stage during experiment 7. A rating of 9 reflected that participants liked the CSs' picture(s), 1 indicated that participants disliked the CSs' picture(s), and 5 suggested that they neither like nor dislike the CSs' picture(s).

3.3.3.2 Pre-training stage

During the pre-training stage, all ratings of CSs were quite steady (see figure 3.8). An ANOVA with discrimination (A or U v. C or V), reinforcement and pre-training block (1-6) as factors, revealed a main effect of reinforcement $F(1,15)=4.85$, $p=0.04$, but no other significant main effects and interactions, the largest $F(1,15)=1.86$, $p=0.11$, suggesting participants gave significantly different ratings to reinforced and non-reinforced stimuli.

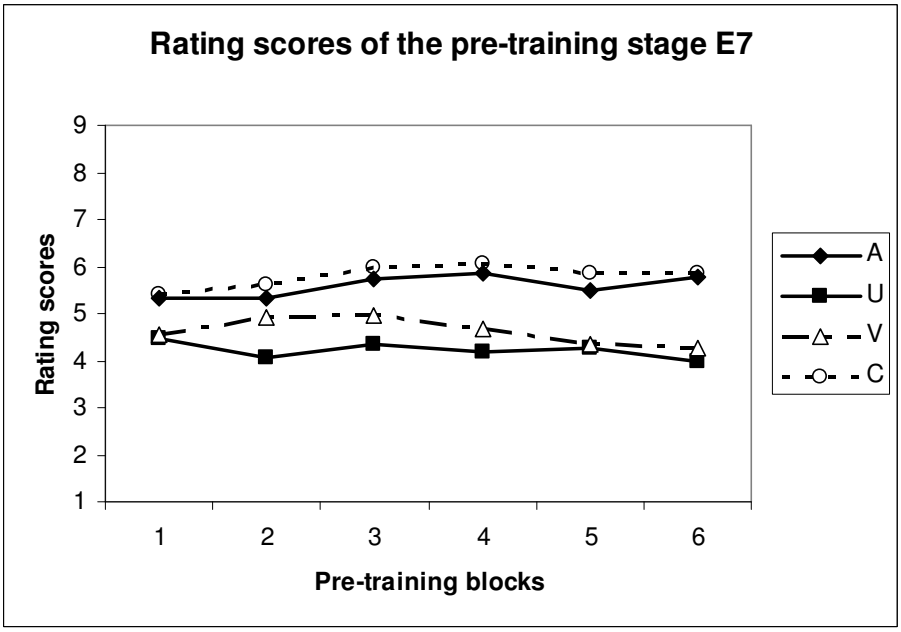


Figure 3.8 Rating scores for A+, U–, V– and C+ at the pre-training stage during experiment 7. A rating of 9 reflected that participants liked the CSs' picture(s), 1 indicated that participants disliked the CSs' picture(s), and 5 suggested that they neither like nor dislike the CSs' picture(s).

3.3.3.3 Training stage

During the training stage, the rating of AZ and CY very slightly increased, but the rating of BX and AP were maintained at the same level over training (see figure 3.9). An ANOVA with discrimination (AZ or AP v. CY or BX), reinforcement and training block (1-8) as factors, revealed no main effect of either training blocks $F(7,105)=2.02$, $p=0.06$, or discrimination $F<1$, but the main effect of reinforcement was significant $F(1,15)=9.90$, $p=0.007$. Furthermore the interaction between training block and reinforcement was also significant $F(7,105)=4.55$, $p<0.001$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. The simple main effects revealed that there was an effect of block on reinforced trials $F(7,105)=4.10$, $p<0.001$, but not on non-reinforced trials $F(7,105)=1.14$, $p=0.34$. The simple main effects also revealed that the differences between reinforced and non-reinforced trials were not significant on any training blocks, the largest $F(1,15)=2.32$, $p=0.15$.

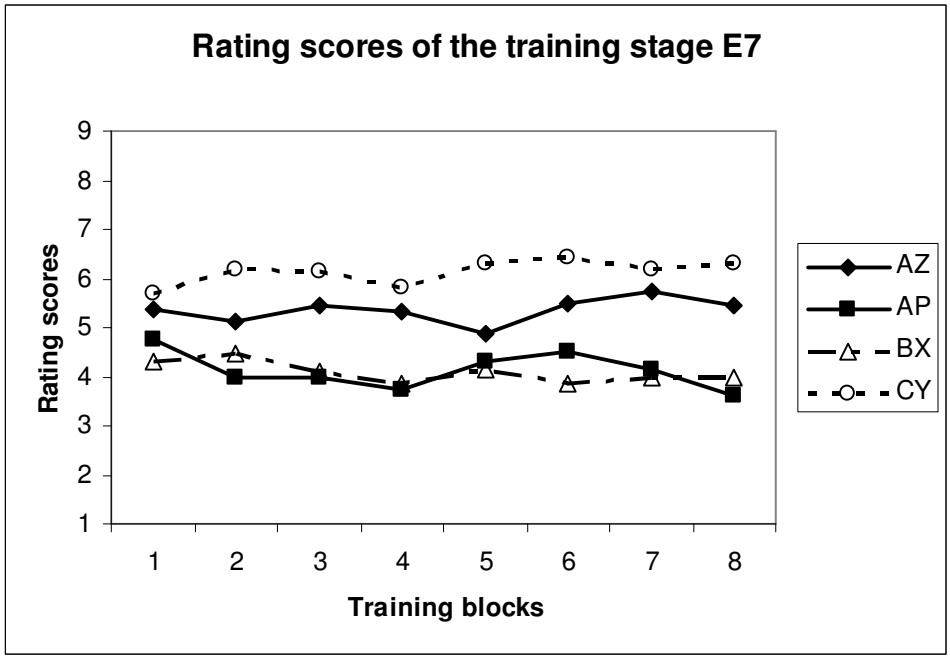


Figure 3.9 Rating scores for AZ+, AP–, BX– and CY+ at the training stage during experiment 7. A rating of 9 reflected that participants liked the CSs' picture(s), 1 indicated that participants disliked the CSs' picture(s), and 5 suggested that they neither like nor dislike the CSs' picture(s).

3.3.3.4 Test stage

Figure 3.10 shows the rating scores during the test stage. It can be seen that the ratings of reinforced trials A, AZ and CY were higher than those of other stimuli, but the rating of C was still around 5. For the non-reinforced trials, the ratings of AP and BX slightly dropped, furthermore, the ratings of CP and CX numerically was in the right direction. An ANOVA with discrimination (AZ or AP v. CY or BX) and reinforcement as factors, revealed no main effect of discrimination $F<1$. However, there was a significant effect of reinforcement $F(1,15)=10.37$, $p=0.006$, suggesting participants gave significantly different ratings to reinforced and non-reinforced stimuli. There was no significant two-way interaction $F(1,15)=3.35$, $p=0.09$.

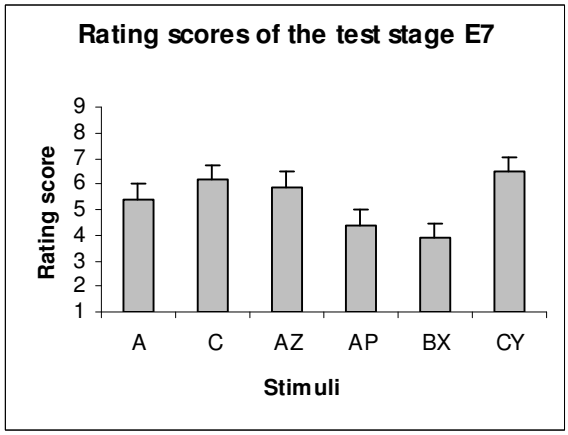


Figure 3.10 Rating scores for A+, C+, AZ+, AP–, BX– and CY+ at the test stage during experiment 7. A rating of 9 reflected that participants liked the CSs' picture(s), 1 indicated that participants disliked the CSs' picture(s), and 5 suggested that they neither like nor dislike the CSs' picture(s).

Figure 3.11 shows the rating scores of two critical stimuli – CP and CX before and after the training. At the pre-test stage, the ratings of CP and CX were very similar; however at the test stage, the ratings of CP were lower than these of CX. An ANOVA with stage (pre-test and test), and stimulus (CP v. CX) as factors, revealed a main effect of stage $F(1,15)=4.59$, $p=0.05$, suggesting participants gave significantly different ratings before and after training. Nothing else was significant, the largest $F(1,15)=1.04$, $p=0.32$. However, numerically the ratings of CP and CX were in the right direction. The results could not provide evidence of CI effects in evaluative conditioning procedures in experiment 7.

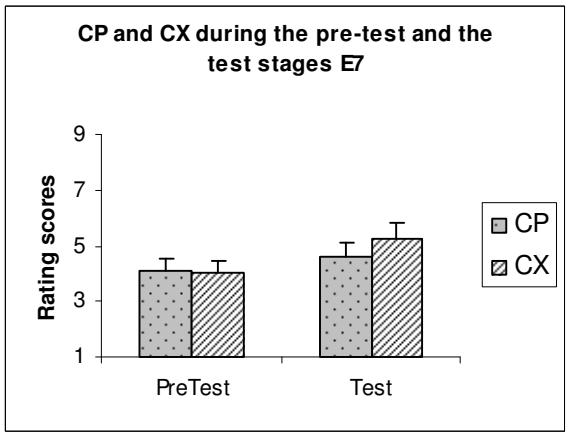


Figure 3.11 Rating scores for the key comparison stimuli CP and CX at the pre-test and the test stages during experiment 7. A rating of 9 reflected that participants liked the CSs' picture(s), 1 indicated that participants disliked the CSs' picture(s), and 5 suggested that they neither like nor dislike the CSs' picture(s). The pre-test ratings showed that the stimuli elicited similar ratings prior to conditioning. The test ratings did not confirm the presence of conditioned inhibition, which was shown as slightly higher ratings to CX than CP.

3.3.4 Discussion

Neither experiment 6 nor experiment 7 found evidence of CI effects in evaluative conditioning procedures. It did not matter whether the CSs and the USs were presented sequentially or simultaneously during the training. However, the results of experiment 7 were more encouraging than those of experiment 6. In experiment 7 at least participants learnt the basic discrimination during the training stages, and the discrimination was maintained in the test stage. Furthermore, comparing the two critical compounds (CP and CX), the ratings of CP were lower than those of CX at the test stage, which indicated that the ratings of CP and CX were numerically in the right direction at the test stage in experiment 7.

The purpose of present EC experiments was to find evidence that the inhibitory learning could occur in EC learning procedures, which would support the suggestion that the EC and CI learning phenomena were similar. However, compared with experiment 4 (which successfully found CI effects) we had to change the experimental procedure quite substantially in experiment 7, so that subjects could learn the basic EC discriminations. Maybe these changes were responsible for our inability to observe evaluative conditioning. In order to investigate this possibility the next experiment tested classical conditioning (CC) and EC learning in the same procedure, to confirm that it is possible to obtain CI in the EC task.

3.4 Experiment 8: Test CI in classical conditioning and EC learning in a same procedure

3.4.1 Introduction

Experiment 8 contained the rating trials of experiment 4 and experiment 6 together, which included two rating tasks for participants. One was to predict the valence of a US picture after a CS's presentation (E4), and

another was to indicate their liking of CS's picture (E6). The first question for the participants was "What type of picture will follow?", and participants were asked to guess or predict what kind of picture would follow the presentation of Lego blocks using a rating scale from 1 (neutral) to 9 (nice), with the rating 5 to reflect uncertainty. The second question for participants was "Do you like the above Lego block(s) or not?", and participants were asked to judge how much they like or dislike the pictures of CSs from 9 (like) to 1 (dislike), 5 as neither like nor dislike. The first rating score was called CC rating score, and the second rating score was called EC rating score.

3.4.2 Methods

All details not mentioned were identical to those of experiment 4.

3.4.2.1 Participants

Experiment 8 was conducted on an opportunity sample of 24 students at the University of Nottingham (13 males, and 11 females), with a mean age of 22.5, range from 19 to 27 years. Three participants were excluded from the experiment because of failing the pre-training stage for the CC ratings. All participants were paid £3 as their inconvenience allowance.

3.4.2.2 Procedure

During experiment 8, the instructions on the computer screen were slightly changed. Participants not only needed to guess and predict the valence of the US, but also needed to rate whether they liked or disliked the CSs (see appendix 5). In order to separate the CC and EC rating, a question appeared above the number buttons ("What type of picture will follow?" for CC rating trials; and "Do you like above Lego block(s) or not?" for EC rating trials) and the number buttons used were two different colours (green for

CC rating trials, and blue for EC rating trials) (see figure 3.12 and 3.13). After participants clicked on a number button to guess the US valence on the CC rating trial, the EC rating trial followed immediately. During the pre-training and training stages, compared with experiment 4, the US presentation time was increased from 1 second to 1.5 sec on the computer. The number of training trials was identical to those of experiment 4.

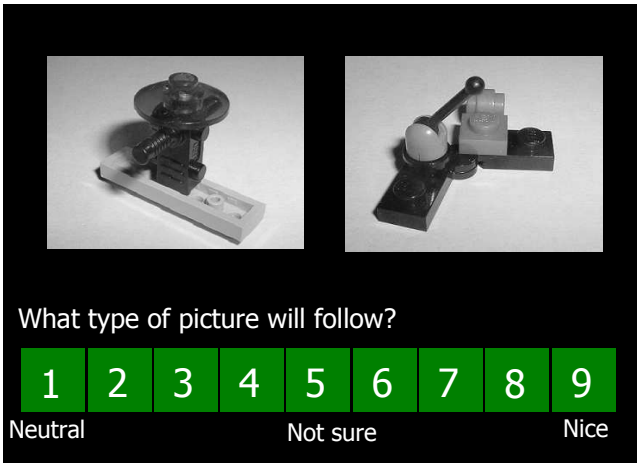


Figure 3.12 The example of a CC rating trial which was shown to participants. According to the two Lego blocks, participants need guess or predict the valence of a US followed this screen.

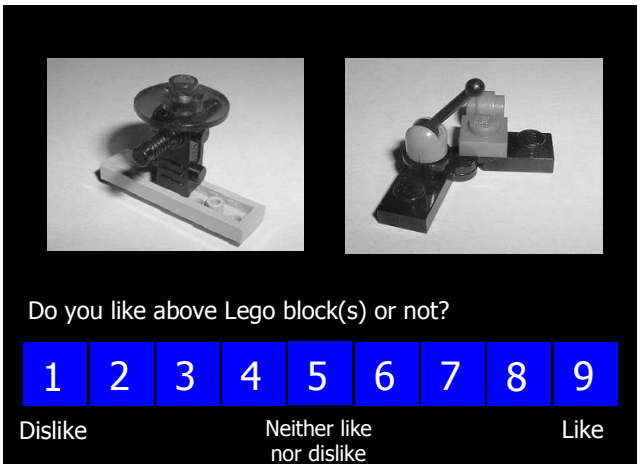


Figure 3.13 The example of an EC rating trial which was shown to participants. According to the two Lego blocks, participants need chose a number which represented they like or dislike the two Lego blocks.

3.4.3 Results and discussion

3.4.3.1 Pre-test stage

Figure 3.14 shows CC rating scores at the pre-test stage; most rating scores were between 4 and 5, but the ratings of AZ were slightly higher

than those of the other stimuli (above 5). Figure 3.15 shows EC rating scores during this stage, and the rating scores of all stimuli were very similar. In CC and EC ratings, an ANOVA with discrimination (AZ or AP v. CY or BX) and reinforcement as factors, revealed nothing was significant, the largest $F(1,23)=2.64$, $p=0.12$. ANOVA revealed no significant difference in responding to CP and CX on both CI and EC ratings, $F(1,23)=-0.58$, $p=0.57$; $F(1,23)=0.21$, $p=0.84$ respectively, suggesting no pre-existing biases on the critical compounds.

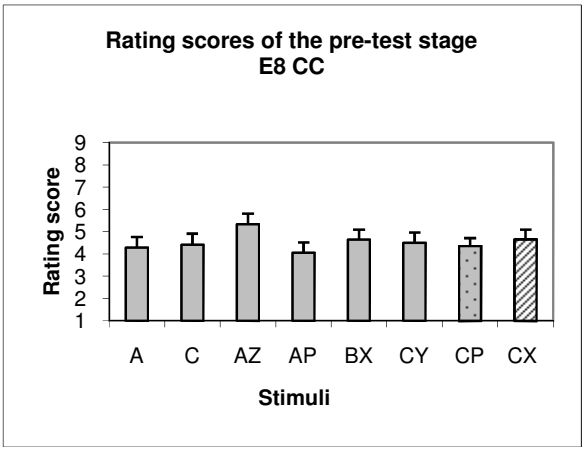


Figure 3.14 CC rating scores for A, C, AZ, AP, BX CY, CP and CX at the pre-training stage during experiment 8. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

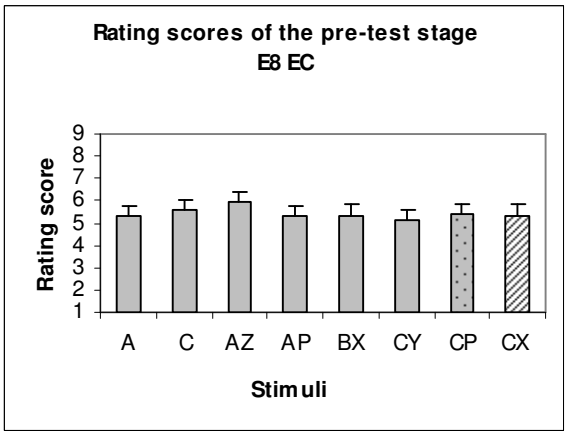


Figure 3.15 EC rating scores for A, C, AZ, AP, BX CY, CP and CX at the pre-training stage during experiment 8. A rating of 9 reflected that participants liked the CSs' picture(s), 1 indicated that participants disliked the CSs' picture(s), and 5 suggested that they neither like nor dislike the CSs' picture(s).

3.4.3.2 Pre-training stage

During the CC rating, A and C steadily increased, while those to U and V fell gradually (see figure 3.16). Participants appeared to learn the discrimination in this phase, an ANOVA with discrimination (A or U v. C or V), reinforcement and pre-training block (1-6) as factors, revealed no main effect of either pre-training block $F(5,115)=1.24$, $p=0.30$, or discrimination $F(1,23)=0.29$, $p=0.59$; however, the main effect of reinforcement was significant $F(1,23)=135.57$, $p<0.001$. The interaction between the pre-training block and reinforcement was significant $F(5,115)=16.99$, $p<0.001$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. The simple main effects revealed that there was an effect of block on both reinforced and non-reinforced trials, $F(5,115)=17.84$, $p<0.001$; $F(5,115)=8.05$, $p<0.001$ respectively. The simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant from second to sixth pre-training blocks, the smallest $F(1,23)=21.44$, $p<0.001$, but not on the first block, $F(1,23)=4.06$, $p=0.06$. Together these effects of reinforcement clearly demonstrated that participants learnt simple Pavlovian discrimination.

There were no other two-way or three-way interactions $Fs<1$.

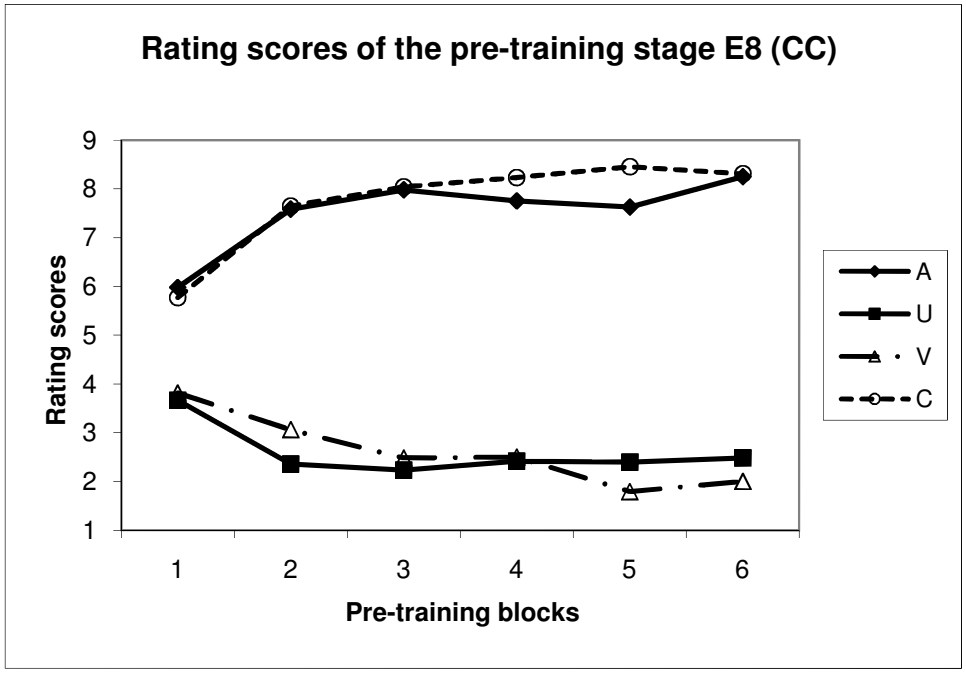


Figure 3.16 CC rating scores for A+, U–, V– and C+ at the pre-training stage during experiment 8. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

In the EC ratings, the reinforced stimuli A and C slightly increased, but for the non-reinforced trials U and V slightly decreased (see figure 3.17). An ANOVA with discrimination (A or U v. C or V), reinforcement and pre-training block (1-6) as factors, revealed no main effect of either pre-training block $F<1$, or discrimination $F(1,23)=2.92$, $p= 0.10$; however, the main effect of reinforcement was significant $F(1,23)=10.28$, $p=0.004$. The interaction between the pre-training block and reinforcement was significant $F(5,115)=3.41$, $p=0.007$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. The simple main effects revealed that there was the effect of block on reinforced approached significance $F(5,115)=2.17$, $p=0.06$, whereas that on non-reinforced trials was not, $F<1$. The simple main effects also revealed that the differences between reinforced and non-reinforced trials were not significant on any of pre-training blocks, the largest $F(1,23)=2.76$, $p=0.11$. In summary there was evidence from the main effect of reinforcement that subjects had successfully learned about A and C by this EC measure.

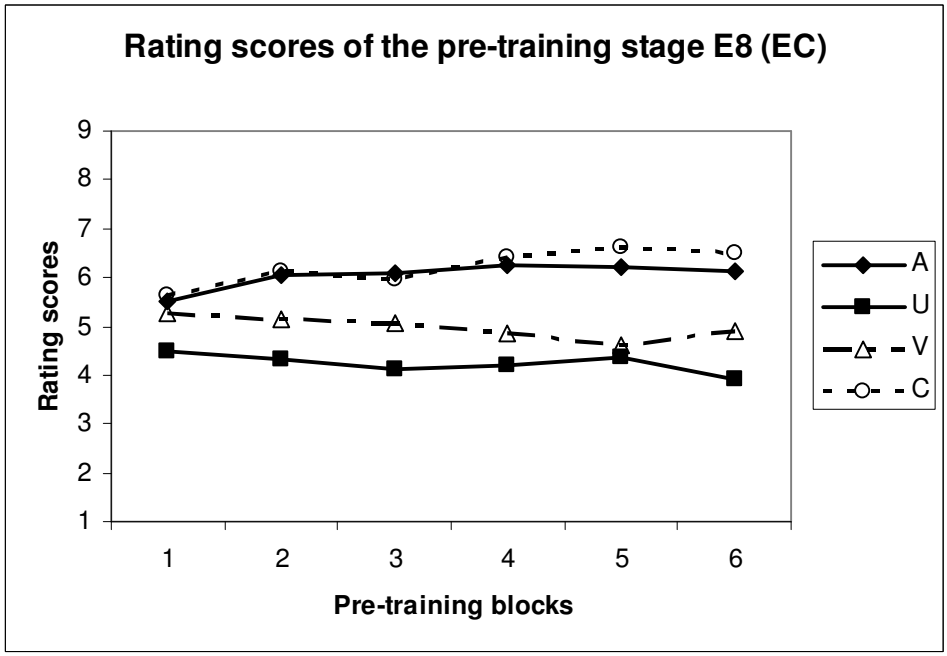


Figure 3.17 EC rating scores for A+, U–, V– and C+ at the pre-training stage during experiment 8. A rating of 9 reflected that participants liked the CSs' picture(s), 1 indicated that participants disliked the CSs' picture(s), and 5 suggested that they neither like nor dislike the CSs' picture(s).

3.4.3.3 Training stage

In the CC ratings of AZ and CY steadily increased, while those to AP and BX fell gradually (see figure 3.18), which suggested that participants had learned the critical discrimination. An ANOVA with discrimination (AZ or AP v. CY or BX), reinforcement and training block (1-2) as factors, revealed no main effect of discrimination $F<1$; however, the main effects of training block and reinforcement were significant, $F(1,23)=10.00$, $p=0.004$; $F(1,23)=119.49$, $p<0.001$ respectively. The interaction between training block and reinforcement was also significant, $F(1,23)=50.93$, $p<0.001$, suggesting the differences between reinforced and non-reinforced trials developed over the blocks. The simple main effects revealed that there was an effect of block on both reinforced and non-reinforced trials, $F(1,23)=15.25$, $p<0.001$; $F(1,23)=70.19$, $p<0.001$ respectively. The simple main effects also revealed that the differences between reinforced and non-reinforced trials were significant on both training blocks, $F(1,23)=37.79$, $p<0.001$; $F(1,23)=86.71$, $p<0.001$ respectively.

There were no other two-way or three-way significant interactions, all *Fs*< 1.

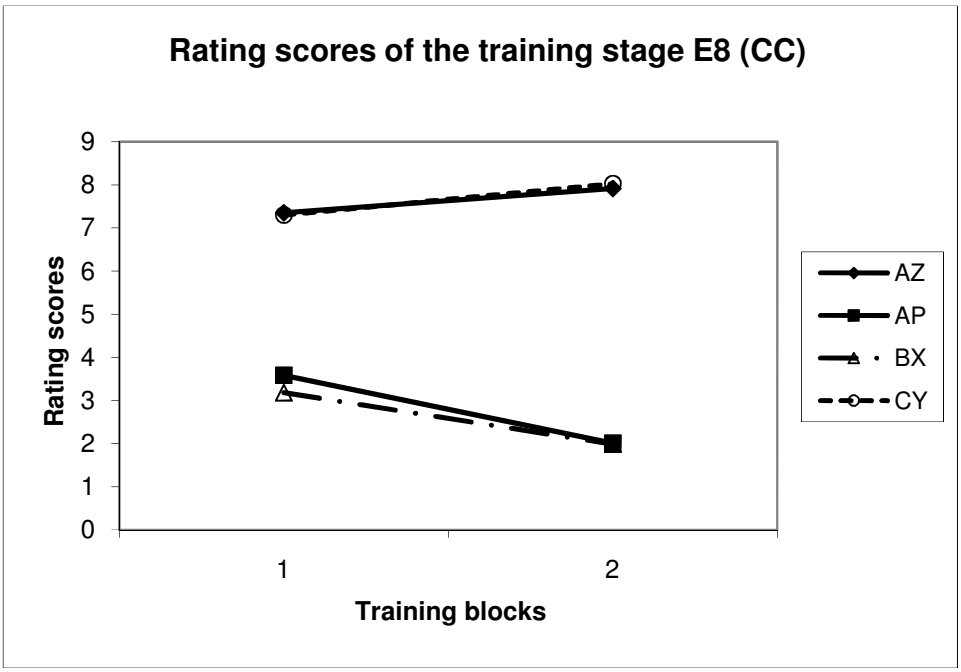


Figure 3.18 CC rating scores for AZ+, AP–, BX– and CY+ at the training stage during experiment 8. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

In the EC ratings, the scores did not change dramatically. The ratings of AZ and CY remained similar, while those to AP and BX fell gently (see figure 3.19). An ANOVA with discrimination (AZ or AP v. CY or BX), reinforcement and training block (1-2) as factors, revealed no main effect of discrimination $F<1$; however, the main effects of training block and reinforcement were significant, $F(1,23)=10.07$, $p=0.004$; $F(1,23)=10.49$, $p=0.004$ respectively.

There were no significant differences of two-way or three-way interactions, the largest $F(1,23)=3.59$, $p=0.07$.

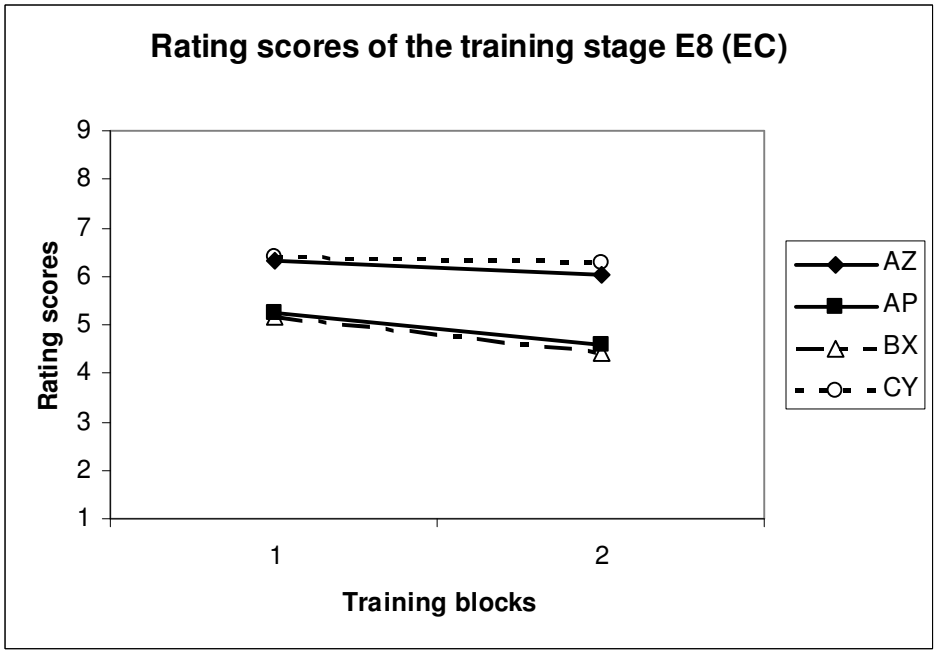


Figure 3.19 EC rating scores for AZ+, AP–, BX– and CY+ at the training stage during experiment 8. A rating of 9 reflected that participants liked the CSs' picture(s), 1 indicated that participants disliked the CSs' picture(s), and 5 suggested that they neither like nor dislike the CSs' picture(s).

3.4.3.4 Test stage

Figure 3.20 shows the CC rating scores at the test stage. Again, ratings of A and C remained high, and the discriminations were maintained. The latter observation was confirmed by the results of an ANOVA with discrimination (AZ or AP v. CY or BX), and reinforcement as factors, this revealed no main effect of discrimination $F(1,23)=1.54$, $p=0.23$. However the effect of reinforcement was significant $F(1,23)=66.96$, $p<0.001$, suggesting participants gave significantly different ratings to reinforced and non-reinforced trials. The interaction between these two factors was not significant $F<1$.

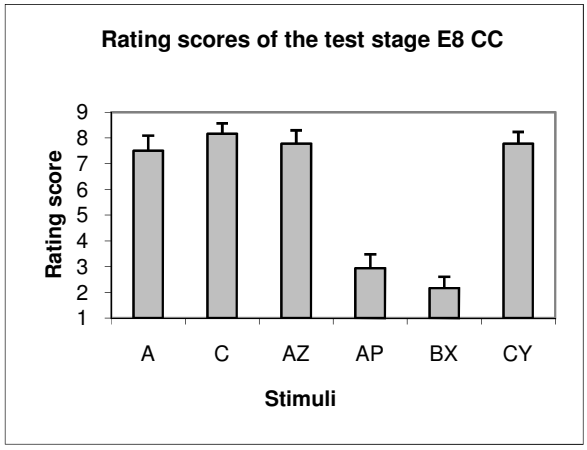


Figure 3.20 CC rating scores for A+, C+, AZ+, AP–, BX– and CY+ at the test stage during experiment 8. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

Figure 3.21 shows two critical stimuli CP and CX before and after training, it can be seen that the rating of CP was lower than CX during the test stage. An ANOVA with stage (pre-test and test) and stimulus (CP v. CX) as factors, revealed no main effect of stage $F<1$; however, the main effect of stimulus was significant $F(1,23)=6.65$, $p=0.02$. The interaction between the two factors was also significant $F(1,23)=4.83$, $p=0.04$. The simple main effects revealed that participants gave a significantly lower rating scores on CP than CX during the test stage $F(1,23)=10.06$, $p=0.004$, but no significant difference was found between CP and CX at the pre-test stage, $F<1$. The results suggest that a replication of the previous findings by summation task – P had become a conditioned inhibitor relative to strong control of pseudo inhibitor in experiment 8.

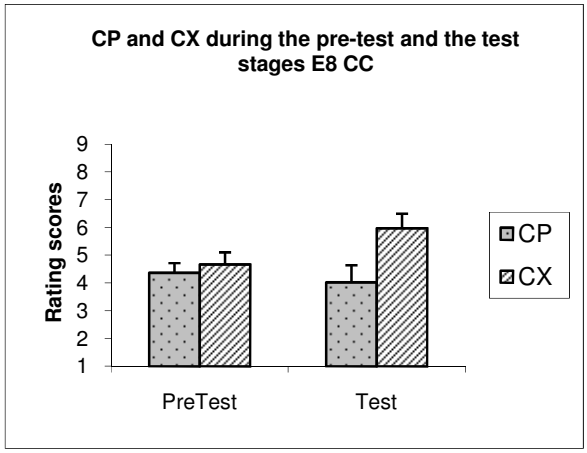


Figure 3.21 CC rating scores for the key comparison stimuli CP and CX at the pre-test and the test stages during experiment 8. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty. The pre-test ratings showed that the stimuli elicited similar ratings prior to conditioning. The test ratings confirmed the presence of conditioned inhibition, which was shown as higher ratings to CX than CP.

Figure 3.22 shows EC rating scores at the test stage, compared these with at the pre-test stage, the rating scores of reinforced stimuli (A, C, AZ, and CY) were a bit higher than these of non-reinforced stimuli (AP and BX). An ANOVA with discrimination (AZ or AP v. CY or BX) and reinforcement as factors, revealed no main effect of discrimination $F<1$; however the effect of reinforcement was significant $F(1,23)=8.72$, $p=0.007$, suggesting participants gave significantly different ratings to reinforced and non-reinforced trials. The interaction between these two factors was not significant $F(1,23)=1.42$, $p=0.25$.

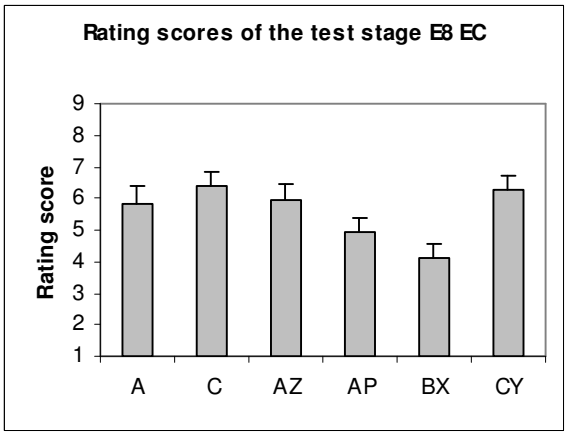


Figure 3.22 EC rating scores for A+, C+, AZ+, AP–, BX– and CY+ at the test stage during experiment 8. A rating of 9 reflected that participants liked the CSs' picture(s), 1 indicated that participants disliked the CSs' picture(s), and 5 suggested that they neither like nor dislike the CSs' picture(s).

Figure 3.23 shows two critical compounds CP and CX at the pre-test and the test stages. It can be seen that the rating of CP was slightly higher than those of CX before the training, but the rating of CP dropped after training to some extent. An ANOVA with stage (pre-test and test), and stimulus (CP v. CX) as factors, revealed nothing was significant, the largest $F(1,23)=1.09$, $p=0.33$. The results suggest no significant difference between CP and CX in EC learning procedures, but numerically it was in the right direction.

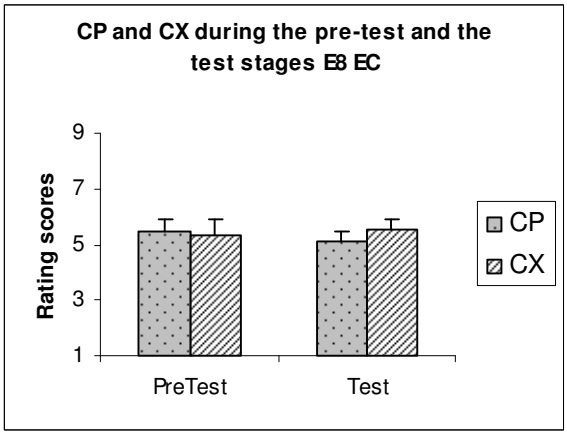


Figure 3.23 EC rating scores for the key comparison stimuli CP and CX at the pre-test and the test stages during experiment 8. A rating of 9 reflected that participants liked the CSs' picture(s), 1 indicated that participants disliked the CSs' picture(s), and 5 suggested that they neither like nor dislike the CSs' picture(s). The test ratings did not confirm the presence of conditioned inhibition, which was shown as the similar ratings at both pre-test and test stages.

3.5 Discussion

The experiment 6, 7 and 8 did not find CI effects in EC procedures. When the CSs and the USs were presented sequentially during the training in experiment 6, participants did not learn the basic discrimination, and showed no evidence of associative learning. Therefore the presentation of CS and US pictures was changed – during the training stage, thus in experiment 7, the CSs and the USs were presented simultaneously. The results indicated that participants learnt the basic discrimination, but CI effects were not evident in this EC learning procedure. Experiment 8 combined a CC rating and an EC rating in the same experimental

procedures, to confirm that it was possible to observe normal CI under these conditioning. The experiment confirmed that the CI effects were found in the CC rating, and this finding was a replication of experiment 4 and 5b. Experiment 8 also found that there was no evidence of the CI effects in EC procedures, although participants learnt the differences between reinforced and non-reinforced trials during both training stages, and these differences were maintained in the test stage, which suggested that they learned the EC discriminations as well as the CC discriminations.

The results of experiment 7 and 8 showed some evidence of learning in this evaluative conditioning task – participants learnt the basic discrimination between reinforced and non-reinforced trials. Furthermore, compared with the pre-test stage, the rating of CP was lower than these of CX in both EC experiments. Although this difference was not significant, at least numerically it was in the right direction. These results suggested that classical conditioning and EC learning are not totally the same and inhibition is hard to get in the EC learning procedure.

The 3 experiments in this chapter tried to examine whether CI could be demonstrated in EC learning procedures. If the rating of CP was significant lower than those of CX during the test stage in EC ratings, then it indirectly illustrates the extinction in EC learning phenomena. However the difference of CP and CX ratings was not significant in EC tasks, which makes it hard to conclude that the extinction exists in EC learning procedures. First, it was a harsh design to check the extinction by using test CI effects in the EC tasks, in which extinction is not only expected, but also required inhibition. The results of the present EC experiments may indicate that evaluative conditioning is more resistant to extinction than is expectancy learning,

which is also proposed by previous studies (Baeyens, Eelen & Crombez, 1995; Vansteenwegen, Francken, Vervliet, De Clercq & Eelen, 2006).

Chapter IV: Conditioned inhibitory learning in relation to disorder (E9-10)

4.1 Experiment 9: CI experiment in community-based schizophrenic patients

4.1.1 Introduction

Schizophrenia is a type of psychotic disorder. As introduced in chapter 1, according to DSM-IV, positive symptoms of schizophrenia include hallucinations, delusions and thought disorder (e.g. disorganized speech); and the common features of negative symptoms are affective flattening, alogia, or avolition. Cognitive dysfunction is a definitive aspect of schizophrenia (Bleuler, 1911; Kraepelin, 1919) that has been the subject of intensive investigation over the last six decades. During the 1960s, Venables (1960) introduced the concept of 'flooding' or sensory inundation in schizophrenia. At the same time, McGhie & Chapman (1961) suggested that schizophrenics show attentional, sensory and perceptual disorders. The information-processing abnormalities subsequently reported have been diverse; however one unifying theme which has emerged is that a variety of impairments seen in schizophrenia can be understood as deficits of inhibition (Beech et al., 1989; Daskalakis, Chen, Christensen & Kapur, 2000; Daskalakis et al., 2002; Enticott et al., 2008; Kaiser et al., 2008). For example, there have been a number of reports of abnormalities in prepulse inhibition (PPI) (Braff et al., 2001; Kumari et al., 2000; Kunugi et al., 2007; Weike et al., 2000) and latent inhibition (LI) (Baruch et al., 1988; Cohen et al., 2004; Gray et al, 1992; Guterman et al., 1996; Kathmann et al., 2000; Rascle et al., 2001; Sitskoorn et al., 1991; Swerdlow et al., 2005) in schizophrenic patients.

As introduced in chapter 1, PPI is demonstrated when a relatively weak version of the later presented startle stimulus (the pre-pulse) reduces the magnitude of the startle response (Graham, 1975), which suggests PPI is defined as a reduction of unconditioned responding. In contrast, LI has

been defined as the retardation in acquisition of conditioned responding which occurs when the CS is given non-reinforced pre-exposure prior to the conditioning stage (Lubow & Moore, 1959). Compared to controls (not pre-exposed to the CS), pre-exposed subjects are slow to form a subsequent association between the CS and an outcome (US); this retardation of learning constitutes LI. However, although so-called LI procedures effectively retard later learning they do not render the pre-exposed stimulus truly inhibitory (Baker & Mackintosh, 1977). PPI and LI are disrupted in several psychiatric diseases, such as schizophrenia, as well as in patients with antisocial and borderline personality disorders (Braff et al., 1978; Braff & Geyer, 1990; Braff et al., 1992; Braff et al., 1999; Geyer et al., 1990; Grillon et al., 1992; Herpertz & Koetting, 2005; Kumari et al., 2000; Weike et al., 2000).

If the cognitive impairments seen in schizophrenia can be characterised as a general impairment in inhibitory processes, then CI might well be affected. However, up to date there is no direct test of CI in schizophrenic patients, although a recent study of CI in human participants was reported, in which CI was found to be reduced in normal participants with high schizotypy scores (Migo et al., 2006). Therefore, it is expected that the inhibitory learning would be reduced or even abolished in schizophrenic patients compared to matched controls. Furthermore, the relationship between positive/negative symptoms of schizophrenia and associative learning performance also would be explored. This chapter reports the CI learning phenomenon in schizophrenic patients at a community-based setting. The successful computer-based CI learning summation test (experiment 4) was used as the CI learning task in these samples.

4.1.2 Methods

All details not mentioned were identical to those of experiment 4.

4.1.2.1 Participants

The experiment was conducted on 34 patients who came from three different adult mental health residential units in the city of Nottingham, UK. Diagnoses of schizophrenia met the International Classification of Diseases (ICD-10, 1992) criteria for schizophrenia. Patients also had a psychiatric assessment scale rating (KGV scale, Krawiecka, Goldberg & Vaughn, 1977) for symptom severity. Five participants were excluded because their symptoms did not meet the criteria for schizophrenia or because of co-morbidity with other mental illnesses. Additionally, four more participants were excluded because they failed the pre-training stage.

The matched controls were an opportunity sample of 28 participants, three of which were subsequently excluded because they failed the pre-training stage. The controls lived in the same county and were recruited at the University of Nottingham (ancillary staff), the Nottingham National Ice Centre and the Nottingham Trent FM Arena. Like the patients, the 25 control participants who completed the study were all without higher education and came from a variety of employment backgrounds, including unemployed, swimming instructor, driver, waiter, shop assistant, and university support staff. None showed any indication of mental illness or substance abuse. Table 4.1 shows the details of participants' age, gender, ethnicity and educational level. The allocation to the counterbalanced conditions of the experiment was identical in both groups.

Table 4.1 Summary details of the final sample of schizophrenic participants

	Schizophrenic patients (n=25)	**Controls (n=25)**
Age (years)	30.64	31.20
Range of age (years)	20-41	19-48
Gender (n=male/female)	18/7	18/7
Educational level	Up to A level*	Up to A level*
Ethnic	24 White and 1 Black	24 White and 1 Black

Note: * In the UK, the number of years in education required to achieve A level is 14.

This study was approved by NHS Research Ethics Committees (Derbyshire Research Ethics Committees, reference No. 08/H0401/65, September 2008). Procedures for testing the control participants were approved by the University of Nottingham, School of Psychology Ethics Committee. Control participants received £5 cash and schizophrenic participants received £10 cash as an inconvenience allowance.

4.1.2.2 Clinical measurement and medication of schizophrenic participants

Twenty out of 25 schizophrenic participants completed the Positive and Negative Syndrome Scale (PANSS) interview (Kay, Fiszbein & Opler, 1987) to assess their current symptoms. The PANSS is a 30-item rating scale, and includes three categories: positive symptoms, negative symptoms, and general symptoms, which was completed by clinically trained research staff. It was possible to complete the PANSS interview and the CI learning task on the same day for 11 participants. The other 9 participants completed the PANSS interview within two months of the CI task.

Participants were under a variety of antipsychotic medication regimes. All antipsychotics were calculated by chlorpromazine (CPZ) equivalent as a standard level. The calculation of the CPZ equivalent was based on: 100mg/day CPZ = 5mg/day olanzapine, 100mg/day clozapine, 200mg/day sulpiride, 1mg/day risperidone (Andreasen, Pressler, Nopoulos, Miller & Ho, 2010; Kane, 1996; Simon et al., 2000; Woods, 2003; Zito, 1994). Table 4.2 shows the details of medication and assessment for the schizophrenic participants.

Table 4.2 Medication and assessment details of the schizophrenic samples

Patient ID	Medication	Chlorpromazine Equivalent	PANSS Positive	PANSS Negative	PANSS General	PANSS Total
P1	Flupenthixol Olanzapine	1000	n/a	n/a	n/a	n/a
P2	Flupenthixol Clonazepam	800	n/a	n/a	n/a	n/a
P5	Clozapine	400	n/a	n/a	n/a	n/a
P6	Clozapine	400	n/a	n/a	n/a	n/a
P10	Risperidone	200	21	11	34	66
P11	n/a	n/a	14	8	19	41
P13	Olanzapine Valproate	400	13	28	27	68
P16	Clozapine Valproate	200	15	25	31	71
P17	Risperidone	400	11	32	27	70
P18	Risperidone	100	7	26	36	69
P19	Medication free	0	9	36	29	74
P20	Flupenthixol	600	n/a	n/a	n/a	n/a
P21	Medication free	0	18	11	24	53
P22	Sulpiride Clozapine	275	10	10	16	36
P23	n/a	n/a	19	17	37	73
P24	Olanzapine	250	8	16	18	42
P25	Clozapine	400	13	24	27	64
P26	Clozapine	150	14	13	30	57
P27	n/a	n/a	7	14	26	47
P28	n/a	n/a	20	17	28	65
P29	Clozapine	400	19	14	34	67
P31	Olanzapine	300	14	10	26	50
P32	Clozapine	300	20	21	32	73
P33	Clozapine	250	15	29	35	79
P34	Clozapine	350	15	11	26	52

Note: n/a = data not available.

4.1.2.3 Materials

Five questionnaires were used for the controls during the experiment (BIS/BAS, EPQ-RS, O-LIFE (Short), STB and UPPS).

4.1.2.4 Design and analysis

The number of participants was tried to equally allocate to 8 CSs counterbalanced groups; however, a total 9 patients were excluded from the study, the number of participants was not equal in the counterbalanced groups. Table 4.3 shows the number of participants in the counterbalanced groups. The controls shared the same counterbalanced pattern as schizophrenic patients.

Table 4.3 The number of schizophrenic participants in 8 counterbalanced groups.

Counterbalanced Groups	1	2	3	4	5	6	7	8
Number of participants	4	4	3	2	3	2	3	4

Note: Please see table 2.5 for details of the counterbalanced groups.

Statistical analyses were by mixed design analyses of variance (ANOVA). The within-subjects factors were identical to those of the CI experiments (E1-5), for example, discrimination (e.g. AZ or AP v. CY or BX), reinforcement (reinforced or not) and trial block. The between-subjects factor was diagnostic group (schizophrenic patients v. controls). Correlational analyses were used to examine the relationship between learning scores and (1) symptom profile as measured by PANSS scores and (2) antipsychotic medication dosage. For learning scores, a summary measure of excitatory learning was provided by the difference in mean ratings on C and V trials during the initial training stage (i.e. C-V). As C was the excitatory stimulus, the greater the C-V score, the higher the level of excitatory learning. A summary measure of CI was provided by the difference between the mean ratings on CX and CP trials given during the test stage (i.e. CX-CP). P was the putative inhibitor, and thus supposed to suppress the evaluation of C more than X; thus the greater the CX-CP score, the higher the level of inhibitory learning. Planned comparisons of the assessment score data were by t-test (ie. to compare the schizophrenic patients on typical and atypical antipsychotics).

4.1.2.5 Procedure

Before the experiment, each participant was invited to read an information sheet and sign a consent form. The documents were approved by NHS Research Ethics Committee. During the CI learning task, some of participants asked irrelevant questions. For example: Do you think a woman will love me? Do you know that I was a teacher before? They were

asked to try to focus on the task and to try to remember or guess which outcome (nice or neutral picture) was predicted by the Lego blocks.

4.1.3 Results

4.1.3.1 Pre-test stage

Figure 4.1 shows the rating scores during the pre-test stage. In both groups, the scores of AZ and CY were around 6, which were slightly higher than those of other stimuli (around 5). ANOVA performed on the pre-test ratings of the two critical comparison stimuli CP and CX, with diagnostic group (schizophrenic patients v. controls) as a factor, confirmed that there was no pre-existing bias in responding to these compounds, the largest $F(1,48)=1.73$, $p=0.19$.

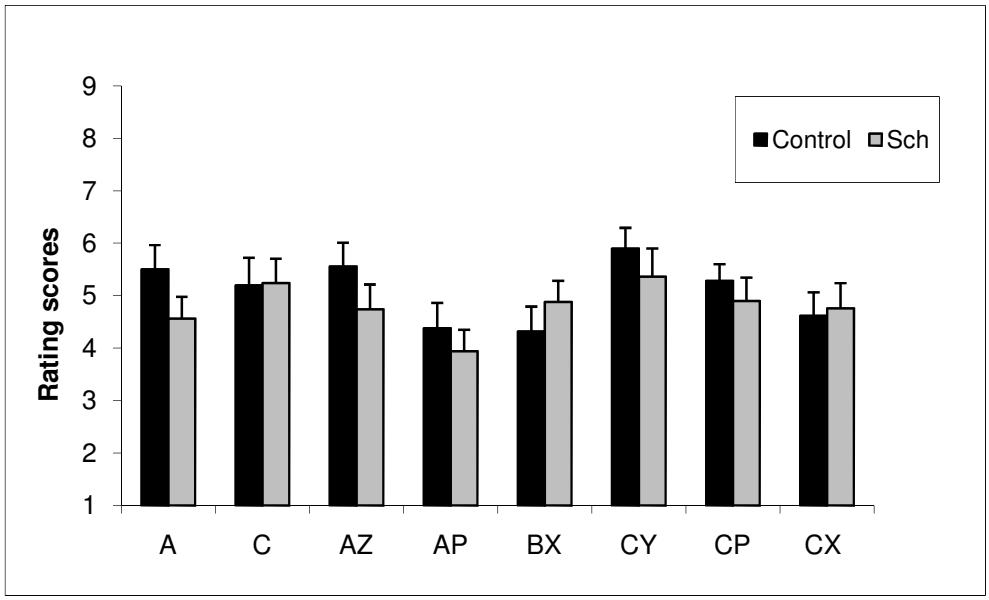


Figure 4.1 Rating scores for A, C, AZ, AP, BX, CY, CP and CX in the controls and schizophrenic groups at the pre-test stage. A rating of 9 reflected expectation of a positive image, 1 of a neutral image and 5 indicated uncertainty.

4.1.3.2 Pre-training stage

During the pre-training stage, the ratings of A and C steadily increased, while those to U and V fell gradually (figure 4.2). This pattern of responding was observed in both groups. However, the ratings of A and C were lower in patients than in controls whilst the ratings of U and V were

higher. Both of these observations suggest that the controls learned the discriminations better than the schizophrenic patients, and this impression was supported by the results of the statistical analysis.

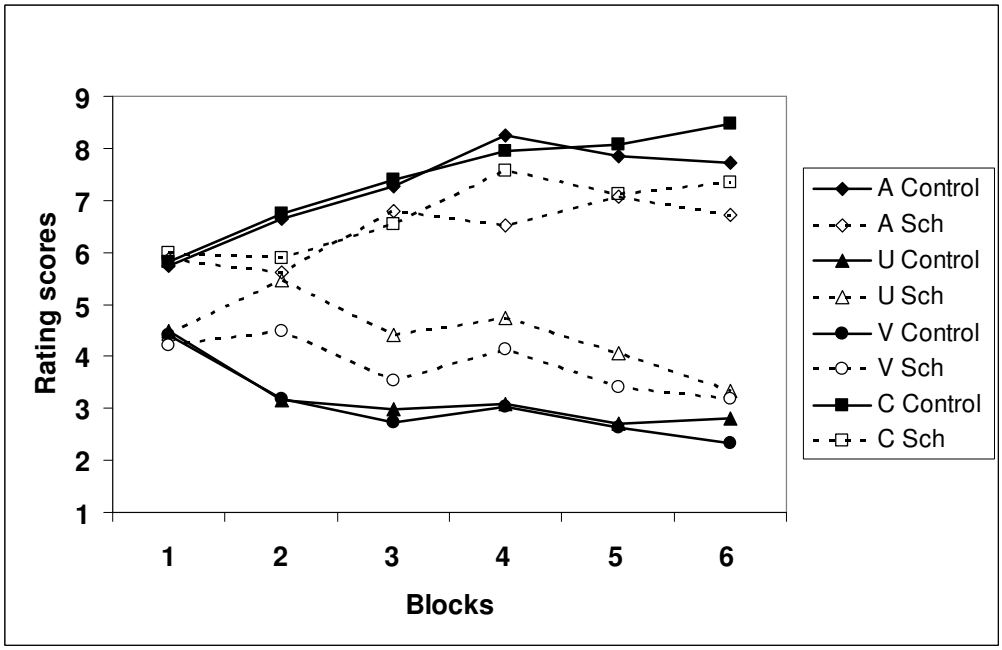


Figure 4.2 Rating scores for A+, U–, V– and C+ in the controls and schizophrenic groups at the pre-training stage. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

ANOVA with group, discrimination (A or U v. C or V) and reinforcement as factors revealed no main effect of group or discrimination, both *F*s<1. However, the main effects of training block and reinforcement were significant, $F(5,240)=2.31$, $p=0.05$ and $F(1,48)=260.66$, $p<0.001$ respectively. The interaction between reinforcement and diagnostic group was also significant $F(1,48)=7.73$, $p=0.008$, suggesting that performance on the discriminations differed in the two groups. Simple main effects analysis confirmed that the groups differed on both reinforced and non-reinforced trials, $F(1,96)=4.40$, $p=0.04$ and $F(1,96)=7.95$, $p=0.006$ respectively, suggesting that the schizophrenic group did not learn as well as the control group about either reinforced or non-reinforced trials. However, the difference between reinforced and non-reinforced trials was significant in both control and schizophrenic groups, $F(1,48)=91.41$,

$p<0.001$, and $F(1,48)=31.68$, $p<0.001$ respectively, demonstrating that both groups nonetheless learnt the discriminations.

There was also an interaction between training block and reinforcement $F(5,240)=17.92$, $p<0.001$, reflecting the development of the discrimination over training; simple main effects revealed that there was an effect of block for both reinforced and non-reinforced trials $F(5,480)=14.34$, $p<0.001$; $F(5,480)=7.68$, $p<0.001$ respectively, and that the difference in ratings between reinforced and non-reinforced trials was significant on all training blocks. Consistent with the difference between the diagnostic groups in the acquisition of the discrimination, there was also an interaction between training block, reinforcement and diagnostic group, $F(5,240)=3.15$, $p=0.009$. Nothing else was significant, the largest $F(1,48)=3.14$, $p=0.08$.

4.1.3.3 Training stage

During the training stage, the ratings of AZ and CY showed some increase, while those to AP and BX decreased slightly. Figure 4.3 shows that overall participants learned the difference between the reinforced and non-reinforced compounds. Comparing the scores in the two groups, it can be seen that, just as in the previous stage, the ratings of AZ and CY were lower in patients than in controls, whereas the ratings of AP and BX were higher. Both of these observations suggest that the controls learned the discriminations better than the schizophrenic patients.

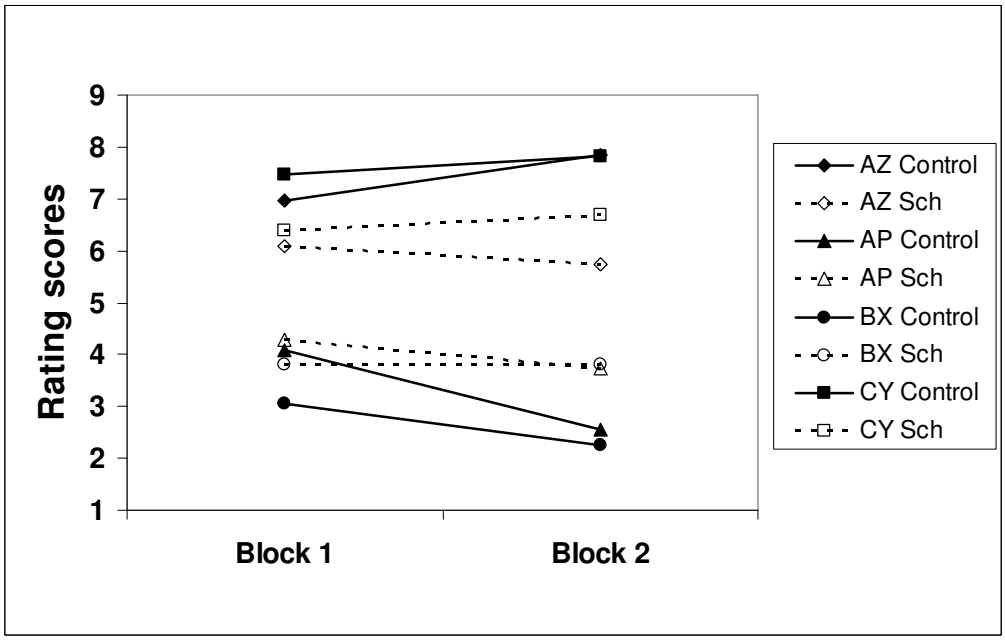


Figure 4.3 Rating scores for AZ+, AP–, BX– and CY+ in the controls and schizophrenic groups at the training stage. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

A mixed ANOVA with diagnostic group (schizophrenic patients v. controls) as between-subjects factor, and discrimination (AZ or AP v. CY or BX), reinforcement (reinforced or not) and training block (1-2) as within-subjects factors, revealed no main effect of diagnostic group, discrimination or training block, the largest $F(1,48)=2.32$, $p=0.13$. However, the main effect of reinforcement was significant $F(1,48)=106.06$, $p<0.001$, and this factor interacted significantly with diagnostic group, $F(1,48)=11.08$, $p=0.002$; simple main effects analysis revealed that the groups differed on both reinforced and non-reinforced trials, $F(1,96)=9.99$, $p=0.002$ and $F(1,96)=5.01$, $p=0.03$ respectively, confirming the suggestion that the control group learned more effectively than the schizophrenic group; however, the difference between reinforced and non-reinforced trials was significant in both control and schizophrenic groups, $F(1,48)=92.84$, $p<0.001$, and $F(1,48)=24.29$, $p<0.001$ respectively, confirming that both groups had nonetheless learnt the discrimination.

As might be expected, there was a significant interaction between training block and reinforcement $F(1,48)=11.12$, $p=0.002$. The simple main effects revealed that there was an effect of blocks for non-reinforced trials $F(1,96)=12.17$, $p<0.001$, but not for reinforced trials $F(1,96)=2.04$, $p=0.16$; the discrimination was nonetheless significant on both training blocks: $F(1,96)=63.76$, $p<0.001$; $F(1,96)=115.64$, $p<0.001$ respectively. A significant interaction was also found between discrimination and reinforcement $F(1,48)=4.84$, $p=0.03$, suggesting that there might have been differences in the ease with which the AZ/AP and CY/BX discriminations were mastered; however, simple main effects revealed that ratings of AZ and CY, and AP and BX, did not differ $F(1,96)=2.23$, $p=0.14$, and $F(1,96)=2.15$, $p=0.14$ respectively, and that the discrimination was significant for both discrimination types, $F(1,96)=59.67$, $p<0.001$ for AZ and CY, and $F(1,96)=99.50$, $p<0.001$ for AP and BX, suggesting that both discriminations were learned effectively. Nothing else was significant, the largest $F(1,48)=2.47$, $p=0.12$.

4.1.3.4 Test stage

Figure 4.4 shows the rating scores during the test stage. Again, the ratings of A and C remained high, and the AZ v. AP and BX v. CY discriminations were maintained. The latter observation was confirmed by the results of an ANOVA with diagnostic group as between-subjects factor, and discrimination (AZ or AP v. CY or BX), and reinforcement (AZ, CY v. AP, BX) as within-subjects factors; this revealed no main effect of either diagnostic group, $F<1$, or discrimination $F(1,48)=1.61$, $p=0.21$; but a main effect of reinforcement $F(1,48)=93.64$, $p<0.001$, suggesting participants gave significantly higher scores to reinforced than to non-reinforced stimuli. As in the previous stage, there was also a significant interaction between reinforcement and group $F(1,48)=15.78$, $p<0.001$, which was due to the

fact that the control group responded more than the schizophrenic group on reinforced, and less on non-reinforced trials, $F(1,96)=7.50$, $p=0.007$, and $F(1,96)=9.77$, $p=0.002$ respectively. However, as before, the discrimination between reinforced and non-reinforced trials was significant in both groups, $F(1,48)=93.16$, $p<0.001$, and $F(1,48)=16.27$, $p<0.001$, for the control and schizophrenic groups respectively. Nothing else was significant, the largest $F(1,48)=2.45$, $p=0.12$.

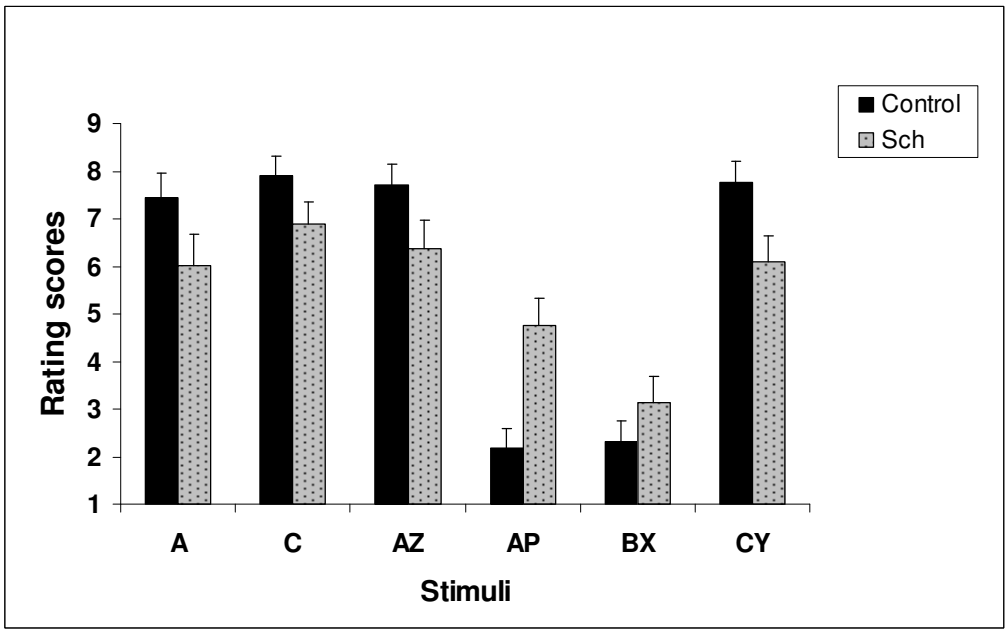


Figure 4.4 Rating scores for A+, C+, AZ+, AP–, BX– and CY+ in the controls and schizophrenic groups at the test stage. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

Figure 4.5 shows the rating scores of the two critical stimuli CP and CX at the pre-test and test stages. It is clear that, while during the pre-test stage ratings of the two stimulus compounds were quite similar in both groups, during the test stage CP was rated lower than CX in both groups, but that this difference was more marked in the control than in the schizophrenic group. A mixed design ANOVA with diagnostic group as between-subjects factor, stage (pre-test and test) and stimuli (CP v. CX) as within-subjects factors, revealed no main effect of diagnostic group, stage and stimuli, the largest $F(1,48)=1.89$, $p=0.18$, but the interaction between stage and

stimuli was significant $F(1,48)=15.48$, $p<0.001$. Unfortunately, there was no significant three-way interaction $F(1,48)=2.26$, $p=0.14$.

To further examine the apparent difference between schizophrenic and control groups, ANOVAs with stage (pre-test and test) and stimuli (CP v. CX) as factors, were performed in each group. In the control group, ANOVA revealed no main effect of either stage $F(1,24)=1.70$, $p=0.21$, or stimuli, $F< 1$; however, the interaction between stage and stimuli was significant, $F(1,24)=14.71$, $p=0.001$. The simple main effects revealed that although the ratings of CP and CX did not differ at the pre-test stage $F(1,24)=1.87$, $p=0.18$; they differed significantly at the test stage $F(1,24)=6.31$, $p=0.02$. In contrast, in the schizophrenic group, ANOVA revealed nothing significant, the largest $F(1,24)=2.97$, $p=0.10$. These results suggested CI effects were verified differently in the two groups, the degree of inhibition appeared to be reduced in the patients.

This impression was confirmed by ANOVA with diagnostic group and stage (pre-test and test) as factors by using another summary measure of CI. {It was statistically difficult to demonstrate a 3-way interaction by using the current summary measure of CI (CX-CP), so a ratio summary measure of CI [CP/(CP+CX)] was used.} The ANOVA revealed no main effect of diagnostic group, $F<1$, but a significant effect of stage $F(1,48)=16.62$, $p<0.001$, and a significant interaction between these two factors, $F(1,48)=4.05$, $p=0.049$. Simple main effects revealed that there was a significant effect of stage in the control group $F(1,48)=18.454$, $p<0.001$, but not in the patients $F(1,48)=2.13$, $p=0.15$. Nothing else was significant, the largest $F(1,96)=2.12$, $p=0.15$. Finally, to ensure that none of these differences could be attributed to differences in responding to CX, which was serving as a baseline against which the effect of P could be evaluated,

an ANOVA was conducted to examine ratings of CX at both pre-test and test stages. This revealed no significant effects or interactions involving group, *Fs*<1; the effect of stage was also not significant $F(1,48)=2.47$ $p=0.12$. This confirms the conclusion that the differences in ratio responding were solely attributable to differences in responding to CP (indeed a corresponding analysis of the CP scores revealed a significant interaction between group and stage $F(1,48)=4.32$, $p=0.04$, and simple main effects revealed a group difference at test $F(1,96)=4.07$, but not at the pre-test stage, $F<1$. This pattern of results suggests that P had become a conditioned inhibitor in the matched control participants, but not in the schizophrenic patients.

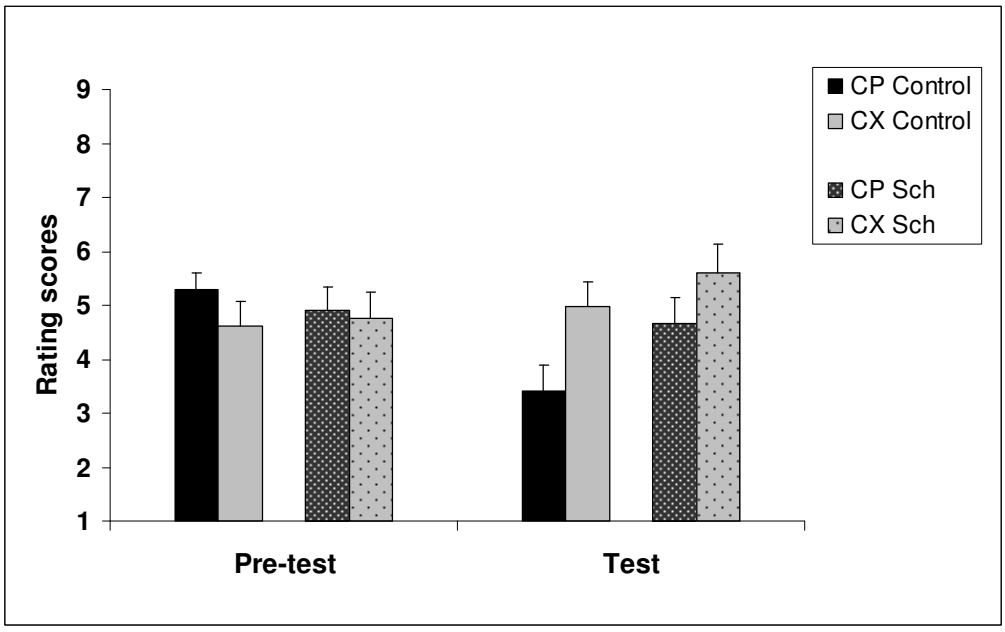


Figure 4.5 Rating scores for the key comparison stimuli CP and CX at the pre-test and the test stages in the controls and schizophrenic groups. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty. The pre-test ratings showed that the stimuli elicited similar ratings prior to conditioning. The test ratings confirmed the presence of conditioned inhibition in controls (shown as higher ratings to CX than CP presentations) and showed that conditioned inhibition was reduced in the schizophrenic group.

4.1.3.5 Differences by symptom profile

There was also no overall correlation between the PANSS General scores and the measure of CI $r(20)=-0.25$, $p=0.29$, nor with the excitatory learning score $r(20)=-0.31$, $p=0.19$. However, PANSS Negative symptom

scores were negatively associated with the measure of CI $r(20)=-0.51$, $p=0.02$, but did not significantly correlate with the excitatory learning score $r(20)=-0.39$, $p=0.09$. There was no significant correlation between PANSS Positive symptom scores and the measures of CI $r(20)=0.36$, $p=0.12$, nor with the excitatory learning score $r(20)=-0.03$, $p=0.91$. Therefore the relationship between symptom profile and performance on the learning measures at test was confined to the greater the negative symptom profile in association with lower expressed CI.

4.1.3.6 Differences by medication

Finally, there were no detectable differences by medication status in that there was no correlation between dose, measured as the CPZ equivalent, and either inhibitory $r(21)=0.36$, $p=0.11$, or excitatory learning scores $r(21)=-0.16$, $p=0.49$. Similarly there were no differences in inhibitory or excitatory learning scores between the schizophrenic patients on typical and atypical antipsychotics, the largest $t(17)=1.21$, $p=0.25$.

4.1.4 Discussion

The present study provided evidence that both excitatory associative and CI learning are impaired in schizophrenia. For excitatory associative learning, in spite of both groups learning to respond differently on reinforced (A+ and C+) and non-reinforced (U– and V–) trials, the patient group responded less on reinforced trials and more on non-reinforced trials than the matched controls, which indicated a general learning impairment in this group. For CI learning, both groups learned discriminations on reinforced (AZ+ and CY+) and non-reinforced (AP– and BX–) trials; again, the patient group responded less on reinforced trials and more on non-reinforced trials than the matched controls. During the test stage, matched controls responded significantly less to the excitatory stimulus C when it

was compounded with the inhibitor P than when it was presented with a matched control stimulus X, participants in the schizophrenic group did not, which suggested the degree of inhibition was reduced in the patients.

It cannot be ruled out that the results were due to differences in general intelligence or motivational factors between the matched controls and schizophrenic samples, although the controls were matched through age, gender, educational level and socio-economic status. Besides, it was suggested that any demographic characteristics (e.g. age, gender) did not affect schizophrenic patients showing intact response inhibition (Sacchetti, Galluzzo, Panariello, Parrinello & Cappa, 2008; Thoma et al., 2007). It can be argued that the majority of the schizophrenic samples were on antipsychotics and these medications generally impair cognitive functions. In fact, associative learning abnormalities in schizophrenia have been reported independent of medication (e.g. Baruch et al., 1988; Serra et al., 2001).

Regardless of whether reduced CI effects were caused by medication or not, the fact that simple associative learning can sometimes be retarded in schizophrenia, which raises the possibility that the attenuation of CI was observed no more than it would be expected given the impairment in associative learning measured in the training stages. A conditioned inhibitor forms because it signals the absence of an outcome that is predicted by an excitatory stimulus. If the patient samples were less able to learn about this excitatory stimulus, then conditioned inhibition would necessarily be impaired. Therefore, whether the CI deficits are a primary effect, or a secondary result of them being poorer at excitatory learning? It is difficult to discount this possibility completely. A full understanding of the nature of the cognitive abnormalities that accompany this condition

would therefore require appreciation of this factor, which might have practical implications for treatments in patients.

The current study also found significant negative correlation between the PANSS negative scores (not positive scores) and the CI learning measures, reflecting schizophrenic patients with higher negative scores on PANSS perform worse on the CI learning task. Negative symptoms are sometimes viewed as adaptive in that they result in withdrawal from the environment and hence reduced arousal levels. Increased CI could contribute to such withdrawal by reducing responding to excess over salient stimuli. The typical feature of negative symptoms is non-response or emotional blunting and an individual showing high CI would effectively ignore complex stimuli which include a signal of non-reinforcement. Farkas, et al. suggested that the enduring negative symptoms of schizophrenic patients may be related to decreased response to cognitive feedback and deficient basal ganglia functioning (Farkas, et al., 2008). Generally speaking, patients with significant negative symptoms are suffering very poor function and quality of life (Katschnig, 2000; Norman et al., 2000; Orse, Akdemir, & Daq, 2004). Moreover, there is no specific medication target to negative symptoms (Kirkpatrick, Fenton, Carpenter & Marder, 2006), and little research has explored the relationship between negative symptoms in schizophrenia and associative learning. The findings from current research may contribute to our understanding of cognitive dysfunctions in schizophrenia, especially patients with significant negative symptoms.

The present study provides a direct investigation of the classical conditioning in schizophrenic patients, and the results show a reduced level of excitatory learning and CI performance compared with matched

controls. The results from the current study allow us to learn that valid predictors of an outcome are ineffective under certain circumstances - namely when the inhibitor is present. Moreover, the demonstration of CI deficit on the summation test specifically demonstrates that such inhibitory contextual cues will not transfer, i.e. suppress excitation to new cues with which they have not previously been paired. Thus, impairment in inhibitory learning will result in inappropriate responding to a variety of stimulus constellations that do not predict an outcome. Casually put, irrelevant cues will remain salient in the sense that they are regarded as significant. Therefore, impaired CI would contribute to understanding of cognitive dysfunctions (e.g. sensory flooding) in schizophrenia (Bleuler, 1911; McGhie & Chapman, 1961; Venables, 1960).

4.2 Experiment 10: CI experiment in patients with PD (forensic settings)

4.2.1 Introduction

As already introduced in chapter 1, personality disorders (PD) includes a set of heterogeneous conditions that have in common a tendency to be deviant, troublesome and persistent. Cluster B characteristics, particularly as seen in antisocial personality disorder (ASPD) and borderline personality disorder (BPD), are overrepresented in forensic populations (Fazel & Danesh, 2002; Hiscoke, Langstrom, Ottosson, & Grann, 2003). Clinical accounts of ASPD and BPD offenders confirm that impulsive and violent behaviours are typical. However, their personality profile is not clear-cut, in that offenders also show a high degree of co-morbidity across PD.

Psychopathy can be differentiated from the PDs on the characteristic pattern affective, interpersonal and behaviour symptoms (e.g. lack of empathy; glibness and superficial charm) (Cleckley 1976; Hare, 1991; McCord & McCord, 1964). Although psychopathy has not been specifically described in either the DSM-IV or ICD-10, the condition clearly shows some overlap with ASPD (Blackburn & Coid, 1998; Coid & Ullrich, 2010; Hare et al., 1991; Hart & Hare, 1996; Kosson, Lorenz & Newman, 2006). Moreover, DSM-IV describes features of psychopathy as 'particularly distinguishing of Antisocial Personality Disorder in prison or forensic settings' (DSM-IV, p. 647), again suggesting that the combination of ASPD and psychopathy may be especially important within forensic populations.

It has been argued that a unifying feature of PD in forensic populations has a poor impulse control: this is well-recognised as a central feature of psychopathy (Johansson et al., 2005; Lesch & Merschdorf, 2000; Prichard, 1837) and some types of personality disorders (Stein et al., 1993, 1995). Within forensic populations of the kind sampled in the present study, poor impulse control may contribute to general learning deficits, whenever unwanted thoughts, emotions and actions interfere with the tasks' performance (Avila & Parcet, 2001; Gullo, Jackson & Dawe, 2010). Notably both psychopathy and ASPD are characterized by impulsivity and disinhibited lifestyles and a tendency to transgress social norms and legal rules.

However, the exact nature of impulsivity has not been unambiguously specified, making further analysis difficult. For example, some have argued that impulsive behaviour results from lack of inhibitory control (Buss & Plomin, 1975), others that it stems from an inability to tolerate delays of reinforcement (e.g. Logue, 1988; Logue et al., 1992; Thiébot, Le Bihan,

Soubrié & Simon, 1985). In any event, individuals with high impulsivity fail to inhibit unwanted actions, and thus behavioural measures of impulsivity include a range of established laboratory behavioural tasks measuring the participants' ability to inhibit pre-potent motor responses (S-R associations: e.g. Go/NoGo, stop-signal, anti-saccadic eye movement procedures). As introduced in chapter 1, deficits in the performance of such tasks have been demonstrated in participants with BPD (e.g. Grootens et al., 2008; Nigg et al., 2005; Rentrop et al., 2007; Rubio et al., 2007; Ruchsow et al., 2008).

However, inhibition is a broad construct, and should not be too narrowly identified with any one behavioural paradigm. For example, in the chain of cause and effect that ultimately results in unwanted actions, environmental cues which trigger associated thoughts and emotions through stimulus-stimulus (S-S) associations can be primary. Furthermore, to date, no studies have demonstrated CI deficits in relation to psychological or psychiatric disorder. The present chapter was devised as a first test of the prediction that a forensic sample of participants with PD (in the absence of comorbid schizophrenia) would show impaired CI effects, and the levels of impulsivity would correlate with the CI learning performance. Again, the computer-based CI learning summation test (experiment 4) was used as the CI learning task in these samples.

4.2.2 Methods

All details not mentioned were identical to these of experiment 4.

4.2.2.1 Participants

A total of 26 forensic PD patients volunteered to participate in the experiment, two of whom were subsequently excluded due to a failure in

the pre-training stage [the scores of (C-V)=<0]. They were all male inpatients at Rampton Hospital, a high security psychiatric hospital in the UK. Of those who completed the study, eight participants were in the Personality Disorder Unit (PDU) and 16 in the Dangerous and Severe Personality Disorder (DSPD) Unit. To meet the criteria for severe PD justifying admission to the DSPD unit, an offender must either: (i) score 30 or more on the PCL-R; or (ii) score between 25 and 30 on the PCL-R plus have at least one DSM-IV PD diagnosis other than ASPD; or (iii) have 2 or more DSM-IV PD diagnoses (Howells, Krishnan & Daffern, 2007). The IPDE and PCL-R had been completed following admission, in the course of their initial assessment by qualified staff at Rampton Hospital.

The matched controls were a community-based sample of 27 participants, three of whom were excluded for the same reason of PD patients, leaving 24 to complete the study. These controls lived in the same county and were recruited at the University of Nottingham (ancillary staff), Nottingham National Ice Centre and the Nottingham Trent FM Arena. They were all without a higher education; some were unemployed, others reported having jobs such as bus driver, waiter, bartender, shop assistant, and university support staff. None reported or showed any indication of mental illness or substance abuse. Other than the fact they were not incarcerated, control participants were tested under comparable quiet environmental conditions in the same way by the same experimenter. Table 4.4 shows the details of PD participants' age, gender, ethnicity, educational level. The number of participants was equally allocated to 8 CSs counterbalanced groups, and the allocation to the counterbalanced experimental conditions was identical for the PD and control groups.

Table 4.4 Summary details of the final sample of PD participants

	PD patients (n=24) in which psychopaths (n=13)	**Controls (n=24)**
Age (years)	39.5	34.92
Range of age (year)	25-58	19-56
Gender	All males	All males
Education level	Up to A level*	Up to A level*
Ethnicity	23 White and 1 Black	23 White and 1 Black

Note: * In the UK, the number of years in education required to achieve A level is 14.

This study was approved by NHS Research Ethics (Derbyshire Research Ethics Committee, Reference No. 08/H0401/65, granted September 2008, amendment to study PD participants approved May 2009). Procedures for testing the control participants were approved by the University of Nottingham, School of Psychology Ethics Committee. Control participants received an inconvenience allowance of £5 cash to cover their travel expenses. No such payment was possible in the case of PD participants, but they had no travel expenses or loss of earnings in the consequence of participation.

4.2.2.2 Clinical assessment and medication of PD participants

For PD patients in the present study, the International Personality Disorder Examine (IPDE; Loranger, et al., 1994) and the PCL-R questionnaire had been completed following admission, in the course of their initial assessment by qualified staff at Rampton Hospital (table 4.5 shows clinical assessment and medication details for PD patients).

Table 4.5 Clinical assessment and medication details of the PD patients

Patients' ID No.	**Psychotropic Medication**	**IPDE dimensional scores**			**PCL-R total score**	**UPPS total score**
		Cluster A	**Cluster B**	**Cluster C**		
PD01	None	3	25	1	20	89
PD02	Diazepam	21	39	16	21	107
PD04	Clozapine Citalopram	8	56	17	22	109

Patients' ID No.	Psychotropic Medication	IPDE dimensional scores			PCL-R total score	UPPS total score
		Cluster A	Cluster B	Cluster C		
PD06	Clozapine Fluoxetine	24	30	9	17.9	108
PD10	None	n/a	n/a	n/a	12	109
PD12	None	16	34	14	17	82
PD20	None	6	38	7	22	111
PD21	None	14	33	15	10	101
DS03	Diazepam Fluoxetine Rispiradone	8	35	6	32.2	70
DS05	None	0	10	1	20	59
DS06	None	4	30	0	28.4	93
DS07	Citalopram	8	61	1	30.5	131
DS08	Diazepam	12	45	3	35	126
DS10	Citalopram	3	30	1	30.5	110
DS11	None	11	47	5	35	86
DS12	Citalopram	3	18	4	23.2	70
DS15	Chlorpromazine	10	31	12	22.2	134
DS16	Diazepam Quetiapine	7	53	5	26	122
DS18	Lorazepam	11	70	7	30	102
DS21	Diazepam Clomipramine Quetiapine	13	45	7	34.7	144
DS22	None	19	52	31	31	114
DS23	Buspirone	13	71	8	34.7	89
DS24	Carbamazepine Rispiradone	13	70	11	29	126
DS25	None	4	42	13	27.4	145

Note: n/a = data not available; PD = participants from Personality Disorder Unit; DS = participants from Dangerous and Severe Personality Disorder Unit; PCL-R score>=25, viewed as indicative of psychopathy.

The IPDE is developed as a standard tool for the assessment of PD, which consists of DSM-IV and ICD-10 modules and aims to obtain classification according to both systems. This comprises both self-report questionnaires and a semi-structured interview rated by the psychiatric or clinical psychological examiner that allows both diagnostic and dimensional scores to be extracted for each patient. The questions are grouped in seven

subjects: work, self, affects, interpersonal relationships, reality testing, impulse control and behaviour before the age of 15 years. During the interview, each item is scored on a 3-point scale (0, 1 or 2), which allows for a negative, probable or definite diagnosis with respect to each personality disorder. The IPDE provides categorical and dimensional scores for PD in the form of 10 sub-scales which relate to the 3 clusters identified by DSM-IV and ICD-10.

According to the IPDE categorical diagnoses, of those participants (n=23) that were finally included, there were definitely (n=17) or possibly (n=4) participants who had confirmed ASPD; there were definitely (n=12) or possibly (n=1) participants who had confirmed BPD; only one participant had a confirmed OCD, but was comorbid with BPD. Psychiatric assessments confirmed that none of the forensic PD patients approached in connection with the study had comorbid schizophrenia. As might be expected, in the DSPD unit (n=16), a majority of participants definitely (n=11) or possibly (n=3) had confirmed ASPD. However, the 17 definite cases of ASPD were not all in the DSPD unit. In total, 14 of the PD participants were on psychotropic medications, including typical (n=1) and atyptical antipsychotics (n=6), anti-depressants (n=7), anxiolytics (n=7), and anticonvulsants (n=1). The remaining 10 participants who completed the study were not on any psychotropic medication.

The PCL-R includes 20 items, which measure individual behaviours and personality traits of special relevance to psychopathy. The items from the PCL-R can be subdivided into two factors; Factor 1 shows interpersonal traits and affective characteristics (e.g. pathological lying, shallow affect and manipulativeness), and Factor 2 assesses antisocial behaviour and impulsivity (e.g. early behavioural problems and impulsivity). Scores are

based on a semi-structured interview and a review of institutional file information. Each item is scored on a 3-point scale (0=clearly not present; 1=may be present; 2=clearly present), and the range of the total score is 0 to 40. A total score of 30 or above can be considered as psychopath (Hare, 1991, 2003).

Whilst a higher cut-off of 30 is used in the USA, a total PCL-R score of 25 or above is the criterion score for a diagnosis of psychopathy in European offenders (Cooke & Michie, 1999; Dolana & Doylea. 2007; Grann, Langstrom, Tengstrom & Stalenheim, 1998; Harris, Rice & Cormier, 1991; Harris, Rice & Quinsey, 1993; Howells, Krishnan & Daffern, 2007; Langstrom et al., 1999); Exceptionally, in European experimental samples, psychopathy has been identified with lower cut-offs of 20 (Flor et al., 2002). According to the majority of European previous research, the present study used a total PCL-R score of 25 or above as the cut-off score for a diagnosis of psychopathy.

4.2.2.3 Stimuli and materials

The USs were selected by a pilot study from the IAPS (Lang et al., 2005), which included 10 positive pictures and 10 neutral pictures, excluding pictures with children (was suggested by a psychiatrist at Rampton hospital, see appendix 1 for pictures' ID no. in IAPS).

The levels of impulsivity were measured by the UPPS scores in both PD participants and matched controls. The controls also completed BIS/BAS, EPQ-RS, O-LIFE (Short), and STB for assessing their individual differences.

4.2.2.4 Analysis

Same as the previous chapter, statistical analyses were by mixed design analyses of variance (ANOVA), again, the within-subjects factors were discrimination, reinforcement and trial block, and the between-subjects factor was diagnostic group (PD patients v. controls). Planned comparisons of the assessment score data were by *t*-test (i.e. to compare the PD patients on different medication), or Kruskal-Wallis where the data were not normally distributed (i.e. IPDE scores).

Correlational analyses were used to examine the relationship between learning scores and (1) levels of impulsivity as measured by UPPS scores, (2) PD dimensions as measured by IPDE scores, and (3) psychopathy as measured by PCL-R. For learning scores, again a summary measure of excitatory learning was provided by (C-V), and a summary measure of CI was provided by (CX-CP). Because the clinical sample size was relatively small for correlational analyses, an effect size was measured by Pearson's correlation coefficient, *r*. According to Cohen's (1988, 1992) suggestion, a different *r* value indicates different effect sizes, which are $0.1<r<0.23$ as small effect size; $0.24<r<0.36$ as moderate effect size; $r>0.37$ as large effect size.

4.2.3 Results

4.2.3.1 Pre-test stage

Figure 4.6 shows the rating scores during the pre-test stage. In the PD group, there was not much difference for rating scores of all stimuli – all were around 5. In the control group, the scores of A and AZ were around 6, which were slightly higher than those of other stimuli (around 5). The pre-test ratings of the two critical stimuli CP and CX confirmed that there were no pre-existing differences. ANOVA with stimulus (CP v. CX) and

group (PD patients v. controls) as factors revealed no significant effects or interactions, the largest $F(1,46)=2.22$, $p= 0.14$.

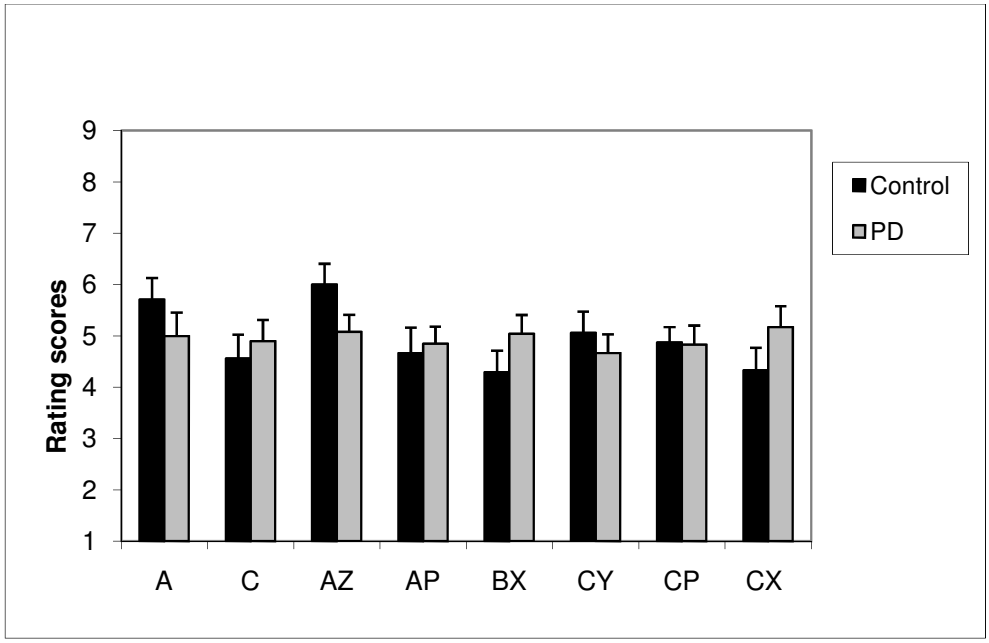


Figure 4.6 Rating scores for A, C, AZ, AP, BX, CY, CP and CX in the controls and personality disordered (PD) groups at the pre-test stage. A rating of 9 reflected expectation of a positive image, 1 of a neutral image and 5 indicated uncertainty.

4.2.3.2 Pre-training stage

During the pre-training stage, the ratings on A+ and C+ trials steadily increased, while those on U- and V- trials fell (figure 4.7). Moreover, this pattern of responding was observed in both groups, with the exception that, in the PD group, the ratings of A appeared somewhat lower than in the control group during the first two training blocks.

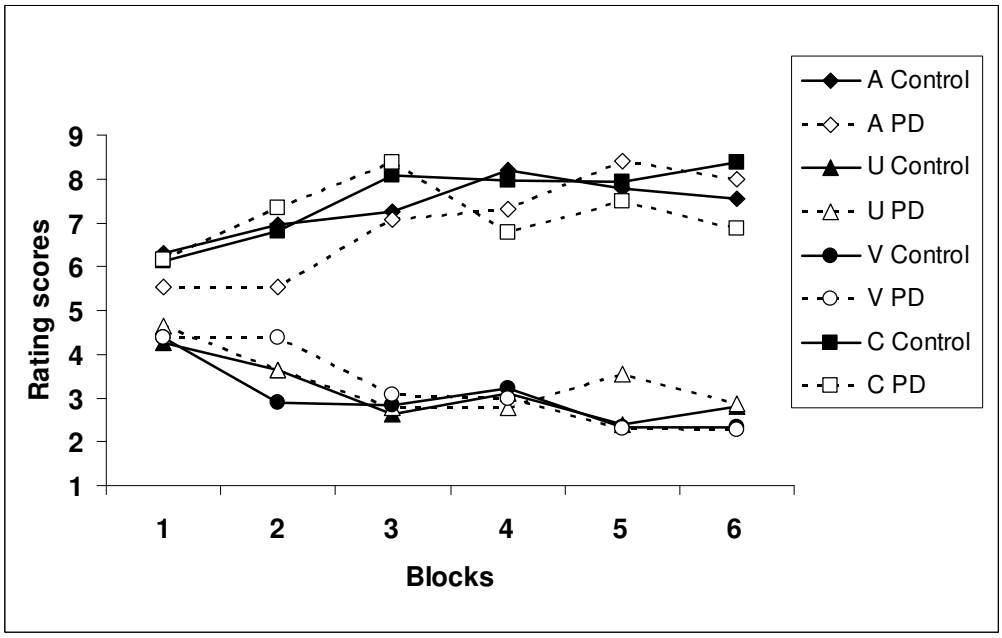


Figure 4.7 Rating scores for A+, U–, V– and C+ in the controls and personality disordered (PD) groups at the pre-training stage. A rating of 9 reflected expectation of a positive image, 1 of a neutral image and 5 indicated uncertainty.

An ANOVA with group, discrimination (A or U v. C or V), reinforcement and training block revealed a main effect of reinforcement $F(1,46)=260.66$, $p<0.001$, confirming that participants gave significantly different ratings to reinforced and non-reinforced stimuli; none of the other main effects were significant, $Fs<1$. The interaction between reinforcement and group was also significant $F(1,46)=4.40$, $p=0.04$. To further analyze this interaction, simple main effects analysis was conducted; this revealed that the groups differed on reinforced trials $F(1,92)=4.14$, $p=0.04$, but not on non-reinforced trials $F(1,92)=3.08$, $p=0.08$, consistent with the suggestion that for reinforced trials, the PD group did not learn about the reinforced stimuli as well as the control group (though inspection of figure 4.7 shows some variation in relation to stimulus). The simple main effects analyses also confirmed that the difference between reinforced and non-reinforced trials was significant in both control and PD groups, $F(1,46)=166.38$, $p<0.001$; $F(1,46)=98.68$, $p<0.001$ respectively. Reinforcement also interacted significantly with training block, $F(5,230)=26.69$, $p<0.001$. Here simple main effects analyses showed an effect of block on both reinforced and

non-reinforced trials, $F(5,460)=16.24$, $p<0.001$; $F(5,460)=16.44$, $p<0.001$ respectively, and that the differences between reinforced and non-reinforced trials were significant on all training blocks, the smallest $F(1,276)=20.32$, $p<0.001$. Together these effects of reinforcement clearly demonstrate that even though the PD group learned marginally less well, both groups had nonetheless learnt the Pavlovian discriminations.

Significant interactions were also found between training block and discrimination, and between training block, discrimination and group, $F(5,230)=2.49$, $p=0.03$ and $F(5,230)=2.87$, $p=0.02$ respectively, suggesting that the change in ratings in the various groups may have varied according to whether the discrimination involved was between A+ and U-, or C+ and V-; however, as none of these interactions involved reinforcement, there is no evidence that the discrimination between reinforced and non-reinforced trials proceeded differently depending on the stimuli employed, and so we did not analyze these effects further. Nothing else was significant, the largest $F(1,46)=1.65$, $p=0.21$.

4.2.3.3 Training stage

During the training stage, the ratings on AZ+ and CY+ trials overall increased, while those on AP- and BX- trials fell (see figure 4.8), suggesting that all participants had learned to discriminate reinforced and non-reinforced compounds. Comparing the scores in the two groups, it can be seen that the ratings of the reinforced compounds AZ and CY were lower in patients than in controls, whereas the ratings of the non-reinforced compounds AP and BX were higher in patients than in controls. Both observations suggested that the controls learned the discriminations somewhat better than the PD patients.

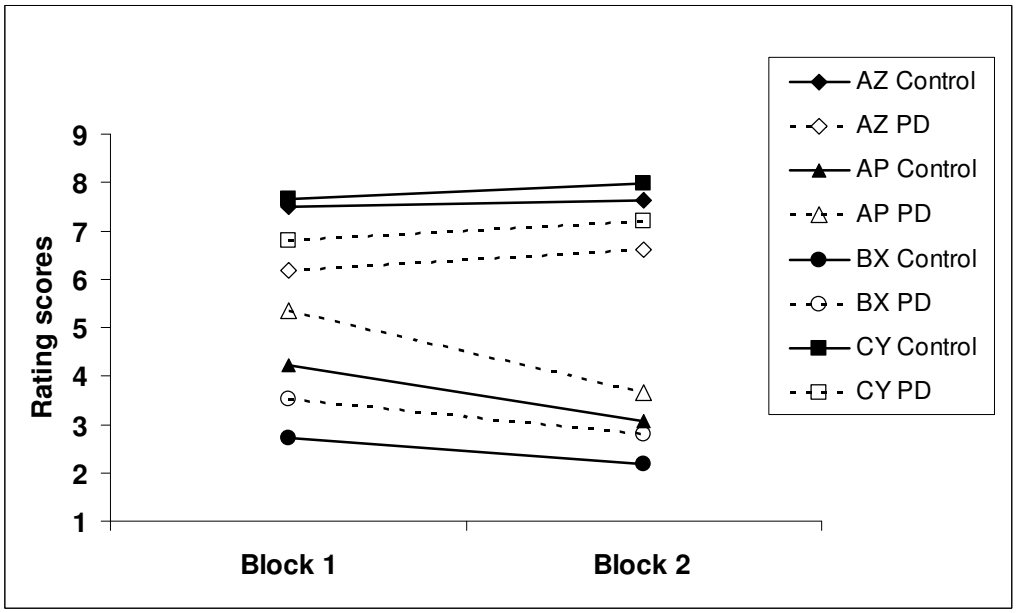


Figure 4.8 Rating scores for AZ+, AP–, BX– and CY+ in the controls and personality disordered (PD) groups at the training stage. A rating of 9 reflected expectation of a positive image, 1 of a neutral image and 5 indicated uncertainty.

A mixed ANOVA with group (PD patients v. controls) as between-subjects factor, and discrimination (AZ or AP v. CY or BX), reinforcement (reinforced or not) and training block (1-2) as within-subjects factors, revealed no main effect of either group $F<1$, or discrimination $F(1,46)=2.25$, $p=0.14$. However, the main effects of training block and reinforcement were significant, $F(1,46)=5.65$, $p=0.02$ and $F(1,46)=168.28$, $p<0.001$ respectively. The interaction between reinforcement and group was also significant $F(1,46) =11.01$, $p=0.002$.

Simple main effects analyses showed that the PD and control groups differed on both reinforced and non-reinforced trials, $F(1,92)=10.55$, $p=0.002$ and $F(1,92)=5.35$, $p=0.02$ respectively, confirming the suggestion that the control group were better at discriminating between reinforced and non-reinforced trials than the PD group. However, the simple main effects analyses also revealed that the difference between reinforced and non-reinforced trials was significant in both control and PD

groups, $F(1,46)=132.70$, $p<0.001$; $F(1,46)=46.60$, $p<0.001$ respectively. Thus both groups had nonetheless learnt the discrimination.

A significant interaction was found between training block and reinforcement, $F(1,46)=32.85$, $p<0.001$. The simple main effects revealed that there was an effect of blocks for non-reinforced trials, $F(1,92)=29.07$, $p<0.001$, but not for reinforced trials, $F(1,92)=2.68$, $p=0.11$, and that the difference between reinforced and non-reinforced trials was significant on both training blocks, $F(1,92)=92.89$, $p<0.001$, and $F(1,92)=201.12$, $p<0.001$ respectively. A significant interaction was also found between discrimination and reinforcement, $F(1,46)=19.52$, $p=0.001$. The simple main effects revealed that the ratings of AP- was significantly higher that those of BX- trials, $F(1,92)=15.70$, $p<0.001$, but not between CY+ and AZ+ trials, $F(1,92)=2.70$, $p=0.10$, suggesting that the inhibition discrimination (AP v. AZ) was harder to learn than the simple discrimination (BX v. CY) at this stage. The simple main effects also showed that the difference between reinforced and non-reinforced trials was significant for both discrimination types, $F(1,92)=64.83$, $p<0.001$, and $F(1,92)=172.83$, $p<0.001$, suggesting both discriminations had been learned effectively.

Nothing else was significant, the largest $F(1,46)=1.92$, $p=0.17$.

4.2.3.4 Test stage

Figure 4.9 shows the rating scores during the test stage. As during the training stage, the ratings of the previously reinforced A and C remained high, and the discriminations were maintained. The latter observation was confirmed by the results of an ANOVA with group as between subjects factor, and discrimination (AZ or AP v. CY or BX), and reinforcement (AZ or

CY v. AP or BX) as within subjects factors. This revealed no main effect of either group, or discrimination, *Fs*<1, but a main effect of reinforcement, $F(1,46)=174.14$, $p<0.001$.

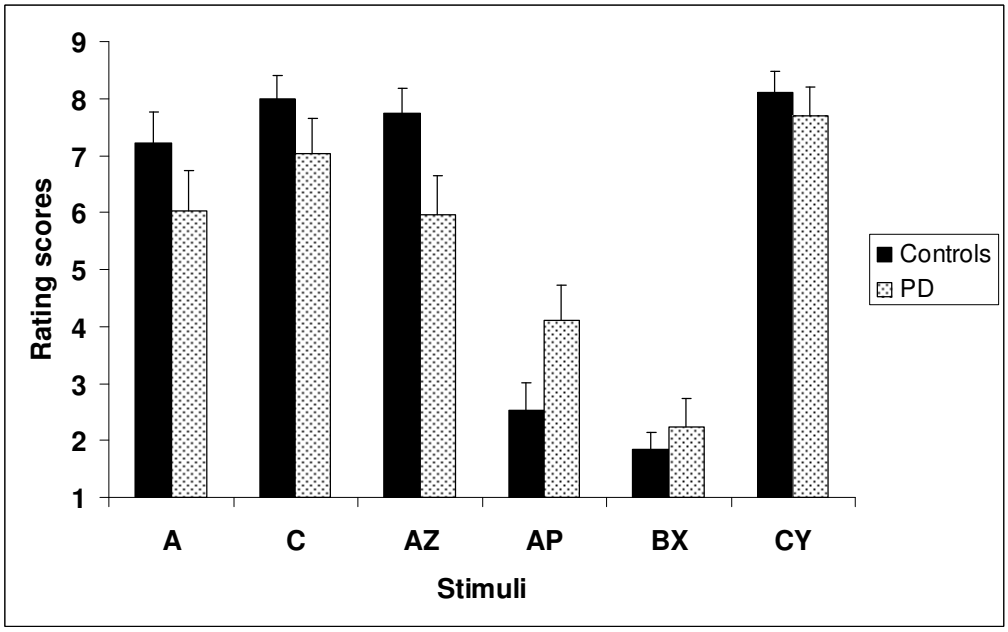


Figure 4.9 Rating scores for A+, C+, AZ+, AP–, BX– and CY+ in the controls and personality disordered (PD) groups at the test stage. A rating of 9 reflected expectation of a positive image, 1 of a neutral image and 5 indicated uncertainty.

There was also a significant interaction between reinforcement history and group, $F(1,46)=8.50$, $p=0.005$. Simple main effects analysis revealed that, as in training, the control group responded overall more than the PD group on previously reinforced, and less on previously non-reinforced trials $F(1,92)=5.43$, $p=0.02$; $F(1,92)=4.18$, $p=0.04$ respectively. Nonetheless, as before, the discrimination between reinforced and non-reinforced compounds was significant in both groups, $F(1,46)=129.78$, $p<0.001$, and $F(1,46)=52.86$, $p<0.001$, for control and PD groups respectively. There was also a significant interaction between discrimination and reinforcement, $F(1,46)=10.70$, $p=0.002$, which was due to the higher ratings given on CY+ than on AZ+ trials, and the lower ratings given on BX- than on AP,- trials $F(1,92)=3.92$, $p=0.05$, and $F(1,92)=5.94$, $p=0.02$ respectively. Again, it suggested that the simple discrimination (BX v. CY) was easier to learn than the inhibition discrimination (AP v. AZ). The simple

main effects analyses also showed that the differences between reinforced and non-reinforced trials were significant for both discrimination types, $F(1,92)=49.38$, $p<0.001$, and $F(1,92)=135.71$, $p<0.001$. The results suggested that both groups maintained the Pavlovian discriminations at the test stage.

There were no three-way interactions $F(1,46)=3.26$, $p=0.08$.

Figure 4.10 shows the rating scores for the two critical stimuli CP and CX at the pre-test and test stages. It is clear that during the pre-test stage, the scores of the two stimuli were quite similar in both groups, but that in the test stage, the rating of CP was lower than the rating of CX in controls. However, this was not true in the PD group. A mixed design ANOVA with group as the between-subjects factor, stage (pre-test v. test) and stimuli (CP v. CX) as within-subjects factors, revealed no main effect of either group $F(1,46)=3.72$, $p=0.06$, or stage $F<1$. However, there was a main effect of stimuli $F(1,46)=4.48$, $p=0.04$, which interacted with stage $F(1,46)=6.39$, $p=0.02$. Most importantly, the three-way interaction was significant $F(1,46)=10.03$, $p=0.003$, suggesting that the change in ratings of CP and CX produced by inhibition training differed in the two groups.

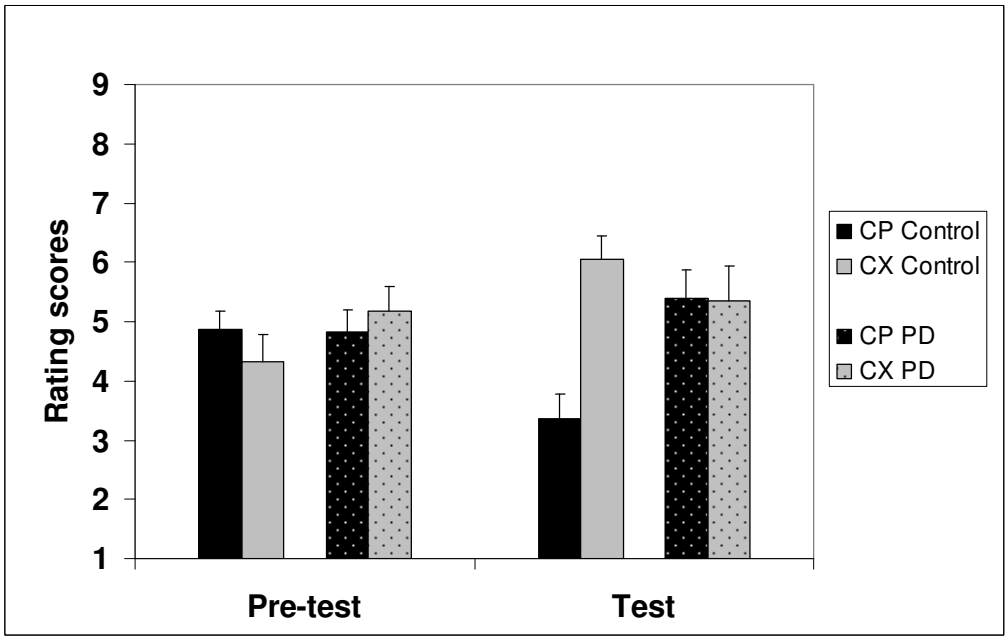


Figure 4.10 Rating scores for the key comparison stimuli CP and CX at the pre-test and the test stages in the controls and personality disordered (PD) groups. A rating of 9 reflected expectation of a positive image, 1 of a neutral image and 5 indicated uncertainty. The pre-test ratings showed that the stimuli elicited similar ratings prior to conditioning. The test ratings confirmed the presence (in controls) or absence (in the PD group) of conditioned inhibition, which was shown as higher ratings to CX than CP.

In order to explore this three-way interaction further, an ANOVA with stage (pre-test v. test) and stimuli (CP v. CX) as factors was performed in each group. In the control group, the ANOVA revealed no main effect of either stage $F<1$, or stimuli $F(1,23)=8.00$, $p=0.10$; however, the interaction between stage and stimuli was significant $F(1,23)=27.89$, $p<0.001$. The simple main effects revealed that the stimuli differed at the test stage $F(1,23)=30.80$, $p<0.001$, but not at the pre-test stage $F(1,23)=2.40$, $p=0.14$. In the PD group, the ANOVA revealed nothing significant, all Fs<1. This pattern of results confirms that although P had acquired the properties of a conditioned inhibitor in the control participants, this had not occurred in the PD patients.

4.2.3.5 Individual differences measured by questionnaires

For measuring of impulsivity by questionnaires, there was no correlation between the UPPS scores, either the total score or any of its sub-scales,

with any of the summary measures of excitatory or inhibitory learning, the largest $r(48)=0.19$, $p=0.20$. However, the UPPS scores were overall no different in the PD and the control group $t(46)=0.33$, $p=0.74$. Only the sensation-seeking scores were significantly different in the PD group $t(46)=3.00$, $p=0.004$ (and these were lower, possibly in response to incarceration). When the key analysis for CI was repeated categorising the samples into high and low UPPS sensation-seeking using a median split analysis, the three-way interaction between stage, stimuli and UPPS was not significant, $F<1$. Therefore the expression of CI was not different in participants with low and high UPPS scores. Moreover, when the analysis by group was repeated using the UPPS sensation-seeking scores as a covariate, the three-way interaction reflecting abolition of CI in the PD group remained significant $F(1,45)=9.89$, $p=0.003$, suggesting the measurement of impulsivity (by UPPS) did not correlate to the excitatory or inhibitory learning performance in current samples.

Within the PD group, there was no significant correlation between any of the IPDE subscales and the summary measure of inhibitory or excitatory learning, the largest $r(23)=0.35$, $p=0.10$. This was also true when the IPDE dimensional scores were sub-grouped as 3 clusters according to DSM-IV, the largest $r(23)=0.16$, $p=0.46$. Similarly, there was no correlation between PCL-R scores, either overall or by subscale, and the summary measure of excitatory or inhibitory learning, the largest $r(24)=-0.29$, $p=0.17$, for factor 2.

4.2.3.6 Individual differences in two units at Rampton hospital

However, there did appear to be differences between participants in the DSPD and PD units. More specifically, participants from the DSPD unit showed less inhibitory learning than those in the PD unit, while levels of

excitatory learning were relatively unaffected. The C-V scores, the measure of excitatory learning, were 4.05, 3.89 and 5.12 for the PD, DSPD and control participants respectively; the corresponding scores for the CX-CP measure of inhibition were 0.27, -1.03 and 2.80. Accordingly, ANOVA with group (PD, DSPD and control) and measure (excitatory v. inhibitory) was performed (using the harmonic mean to deal with the unequal sample size created by this post hoc comparison). This revealed a significant interaction between these two factors $F(2,45)=10.41$ $p<.001$, $r=0.43$; simple main effects showed that there was an effect of group on the inhibition measure, $F(2,90)=11.63$ $p<0.0001$, but not on the excitation measure $F(2,90)=1.43$ $p=0.25$. Tukey's test showed that whereas the DSPD subjects differed from the control participants $p=0.001$, the PD subjects did not $p=0.78$. We therefore conclude that the deficit in CI was greater in the DSPD participants. Further support for this interpretation comes from the fact that, in an analysis of the CP and CX ratings before and after training that excluded the PD participants, the critical 3-way interaction between group, stimulus compound and stage was still highly significant $F(1,38)=10.68$ $p=.002$.

The IPDE dimensional scores were not significantly different in the PD and DSPD units on any of the 10 subscales, the largest $\chi^2(1,N=23)=2.96$, $p=0.09$. Furthermore when the IPDE dimensional scores were sub-grouped as the 3 DSM-IV clusters, there was no significant difference between the two units, the largest $t(21)=1.28$, $p=0.22$. However, consistent with the admissions criteria, participants in the DSPD unit had significantly higher PCL-R scores (by both the individual factors and the total scores) than those in the PD unit, smallest $t(22)=2.53$, $p=0.02$, power=0.47. Thus participants with sufficiently high PCL-R scores to warrant DSPD admission showed overall less CI than those with lower PCL-R scores and the

difference between the units points to the combination of PDs, dangerousness and psychopathy as likely underlying mediators of differences in CI.

4.2.3.7 Medication differences

Finally, medication status made no difference to performance on the task. There were no differences in excitatory learning scores (both measures), or in inhibitory learning scores (both measures), between the PD patients with (n=14) and without (n=10) medication: for antidepressants, the largest $t(22)=1.11$, $p=0.28$; for anxiolytics, the largest $t(22)=0.78$, $p=0.44$; for antidepressants and/or anxiolytics, the largest $t(22)=1.27$, $p=0.22$; for antipsychotics, the largest $t(22)=1.54$, $p=0.14$; for any form of psychotropic medication, the largest $t(22)=1.51$, $p=0.15$.

4.2.4 Discussion

The results clearly showed CI effect in control participants, but the CI effect was abolished in the forensic PD samples. During the pre-test, there were no pre-existing differences in the ratings for the critical stimuli (CP and CX). At the pre-training stage, the PD group showed some sign of reduced excitatory learning, although the discrimination was learned - indeed participants who did not learn at this stage were excluded from the study (2 PD and 3 matched controls). At the training stage, PD participants gave lower ratings on reinforced trials and higher ratings on non-reinforced trials than did controls. Nonetheless they learned the discrimination, albeit at a lower level. This difference in prior learning was also evident in the test stage.

It can be arguable that there was some evidence of a more general learning deficit in the PD group, so one must consider the possibility that

the results do not represent a specific impairment in CI, but a more nonspecific effect on learning. However, the evidence for an impairment in excitatory conditioning in the PD group was statistically inconsistent, as well as being numerically more modest than the impairment in CI, and the CI deficit was significantly greater than the effect on excitatory learning in these PD participants. Moreover, although there was some sign of an impairment in learning the key CI discrimination between AZ and AP in the PD group, by the end of training the PD were performing as efficiently as the controls were on this task. The key result of the study was thus not strictly an impairment in inhibitory learning, but rather in the *expression* of that learning, when P was paired with the excitatory C in the summation test. The difference between the groups lay in the extent to which they were able to transfer what they had learned about P to other excitatory stimuli - the controls could transfer this information whereas the PD group showed no sign of being able to do so. It is difficult to explain this pattern of results in terms of a general learning deficit.

It was unexpected that there was no direct evidence in the present study that the difference in CI related to individual differences in impulsivity as measured by the UPPS (either overall or in relation to its subscales), which was predicted before the experiment. However, self-report and behavioural measures of impulsivity often show a weak relationship (Claes et al., 2006; Helmers, Young & Pihl, 1995; Moeller et al., 2001). Although a high proportion of the sample had confirmed ASPD and/or BPD according to the IPDE categorical diagnoses, there was no correlation between any of the IPDE dimensional measures and CI scores. Similarly, there was no correlation between CI scores and psychopathy levels as measured by the PCL-R, either overall or by either of the subscales (Hare, 1991; Lykken, 1995). In spite of these results, one cannot place too much weight on

these observations as, in common with other experimental studies, the sample size was underpowered for these kinds of analyses (observed power for the correlations between 0.11 and 0.35).

There was also a significant difference in the CI effect between patients in the PD and the DSPD units. Specifically participants in the DSPD unit showed significantly less CI; indeed the demonstration of abolished CI remained significant when the analysis was restricted to the samples. The difference between the PD and ASPD units should be further considered. DSPD unit patients are typically characterised by the co-occurrence of high PCL-R scores with an ASPD diagnosis and, frequently, a BPD diagnosis (Howard & Duggan, 2009). This pattern of co-morbidity is associated with a significant degree of serious, in particular violent, offending (Kosson et al., 2006; Coid & Ullrich, 2010) and with high scores on a dimension of hostile impulsivity, characterised by aggression, resentment, deviance and paranoid beliefs together with affective dyscontrol (Blackburn, 2009). Since this particular quality of deviant disinhibition is not captured by UPPS, it is not surprised that no significant association was found here between UPPS scales and CI. Nor is it surprising that the CI deficit failed to correlate significantly with PCL-R scores, since it is the co-occurrence of psychopathy with ASPD (and frequently BPD as well) that characterises these deviant and disinhibited patients, rather than simply a high PCL score. In the present study, the more dangerous participants showed less CI.

Any firm conclusion that CI is impaired in relation to PD within a forensic population depends on the adequacy of the matched control condition. The control participants were matched as far as possible with the PD group in terms of general factors, including educational level and socio-economic

status. Moreover, participants who did not learn in the first training stage were excluded; but of course differences in general intelligence or motivational factors between the control and forensic PD groups cannot be ruled out. It is also important to consider the possibility that medication might be the sufficient explanation of the loss of CI in the PD patients, as a relatively large proportion of the sample was on benzodiazepines or antipsychotics of some description and such medications generally impair cognitive function.

A contradiction of non-specific differences, the diversity of medication regime would seem unlikely to provide any systematic account of the failure of forensic PD participants to express CI. Non-specific effects of medication, e.g. on arousal, attention or motivation to engage with the task, would be expected to depress performance throughout, and this was not the pattern of effects observed in the present study. Most importantly, the change in CI was selective, demonstrated over and above any difference in excitatory learning. However, such arguments do not exclude the possibility that confounded factors contribute to the observed difference in CI in the forensic PD and control groups. Moreover, the controls were not matched for incarceration or substance abuse history. Nonetheless, given the significant difference in CI between the participants from the PD and DSPD units, it could be argued that incarceration *per se* does not seem to be the critical issue. The results of current study suggested a more natural conclusion – inhibitory learning deficits may contribute to the cognitive profile of an individual whose behaviours result in incarceration – rather than suggest that incarceration *per se* has a selective cognitive effect. In summary, the pattern of results obtained is

not obviously explicable in terms of the nature of the matched control condition.

Chapter V: Individual differences and learning

5.1 Introduction

This chapter aims to explore the relationship between individual differences and associative learning performance. The individual differences were assessed by 5 questionnaires: BIS/BAS, UPPS, EPQ-RS, O-LIFE (short), and STB. These measures were closely related to the clinical samples in the present study – schizophrenic patients and patients with personality disorder in forensic settings. For example, BIS measures levels of anxiety. According to Eysenck's dimensional model of psychological disorder, anxiety may link to avoidant personality disorder (Eysenck, 1957; Eysenck & Eysenck 1976a, 1976b); and anxiety is often comorbid with schizophrenia and PD (Braga, Petrides, & Figueira, 2004; Dowson, 1992). BAS and UPPS measure levels of impulsivity, and impulsivity is one of the core features for some clinical populations (e.g. schizophrenic patients, and patients with PD in forensic settings).

Again, according to Eysenck, individuals with high neuroticism scores (measured by EPQ-RS) may suffer from anxiety-related conditions and antisocial behaviours when combined with high introversion and high extraversion, respectively; these with high psychoticism scores are more susceptible to schizophrenia and mood disorder (Eysenck, 1957; Eysenck & Eysenck 1976a, 1976b). In relation to susceptibility to disorder, O-LIFE (short), and STB measure schizotypal personality disorder and borderline personality disorder respectively in normal populations. It is clear that the symptoms of schizotypal personality disorder (e.g., odd beliefs and behaviours) are closely related to some of the symptoms among schizophrenic patients.

Generally speaking, it was predicted that anxiety, impulsivity, neuroticism, psychoticism, schizotypy and borderline personality disorder tendencies should be negatively related to CI learning performance.

The BIS/BAS scales were developed to assess two general motivational systems (behavioural inhibition and behavioural activation systems) underlying behaviour and affect. According to Gray (1982), individual with higher BIS scores shows sensitivity to non-reward cues. The typical emotion accompanying BIS activity is characterised as anxiety. Previous research suggested that people with a higher BIS score were vulnerable to states of anxiety and other negative affects (Fowles, 1980, 1993; Gray 1985). Only one study has explored BIS scores in relation to CI learning performance (Migo et al., 2006); however no significant correlation was found. Results previously reported in the thesis (chapter 2, experiment 5) showed a negative correlation between BIS scores and CI learning performance. Therefore, it can be expected that participants scoring higher on BIS would perform worse on the CI learning task.

BAS scales are developed to explain sensitivity to signals of reward, non-punishment, and escape from punishment. People with high BAS sensitivity should respond towards the reward signals behaviorally, and should experience a positive affect when these signals are presented. The high BAS sensitivity reflects high impulsivity or antisocial tendencies (Gray, 1985, 1987). BAS scales include three sub-scales: BAS drive, BAS fun seeking and BAS reward responsiveness (listed in table 5.2). Previous studies proposed a negative relationship between BAS activity and inhibitory control – participants with higher BAS scores would show more inhibitory problems (Logan et al., 1997; Patterson & Newman, 1993). The earlier study of CI also found that BAS reward responsiveness was

negatively correlated with inhibitory learning (Migo et al., 2006), thus it is anticipated that participants scoring higher on BAS or BAS sub-scales would perform worse on the CI learning task used in the present study.

The UPPS questionnaire was proposed to measure impulsiveness, which includes: (Lack of) premeditation, Urgency, Sensation Seeking, and (Lack of) perseverance. Lack of inhibitory control could be one of the core features of impulsivity; therefore, theoretically any scale that indicates high impulsivity should predict poor CI. Furthermore, some previous research suggested that people with high impulsivity performed worse on behavioural inhibitory tasks (Enticott et al., 2006; Logan et al., 1997; Swann et al., 2009; Visser et al., 1996). However, other studies have demonstrated no correlations between the questionnaire measures (e.g. Eysenck's Impulsiveness Scale, Barrett's Impulsiveness Scale, and the BIS/BAS scale) and behavioural measures of impulsivity (Claes et al., 2006; Helmers, Young & Pihl, 1995; Milich & Kramer, 1984; Paulsen & Johnson, 1980). On balance these earlier findings, it could be expected that a negative correlation would be found between impulsivity and CI learning performance.

The EPQ-RS scale was developed to assess the major dimensions of personality, which contains 4 subscales: extraversion (E), psychoticism (P), neuroticism (N) and response distortion (lie scale, L) (Eysenck et al., 1985). Helmers et al. suggested a positive correlation between extraversion and impulsivity, the study also found that extraverts demonstrate greater errors of commission than introverts during Go/NoGo tasks (Helmers et al., 1997). The psychoticism scale is related to several different facets, such as hostility, cruelty, lack of empathy, and non-conformity (Eysenck et al., 1985), and this subscale has been found to

correlate negatively with LI (e.g. Baruch, Hemsley & Gray, 1988b). Individuals with higher neuroticism scores may suffer strong, changeable mood, and overreact in emotional situations (Eysenck & Eysenck, 1976a, 1991). Eysenck proposed that anxiety was a typical profile for neuroticism. Previous studies found a negative correlation between anxiety and associative learning (Braunstein-Bercovitz, 2000; Braunstein-Bercovitz, Rammsayer, Gibbons & Lubow, 2002). Moreover, the earlier result described in this thesis (chapter 2, experiment 5) also confirmed that anxiety (as measured by BIS) was negatively correlated with CI learning as measured in the present task. Up to date, no study has explored the relationship between associative learning and EPQ-RS lie subscale. Based on previous findings, it is therefore predicted that E, P and N should be negatively correlated with the CI learning measure.

The O-LIFE (short) scale was based on a schizotypal personality scale (STA, Claridge & Broks, 1984; Mason et al., 2005), and has been developed for measuring schizotypal personality in normal population. The O-LIFE has four sub-scales: unusual experiences, cognitive disorganization, introverted anhedonia, and impulsive non-conformity. Previous studies have shown participants scoring higher on schizotypal personality scales (i.e. STA or O-LIFE) and performing worse on inhibitory learning tasks (e.g. PPI and CI learning tasks) (Abel, Jolley, Hemsley, & Geyer, 2004; Migo et al., 2006), so it is predicted that high scores on the O-LIFE and its subscales should be negatively related to the CI learning measure.

The STB questionnaire has been used for measuring borderline personality traits in non-clinical individuals, which contains two subscales: hopelessness and impulsiveness (Claridge & Broks, 1984). According to previous research, impulsivity is negatively correlated with inhibitory

control (Claes et al., 2006; Horn et al., 2003; Lansbergen et al., 2007), consequently participants with higher STB scores should perform worse on CI learning tasks. It is therefore expected that there should be a negative relationship between the STB scores and the CI learning measure.

The present study also will check the relationship between demographic variables and CI learning measures. Previous studies demonstrated significant associations among age, gender and measure of impulsivity. For example, younger people showed higher impulsivity than older people (Helmers et al., 1995). Males are more impulsive than females (Chappel & Johnson, 2007; Waldeck & Miller, 1997). It is expected that age may positively correlate with CI learning measure, and females perform better than males in the CI learning task.

5.2 Methods

5.2.1 Participants

A total of 237 healthy participants took part in a computer based learning task, and all participants completed a set of questionnaires [BIS/BAS, EPQ-RS, O-LIFE (Short), and STB]. Twenty out of 237 participants failed the excitatory associative learning task (the pre-training stage: i.e. rating scores (C–V)=<0); as in the previous experiments, these participants were excluded from the CI analyses. Only 106 participants were assessed by UPPS. It was because the UPPS questionnaire was only added in the experiments 5, 9 and 10, after confirming the scales used for the assessment of impulsivity in PD patients.

Table 5.1 shows the number, gender and age for participants in each of the experiments, whose scores were used for data analysis in the chapter.

Table 5.1 Participants information

	Number of participants	Number of male/female participants	Participants failed the pre-training stage	Average age (year)	Age range (year)
Experiment 1	16	14/2	Not applied	21.31	19-28
Experiment 2	43	20/23	3	21.56	18-39
Experiment 3	19	9/10	3	21.26	18-28
Experiment 4	26	12/14	2	21.42	18-33
Experiment 5a	36	17/19	4	22.10	18-33
Experiment 5b	34	12/22	2	25.71	19-47
Experiment 8	27	15/12	3	22.26	18-31
Experiment 9 & 10	36	28/8	3	35.11	19-56
Total participants	**237**	**127/110**	**20**	**23.84**	**18-56**

Note: There was no pre-training stage in experiment 1 (n=16), so for the assessment of the excitatory associative learning: n=237-16=221.

5.2.2 Materials

The details for the questionnaires were listed in chapter 2. Table 5.2 shows all the subscales for 5 questionnaires; scores of the subscales were also used in the analyses of the relationship between individual differences and CI learning performance.

Table 5.2 The subscales for 5 questionnaires.

Questionnaire	Subscales	
BAS	1. BAS Drive	2. BAS Fun seeking
	3. BAS Reward responsiveness	
UPPS	1. (Lack of) premeditation	2. Urgency
	3. Sensation Seeking	4. (Lack of) perseverance
EPQ-RS	1. Extraversion	2. Psychoticism
	3. Neuroticism	4. Response distortion (lie)
O-LIFE (short)	1. Unusual experiences	2. Cognitive disorganisation
	3. Introverted anhedonia	4. Impulse non-conformity
STB	1. Hopelessness	2. Impulsiveness

5.2.3 Analyses

The relationships between individual differences and associative learning were examined by Pearson's correlational analyses in the current study. For learning scores, again the summary measure of excitatory associative learning was provided by comparison of the ratings of the excitatory C and the non-reinforced V [i.e. (C-V)], and the summary measure of CI was provided by comparison of responding on the test trials with CX and CP

[i.e. (CX-CP)]; the greater the (C-V) and (CX-CP) scores, the higher the level of excitatory learning and inhibitory learning.

It is suggested that Bonferroni adjustments can be employed to reduce Type I errors when multiple tests are conducted (Larzelere & Mulaik, 1977). Both standard Bonferroni procedure and sequential Bonferroni procedure are commonly used when examining multiple correlation coefficients (Holm, 1979; Rice, 1989). Nevertheless, Jennions and Møller (2003) argued that both procedures exacerbate a serious problem – a substantial reduction in the statistical power of rejecting an incorrect null hypothesis. This is to say the likelihood of Type II error is increased after the Bonferroni adjustments. Besides, the Bonferroni method suggests that all null hypotheses are true simultaneously (Perneger, 1998); however, the general null hypothesis is not the most important point in the current study. Furthermore, there is no formal consensus for when the Bonferroni adjustments should be used (Perneger, 1998), thus it may contribute to publication bias (a basis for adjusting *p* values). In brief, Bonferroni corrections created more problems than they had actually solved, especially when the multiple tests are performed in analysing the data from a clinical study or a behaviour experiment (Perneger, 1998; Nakagawa, 2004). Therefore, Bonferroni adjustments were not conducted in the current study.

5.3 Results

The data of all the CI experiments in normal populations were added up to examine condition inhibitory effects. If there was evidence of the CI effects in these participants, then further analyses could be applied to explore the relationship between the individual differences and the CI learning performance.

5.3.1 Analyses of CI effects

5.3.1.1 Pre-test stage

Figure 6.1 shows the rating scores during the pre-test stage. There was not much difference on the rating scores of all the stimuli which were around 5. There was no significant difference in responding to the two critical test compounds (CP v. CX), $F<1$. The analysis during the pre-test stage suggested no pre-existing biases in responding to the stimuli.

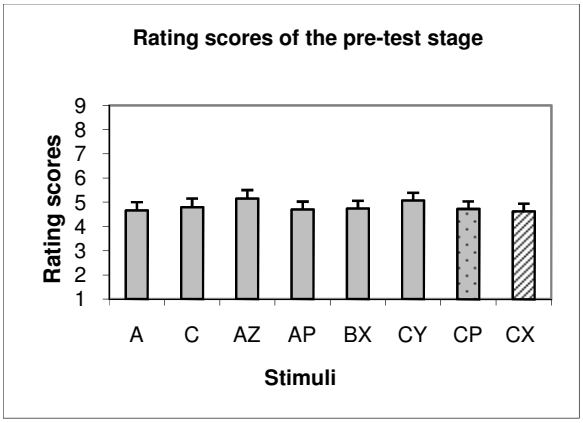


Figure 6.1 Rating scores for A, C, AZ, AP, BX, CY, CP and CX at the pre-test stage for all CI experiments. A rating of 9 reflected expectation of a nice picture, 1 of a neutral picture and 5 indicated uncertainty.

5.3.1.2 Pre-training stage

During the pre-training stage, the ratings of A and C steadily increased, while those to the U and V stimuli fell gradually. Participants appeared again to learn the discrimination in this phase (see figure 6.2). An ANOVA with discrimination (A or U v. C or V), reinforcement and pre-training block (1–6) as factors, revealed no main effect of discrimination $F<1$. However, the main effect of the pre-training block and reinforcement was significant, $F(5,1000)=5.80$, $p<0.001$; $F(1,200)=563.86$, $p<0.001$ respectively. The interaction of these two factors was also significant $F(5,1000)=133.20$, $p<0.001$; furthermore, there was also a significant three–way interaction $F(5,1000)=3.39$, $p=0.005$, suggesting the differences between reinforced and non-reinforced trials in both discrimination types developed over the

blocks. No other two–way interactions were significant, the largest $F(5,1000)=1.81$, $p=0.11$.

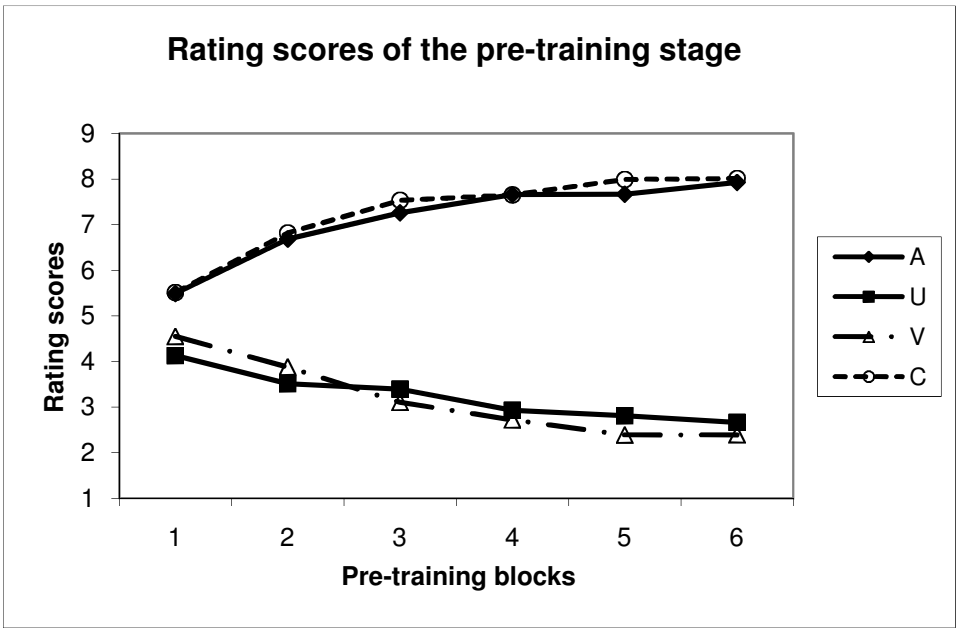


Figure 6.2 Rating scores for A+, U–, V– and C+ at the pre-training stage for all CI experiments. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

5.3.1.3 Training stage

During the training stage, the ratings of AZ and CY steadily increased, while those of AP and BX fell gradually (see figure 6.3), which suggested that participants had learned the critical discrimination. An ANOVA with discrimination (AZ or AP v. CY or BX), reinforcement and training block (1–4) as factors, revealed no main effect of discrimination $F<1$. However, the main effect of the training block and reinforcement was significant, $F(3,648)=31.87$, $p<0.001$; $F(1,216)=35.05$, $p<0.001$ respectively.

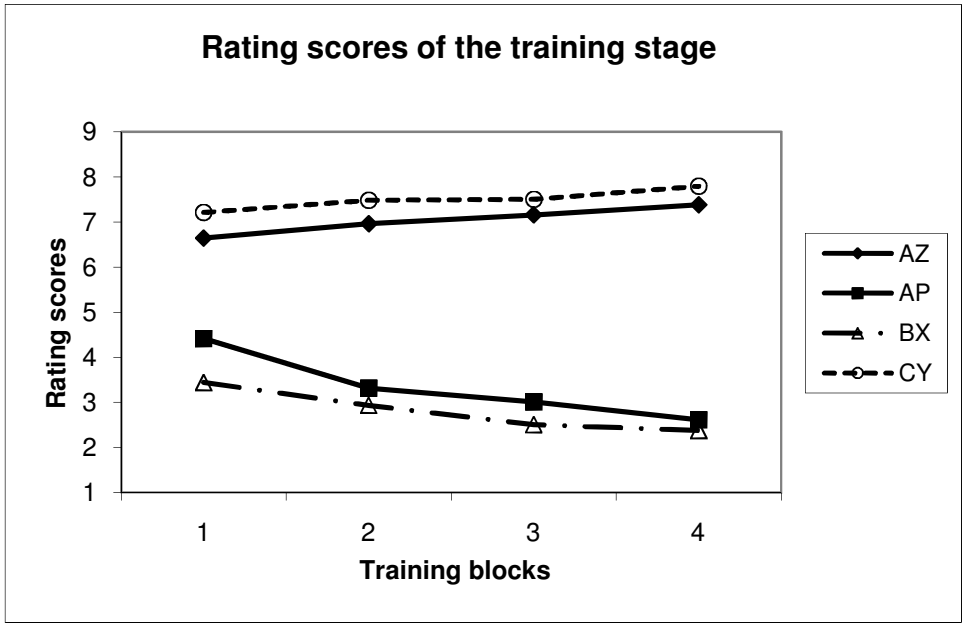


Figure 6.3 Rating scores for AZ+, AP–, BX– and CY+ at the training stage for all CI experiments. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

The two-way interactions between training block and discrimination, training block and reinforcement, discrimination and reinforcement, were also significant $F(3,648)=3.35$, $p=0.02$; $F(3,648)=5.28$, $p<0.001$; $F(1,216)=541.53$, $p<0.001$ respectively. Furthermore there was also a significant three–way interaction $F(3,648)=94.87$, $p<0.001$, suggesting the differences between reinforced and non-reinforced trials in both discrimination types developed over the blocks. This indicated that both sets of stimuli were sufficiently distinctive to support the learning of the discrimination.

5.3.1.4 Test stage

Figure 6.4 shows the rating scores during the test stage. Again, the ratings of A and C remained high, and the AZ or AP v. CY or BX discriminations were maintained; the latter observation was confirmed by the results of an ANOVA with discrimination and reinforcement as factors, which revealed no main effect of discrimination $F(1,216)=1.51$, $p=0.22$. However, the effect of reinforcement was significant $F(1, 216)=545.73$, $p<0.001$. The

interaction between discrimination and reinforcement was also significant $F(1, 216)=8.05$, $p=0.005$, suggesting both discrimination and reinforcement were learned effectively and maintained in the test stage.

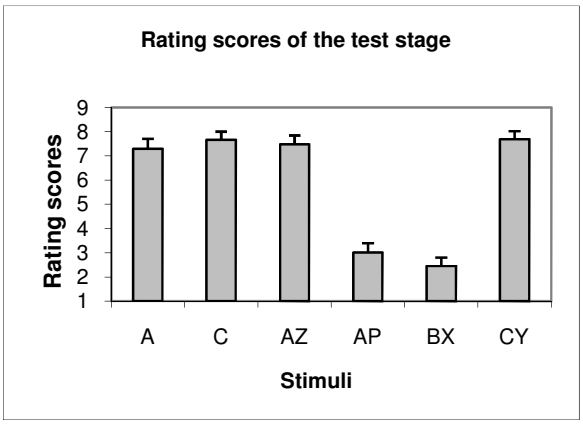


Figure 6.4 Rating scores for A+, C+, AZ+, AP–, BX– and CY+ at the test stage for all CI experiments. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty.

Comparing the two critical stimuli CP and CX during the pre-test and the test stages, it can be seen from figure 6.5 the rating of CP was noticeably lower than CX during the test stages. The difference was confirmed by statistical analysis: an ANOVA with stage (pre-test and test), and stimulus (CP v. CX) as factors, revealed no main effect of stage $F<1$. However the effect of stimulus was significant $F(1,216)=26.13$, $p<0.001$. The interaction between the two factors was also significant $F(1,216)=31.50$, $p<0.001$. The simple main effects revealed that participants gave significantly lower rating scores to CP than to CX during the test stage $F(1,216)=6.98$, $p<0.001$, but not at the pre-test stage $F<1$. The results suggest that P had become a conditioned inhibitor when the data from all CI experiments were added together.

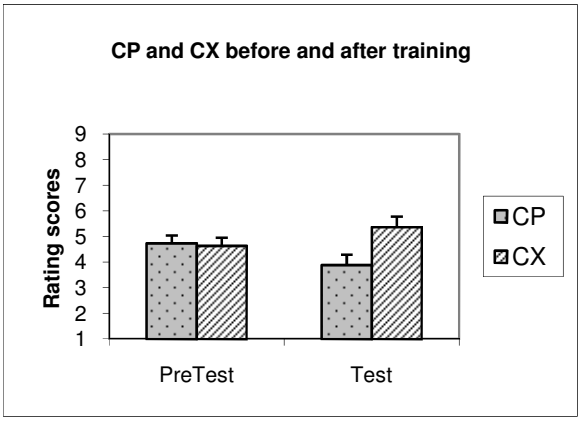


Figure 6.5 Rating scores for the key comparison stimuli CP and CX at the pre-test and the test stages for all CI experiments. A rating of 9 reflected expectation of a nice image, 1 of a neutral image and 5 indicated uncertainty. The pre-test ratings showed that the stimuli elicited similar ratings prior to conditioning. The test ratings confirmed the presence of conditioned inhibition, which was shown as higher ratings to CX than CP.

5.3.2 Individual differences

5.3.2.1 Excitatory associative learning and questionnaire measures

5.3.2.1.1 BIS/BAS

There was a significant correlation between the BAS drive scores and the summary measure of excitatory learning (C-V), $r(221) = -0.17$, $p=0.01$. However, there was no correlation between the other subscales of the BIS/BAS and (C-V), the largest $r(221)=-0.10$, $p=0.16$.

5.3.2.1.2 UPPS

There was a significant correlation between the UPPS (urgency scores) and the summary measure of excitatory learning (C-V), $r(106)=-0.21$, $p=0.03$. However, there was no correlation between the other subscales of the UPPS and (C-V), the largest $r(106)=-0.17$, $p=0.07$.

5.3.2.1.3 EPQ-RS

There was a significant correlation between the EPQ-RS (neuroticism scores) and the summary measure of excitatory learning (C-V), $r(221)=-0.18$, $p=0.009$. However, there was no correlation between the other

subscales of the EPQ-R (Short) and (C-V), the largest $r(221)=0.12$, $p=0.09$.

5.3.2.1.4 O-LIFE (Short)

The correlation between the O-LIFE total scores and the summary measure of excitatory learning (C-V) was significant, $r(221)=-0.16$, $p=0.02$. There was also a significant correlation between the O-LIFE (unusual experiences scores) and (C-V), $r(221)=-0.14$, $p=0.04$. At the same time, there was a significant correlation between the O-LIFE (cognitive disorganisation scores) and (C-V), r $(221)=-0.16$, $p=0.02$. However, there was no correlation between the other subscales of the O-LIFE (Short) and any of the summary measures of excitatory learning, the largest $r(221)=-0.11$, $p=0.12$.

5.3.2.1.5 STB

There was no correlation between the STB scores, either the total score or any of its sub-scales, with the summary measures of excitatory learning, the largest $r(221)=-0.12$, $p=0.07$, for STB total score and hopelessness subscale.

5.3.2.2 CI learning and questionnaire measures

5.3.2.2.1 BIS/BAS

There was a significant correlation between the BIS scores and the summary measure of inhibitory learning (CX-CP), $r(217)=-0.14$, $p=0.04$. However, there was no correlation between the other scales/subscales of BIS/BAS and (CX-CP), the largest $r(217)=0.09$, $p=0.21$.

5.3.2.2.2 UPPS

There was no correlation between the UPPS scores, either the total score or any of its sub-scales, with the summary measure of inhibitory learning, the largest $r(106)=-0.11$, $p=0.27$.

5.3.2.2.3 EPQ-RS

There was a significant correlation between the EPQ-RS (neuroticism scores) and the summary measure of inhibitory learning (CX-CP), $r(217)=-0.16$, $p=0.02$. However, there was no correlation between the other subscales of the EPQ-RS and (CX-CP), the largest $r(217)=0.13$, $p=0.06$.

5.3.2.2.4 O-LIFE (Short)

There was a significant correlation between the O-LIFE (total scores) and the summary measure of inhibitory learning (CX-CP), $r(217)=-0.14$, $p=0.05$. There was also a significant correlation between the O-LIFE (cognitive disorganisation scores) and (CX-CP), $r(217)=-0.16$, $p=0.02$. However, there was no correlation between the other subscales of the O-LIFE (Short) and (CX-CP), the largest $r(217)=-0.11$, $p=0.10$.

5.3.2.2.5 STB

There was no correlation between the STB scores, either the total score or any of its sub-scales, with the summary measure of inhibitory learning, the largest $r(217)=-0.08$, $p=0.24$.

5.3.2.3 Demographic characteristics and learning

5.3.2.3.1 Age and learning

There was a significant correlation between the age and the summary measure of excitatory learning (C-V), $r(221)=0.16$, $p=0.02$. However,

there was no correlation between the age and the summary measure of inhibitory learning $r(217)=0.10$, $p=0.13$.

5.3.2.3.2 Gender and learning

There was no difference between the gender and any of the summary measures of excitatory or inhibitory learning, the largest $t(217)=-1.0$, $p=0.13$.

5.3.2.4 Link between excitatory and CI learning

Three scales (O-LIFE total, O-LIFE cognitive disorganization sub-scale and EPQ-RS neuroticism sub-scale) were not only related to the summary measure of excitatory associative learning (C-V), but also correlated with the summary measure of CI learning (CX-CP), which may indicate a link between excitatory and CI learning. In order to further explore this relationship, the rating scores of (C-V) and (CX-CP) were analyzed by Pearson correlation as well. The results showed that there was no significant correlation between the two ratings $r(221)=0.12$, $p=0.07$, suggesting that inhibitory learning is dissociable from excitatory learning.

5.4 Discussion

In terms of individual differences for the excitatory associative learning task, it showed that individuals with higher BAS Drive, impulsive neuroticism, and schizotypy scores performed worse on the learning task. Significant negative correlations were found between the measure of excitatory learning performance and BAS drive, UPPS urgency, EPQ-RS neuroticism subscales, O-LIFE total score and two O-LIFE subscales (unusual experiences and cognitive disorganization) (see table 5.3).

Table 5.3 Summary of correlation between the excitatory measures and the questionnaires scores.

	n	*r*	*p*
BAS Drive and (C-V)	221	-0.17	0.01
UPPS Urgency and (C-V)	106	-0.21	0.03
EPQ-RS Neuroticism and (C-V)	221	-0.18	0.009
O-LIFE Total score and (C-V)	221	-0.16	0.02
O-LIFE Unusual experiences and (C-V)	221	-0.14	0.04
O-LIFE Cognitive disorganization and (C-V)	221	-0.16	0.02

Note: C was the excitatory stimulus, the greater the C-V score, the higher the level of excitatory learning.

The present study found that people with high BAS drive sensitivity did worse on the excitatory learning task. Furthermore, people with high UPPS urgency did worse on the excitatory learning task. The results suggested that people with higher impulsive scores performed worse on the excitatory learning task. Previous studies have demonstrated negative correlations between measures of impulsivity and behavioral inhibition, e.g. as measured by the Go/NoGo task and the Stop Signal task (Enticott et al., 2006; Logan et al., 1997; Visser et al., 1996). However, up to now, no published research examined the relationship between impulsivity and associative learning. The current study aimed to gain insight into the correlation between the measures of impulsivity and stimulus-stimulus associative learning. The results may suggest that the impaired associative learning processes may be responsible for impulsive behaviors in some of the clinical groups, such as ASPD and psychopathy.

The significant negative correlation between excitatory learning performance and EPQ-RS neuroticism may indicate that individuals who are prone to suffer strong, changeable mood, and to overreact in emotional situations show poorer excitatory learning ability. People who score higher on neuroticism are also more likely to experience anxiety (Eysenck, 1957; 1967), and these people performed worse on the excitatory learning task.

It was hypothesized that a negative correlation would be found between anxiety and associative learning measures, and the results support this hypothesis. The current study may provide some explanation for the impaired associative learning processes in anxiety and phobia patients (Davey, 1992; Grillon, 2002).

The significant negative correlation between excitatory learning performance and O-LIFE total scores suggested that people who scored higher on O-LIFE (especially on O-LIFE cognitive disorganization subscales) showed less evidence of simple associative learning. This finding is consistent with a previous study (Migo et al., 2006) in which higher schizotypal personality traits was accompanied by poorer associative learning performance. It may suggest that the impaired excitatory learning processes are possibly responsible for the associative learning dysfunctions in schizophrenia (Claridge, 1997; Claridge & Broks, 1984; Frith, 1979).

In terms of individual differences for the inhibitory learning task, significant negative correlations were found between the measure of CI learning performance and BIS scores, EPQ-RS neuroticism subscale, O-LIFE total scores, and O-LIFE subscales (cognitive disorganization) (see table 5.4).

Table 5.4 Summary of correlation between the CI measures and the questionnaires scores.

	***r* (n=217)**	***p***
BIS and (CX-CP)	-0.14	0.04
EPQ-RS Neuroticism and (CX-CP)	-0.16	0.02
O-LIFE Total score and (CX-CP)	-0.14	0.05
O-LIFE Cognitive disorganization and (CX-CP)	-0.16	0.02

Note: P was the putative inhibitor, and thus supposed to suppress evaluation of C more than X; thus the greater the CX-CP score, the higher the level of inhibitory learning.

The current study indicates that people with higher BIS scores performed worse on the CI learning task. Individuals with higher BIS sensitivity could be more vulnerable to anxiety or depressive disorders (Fowles, 1980,

1993; Gray 1985). Besides, a significant negative correlation was also found between the EPQ-RS neuroticism sub-scales and the measure of CI learning performance. Again, the higher neuroticism scores indicate the higher levels of anxiety (Eysenck, 1957; 1967). The results confirmed the levels of anxiety negatively correlated with the CI learning performance, which was consistent with the findings in experiment 5. The results of present study supported the hypothesis and consisted with some previous studies (Barlow, 2000; Grillon, 2002), which suggested inhibitory learning deficits in anxiety.

Furthermore, significant negative correlations were found between the O-LIFE total scores, O-LIFE cognitive disorganization subscales and the measure of CI learning performance. The results indicated that individuals with higher schizotypy scores performed worse on the conditioned inhibitory learning task. These results replicated previous findings that people with higher schizotypy scores performed worse during the CI learning task (Migo et al., 2006).

It was unexpected that the current study did not find a correlation between impulsivity (measured by the BAS and UPPS scores) and CI learning performance. There are several possibilities, first, some previous studies suggested low correlations between the paper-and-pencil and behavioural measures of impulsivity (Claes et al., 2006; Helmers et al., 1995; Milich & Kramer, 1984; Paulsen & Johnson, 1980). Second, research has suggested that the low arousal conditions typical of laboratory testing underestimate impulsivity (Helmers et al., 1997). Up to now, no published study has investigated CI learning in relation to impulsivity. Further research is essential to explore the link between CI learning and impulsive personality

traits in non-clinical populations, which also can benefit our understanding of the cognitive abnormalities in clinical patients.

The failure to find a correlation between STB measures and both excitatory and inhibitory learning was unexpected. However, the STB questionnaire not only indicates participants' impulsiveness, but also reflects their physical anhedonia (Rawlings et al., 2001). Some previous research suggested that no significant correlation was found between STB measures and inhibitory learning performance. For example, there was no significant correlation between CI learning and STB scores in Migo et al.'s study. Furthermore Gray and colleagues suggested that the measures of normal participants' introvertive anhedonia (measured by STA/STB) were not related to a reduction in LI (Gray, Fernandez, Williams, Ruddle & Snowden, 2002), which suggested that the STB scores in relation to associative learning is hard to demonstrate. The STB has been used in little published research. Further studies are needed to help us understand the associative learning ability in relation to borderline personality.

With regards to Eysenck's I-E theory and his biological explanation of behaviours, the present research did not find any correlation between I-E measures and excitatory/inhibitory learning. This result is contrary to those suggested by Eysenck, (1957; 1967), which indicated that on average introverts were able to form conditioned responses more easily than extraverts. Finally, there was no relationship between gender and associative learning, but the data did show a correlation between age and associative learning: older participants showed relatively better excitatory learning.

In conclusion, consistent with the theories of Gray and Eysenck, the present research findings suggested that anxiety, impulsivity, neuroticism, and schizotypal personality traits, but not introversion/extraversion, psychoticism and borderline personality traits all exerted main effects on associative learning. The negative correlation between CI learning performance and anxiety, neuroticism and schizotypy may help us to understand cognitive dysfunctions in a wide range of disorders including schizophrenia and personality disorder. Demographic variables (eg. age and gender) play some role in associative learning, which underlines the importance of recruiting matched control participants for patients.

Chapter VI: General discussion

6.1 Summary of current research

The purpose of this PhD research was to develop suitable conditioned inhibition learning procedures in humans, and explore the CI learning effects in relation to individual differences and disorder. Conditioned inhibition is fundamental for cognitive processes in both animals and humans, and it is involved in a wide range of normal behaviours. Disruption of CI could produce a wide range of behavioural deficits, for example, lack of inhibitory control has been argued to lie at the core of impulsivity (Buss & Plomin, 1975). Impulsivity is one of the core features in some clinical groups, such as schizophrenic patients and cluster B personality disorders (PD), especially PD within forensic populations (Hare et al., 1991; Munro et al., 2007).

Previous research studied impulsivity by using some laboratory behaviour learning tasks (e.g. Go-NoGo tasks). People with higher impulsivity have difficulty withholding respones which is demonstrated by poor performance in these tasks, especially in clinical groups, such as patients with BPD and ASPD (Grootens et al., 2008; Nigg et al., 2005; Rentrop et al., 2007; Rubio et al., 2007; Ruchsow et al., 2008). Such tasks are usually thought to involve inhibition of stimulus-response (S-R) association. To date, little research has explored the inhibition of stimulus-stimulus (S-S) associations (formally 'conditioned inhibition', CI) in relation to individual differences, and no research has explicitly examined CI learning in any clinical groups.

The present study used a computer-based task to explore excitatory and inhibitory learning performance within the same learning procedures. The computer-based task tested the inhibition of stimulus-stimulus (S-S) associations in university students, psychiatric patients and their matched controls. The psychiatric patients participating in the current study included

schizophrenic patients in community bases, and patients with personality disorder and psychopaths in forensic settings. It was hypothesized that the CI learning performance would negatively correlate with some personality traits (e.g. extraversion, impulsivity, anxiety, neuroticism, schizotypal and borderline personality) in normal populations. For the clinical groups (schizophrenic patients, patients with PD and psychopaths), these patients would show reduced or even abolished CI effects (Appendix 7 shows a summary of all experiments for present thesis).

The experiments successfully demonstrated a well controlled conditioned inhibitory learning procedure, and the results confirmed robust conditioned inhibitory effects in human participants using a summation test. The learning of CI was confirmed by the results of the summation test (Rescorla, 1969), specifically by the transfer of inhibition to an excitatory CS not previously presented with the conditioned inhibitor during training (stimulus C in the present study). Before the training, the critical comparison stimulus compounds (CX and CP) were overall well-matched and fully counterbalanced, in that there were no pre-existing differences in the ratings. Importantly the training history of the critical test stimuli X and P was identically matched in all respects apart from the fact that P only was trained as an inhibitor – both were previously non-reinforced in compound stimulus presentations on an equivalent number of trials. The only difference was that during this compound training stage P but not X was presented with a stimulus (A) that was reinforced during the first training stage, so that P uniquely specified that an otherwise expected reinforcement would not now occur. The ratings of CX and CP were compared at the test stage, and the CI learning was examined by (CX-CP). If CP was significantly lower than CX, it would suggest the evidence of CI effect. At the same time, the experiments also tested excitatory learning in

the same experimental procedures. At the pre-training stage, the Pavlovian excitatory learning was measured by (C-V), indeed participants who did not learn at this stage were excluded from the study.

In normal populations, the present research findings suggested that impulsivity, anxiety, neuroticism, and schizotypal personality traits were in relation to associative learning performance, but not introversion/extraversion, psychoticism and borderline personality traits. Demographic variables (eg. age and gender) played a small role on associative learning measures. In schizophrenic samples, compared with matched controls, the degree of excitation and inhibition was reduced among the schizophrenic patients; moreover, PANSS negative scores were negatively associated with the expression of inhibitory learning. However, there was no correlation between other PANSS scores (general and positive scores) and the CI learning measures. In addition, there was no correlation between medication (measured by CPZ equivalent) and either inhibitory or excitatory learning scores. In the forensic PD samples, some signs of excitatory learning were reduced and the CI effects were abolished. However, there was no evidence to suggest that this difference was due to impulsive levels, medication or PCL-R scores. The only clear difference in CI was shown between patients in the PD and the DSPD units at Rampton hospital; more specifically, participants in the DSPD unit showed significantly less CI than the matched controls, whereas the participants from the PD unit did not.

6.2 Associative learning in relation to individual differences

The individual differences were assessed by 5 questionnaires: BIS/BAS, UPPS, EPQ-RS, O-LIFE (short) and STB, in which the BIS scales measure the levels of anxiety; the BAS and UPPS questionnaires measure the levels of impulsivity; the EPQ-RS questionnaire measures 4 personality traits (extraversion, psychoticism, neuroticism and response distortion); the O-LIFE (short) scales measure schizotypal personality traits; and the STB scales measure borderline personality traits. Empirically, previous studies suggested individuals with high scores on measures of anxiety, impulsivity, schizotypy, extraversion, and neuroticism would show less inhibition (e.g. Van de Bergh et al., 2006; Migo et al., 2006). Theoretically, lack of inhibitory control could be a core feature for impulsivity (Buss & Plomin, 1975), so any scale that indicates high impulsivity should predict poor CI learning performance. Therefore, it was hypothesised that some personality traits, for example anxiety, impulsivity, schizotypy, extraversion, neuroticism, psychoticism, and borderline personality would negatively correlate with the CI learning performance.

The present study suggested associative learning was related to various personality traits, for example, anxiety (measured by BIS), impulsive or antisocial tendencies (measured by BAS and UPPS), schizotypy (measured by O-LIFE) and neuroticism (measured by EPQ-RS); however, there was no correlation with self-harm or destructive behaviours (measured by STB), and extraversion or introversion (measured by EPQ-RS), sensation seeking, premeditation, and perseverance (measured by UPPS). The present study suggested significant negative correlations between impulsivity, schizotypy, neuroticism and excitatory learning performance. The results confirmed

that people with higher BAS drive, UPPS urgency, EPQ-RS neuroticism and O-LIFE scores performed worse in the excitatory learning task.

Furthermore, significant differences were also found between the BIS, neuroticism, O-LIFE scores and the measure of conditioned inhibition, which indicated individuals who scored higher on the BIS, neuroticism and schizotypal personality measures performed worse in the CI learning task. The results were consistent with those of Grillon (2002) who reported a negative correlation between the measures of anxiety and associative learning performance; and also consistent with those of Migo et al. (2006) who reported a negative correlation between the measures of schizotypy and the CI learning performance. As discussed in chapter 1, Eysenck (1957, Eysenck & Eysenck, 1976a, 1976b, 1991) proposed statistically dimensions in accounting for normal and abnormal personality differences. According to Eysenck, the continuum of personality helps us to bridge the gap between personality as healthy individual variation, and mental illness as malfunction. He considered that the various forms of psychological disorder actually defined the extremes of the personality dimensions. Later Mason et al., (2005) developed O-LIFE (short) form measuring psychosis-proneness, principally schizotypy in normal populations, and the items from the scale deliberately chose for those who tapped psychotic characteristics in healthy individuals. Therefore, the negative correlation between the BIS, EPQ-RS neuroticism and O-LIFE measures could help us to understand the cognitive dysfunctions of a wide range of disorders, especially anxiety, schizotypal personality disorder and schizophrenia. It was expected that schizophrenic patients and patients with PD would show reduced or abolished CI effects.

It was predicted that impulsivity would negatively correlate CI learning, but the present study did not find any relationship between the UPPS scores (measures impulsivity) and CI learning measures. Regarding these findings, cautious interpretation of correlational analyses is necessary, as a unified psychometric self-report measure of impulsivity has not been defined, and a uniform pattern of association between the psychometric measures and behaviour measures was not evident in prior work. The results from the current study were consistent with the findings of Horn et al.'s study (2003), in which there was no evidence for correlations between impulsivity measures (measure by BIS-11) and errors of commission on the Go/NoGo task. Other studies also have demonstrated no correlations between the questionnaire measures (e.g. Eysenck's Impulsiveness Scale, Barrett's Impulsiveness Scale, and the BIS/BAS scale) and behavioural measures of impulsivity (Claes et al., 2006; Helmers, Young & Pihl, 1995; Milich & Kramer, 1984; Paulsen & Johnson, 1980), although some studies suggested that people with higher self-report impulsivity measures showed more errors of commission on the behaviour inhibitory learning task (Logan, Schachar & Tannock, 1997; Swann et al., 2009). Helmers et al. (1997) proposed one reason for the low/no correlation between paper-and pencil (questionnaires) and behavioural measures of impulsivity in normal participants – the laboratory testing impulsivity was under low arousal conditions that allows impulsive participants to restrain their impulsive behaviours.

In summary, the present PhD research explored the relationship between CI learning and individual differences. It was predicted that the CI learning performance would negatively correlate with impulsivity (measured by BAS, UPPS), anxiety (measured by BIS), extraversion, psychoticism, neuroticism (measured by EPQ-RS), schizotypal personality traits

(measured by O-LIFE) and borderline personality traits (measure by STB). The results have met the predictions on the negative correlation between the CI learning performance and the EPQ-RS neuroticism and O-LIFE scores, which suggested individuals with higher levels of neuroticism and schizotypal personality traits performed worse on the CI learning task. Nevertheless, the findings from the current study did not support the hypothesis on the negative correlation between the CI learning performance and impulsivity, extraversion, psychoticism, and borderline personality traits. Regarding the relationship between CI learning and anxiety, the results of experiment 5 showed some signs of negative correlation between these two factors (see chapter 2); however, when the data of all the experiments was drawn together, the correlation was not significant.

6.3 Associative learning in clinical groups

6.3.1 Excitatory and CI learning in schizophrenia and PD

Chapter 4 and 5 reported excitatory learning and CI learning in schizophrenic patients and patients with PD at Rampton Hospital. This novel conditioned inhibition task suggested evidence that both excitatory and CI conditioning were impaired in schizophrenia. For excitatory learning, during the pre-training stage, the results suggested that the controls learned the discrimination (A or U v. C or V) better than the schizophrenic patients. Regarding CI learning performance, comparing the pre-test and the test stages, control participants responded significantly less to the excitatory stimulus C when it was compounded with the inhibitor P than when it was presented with a matched control stimulus X, but participants in the schizophrenic group did not. The current study also yielded novel findings in forensic PD patients. There were some signs of reduced excitatory learning at the pre-training stage, although the discrimination

was learned - indeed participants who did not learn at this stage were excluded from the study. At the training stage, PD participants gave lower ratings on reinforced trials and higher ratings on non-reinforced trials than did controls. Nonetheless they learned the discrimination, and the difference between reinforced trials (AZ and CY) and non-reinforced trials (AP and BX) was also evident in the test stage. Comparing the rating scores before and after the training, the results clearly showed CI effect in matched controls; but the CI effect was abolished in the forensic PD samples. Both clinical groups showed some signs of reduced excitatory learning, which could be one of the explanations for the reduced/abolished CI effect in these groups.

6.3.2 Medication and learning performance

It is important to consider the possibility that medication might be the sufficient explanation of the loss of CI in the schizophrenic and PD patients, as all the schizophrenic patients were under a variety of antipsychotic medication regimes, and the majority of PD patients were on benzodiazepines or antipsychotics. The results of the current study suggested that there were no detectable differences between medication and the learning performance in the clinical groups. To be more precise, there were no correlation between the antipsychotic dose (measured by CPZ equivalent) and either excitatory or inhibitory learning scores in schizophrenic patients, and there was no correlation between medication and learning performances in PD patients.

There have been vigorous debates whether antipsychotics impacted on cognitive functions in the patients. Some studies reported antipsychotics may impair neurocognitive processes (Kumari & Sharma, 2002; Weickert &

Goldberg, 2005). In particular, Clozapine, may reduce impulsivity (Dursum, Szemis, Andrews, Whitaker & Reveley 2000; Spivak, Mester, Wittenberg, Maman & Weizman, 1997; Strous et al., 2006). However, other studies recommended atypical antipsychotics could improve cognitive functions in patients with schizophrenia (see a review, Keefe, Silva, Perkins & Lieberman, 1999). There is also previous evidence of associative learning abnormalities in schizophrenia which have been independent of medication (e.g. Baruch et al., 1988; Serra et al., 2001). It is difficult to discount completely whether medication impacted on the CI learning performance in the samples for the current study. A full understanding of the nature of CI learning defects in clinical groups would therefore require appreciation of the medication factor.

6.3.3 Schizophrenic symptom and learning performance

A PANSS structured interview was conducted to assess current symptom (positive, negative and general symptoms) for schizophrenic patients during the experiment. Surprisingly the results of the current study revealed that negative scores (not positive scores) were negatively associated with the expression of inhibitory learning. This is to say, schizophrenic patients with higher negative scores on PANSS perform worse on the CI learning task. It was not expect to find a significant difference for the correlational analysis since the sample size of the clinical group was relatively small (there were only 25 participants in the group, which usually indicated the data was underpowered for correlational analysis). Furthermore, it was expected that the CI learning performance should negatively correlate to positive symptoms. Schizophrenic patients with significant positive symptoms usually experienced delusions and hallucinations, which could impact on their capacity for associative thought and cognitive processes (Bleuler, 1911; Kraepelin, 1919; Venables, 1960,

1964). Because of these positive symptoms, the patients may fail to inhibit ideas as normal populations do.

The typical feature of negative symptoms is non-response or emotional blunting and an individual showing high CI would effectively ignore a complex stimuli which include a signal of non-reinforcement. Generally speaking, patients with significant negative symptoms are suffering very poor functions and quality of life (Katschnig, 2000; Norman et al., 2000; Orse et al., 2004); moreover, there is no specific medication target to negative symptoms (Kirkpatrick, Fenton, Carpenter & Marder, 2006), and little research has explored the relationship between negative symptoms in schizophrenia and associative learning. The findings from current research may contribute to our understanding of cognitive dysfunctions in schizophrenia, especially patients with significantly negative symptoms.

6.3.4 Forensic PD and learning performance

What explanations can be offered for the lack of correlation between CI and impulsivity measures in forensic PD patients and their matched controls? First, empirical evidence suggested low correlations between the questionnaire and behavioural measures of impulsivity (Claes et al., 2006; Helmers et al., 1995; Milich & Kramer, 1984; Paulsen & Johnson, 1980). It has also been suggested that the low arousal conditions typical of laboratory testing underestimate impulsivity (Helmers et al., 1997). Second, forensic PD patients in a locked environment may suppress their impulsive levels; especially some of the PD patients who have lived in the Rampton hospital for several decades. In fact, the UPPS scores were overall no different in the PD and the control group. Only the sensation-seeking scores were significantly lower in the PD group than those of in the controls, which were very possibly in response to incarceration.

Longitudinal studies might help to clarify whether incarceration impacts on impulsiveness. Finally, the sample size was underpowered for the correlational analyses. Thus, we cannot place too much weight on this unexpected finding.

IPDE and PCL-R scores were collected in patients with personality disorder at Rampton Hospital, which assessed categories of Personality Disorder and defined psychopaths for current PD samples. The results revealed no significant correlation between CI learning performance and either IPDE scores or PCL-R scores. However, there did appear to be differences between participants in the DSPD and PD units. More specifically, participants from the DSPD unit showed less inhibitory learning than those in the PD unit, while levels of excitatory learning were relatively unaffected. It is not clear what this might mean, it seems only the PCL-R score of the patients was the different personality profiles between the two units. Generally speaking, admission criteria for the DSPD unit are patients with sufficiently high PCL-R scores or those with 2 or more DSM-IV PD diagnoses (Howells et al., 2007). The results of current study suggested that combination of PDs, dangerousness and psychopathy as likely underlying mediators of differences in CI.

6.3.5 Theoretical and clinical implications in schizophrenia and PD

The present study confirmed that the reduced excitatory and inhibitory effects in schizophrenia suggesting that impairment in excitatory and inhibitory learning is a feature of schizophrenia. Reduced CI effects in patients may be the consequence of an excitatory associative learning deficit since there was a positive correlation between excitatory and CI learning performances. Besides, the current study found that significant negative correlation between the PANSS negative scores and CI learning

expression. The negative correlation between excitatory learning and negative schizophrenic symptom was also close to significant (p=0.09) in the relatively small samples. Negative schizophrenic symptoms (i.e. apathy, lack of emotion, poor or non-existent social functioning) may indicate less information was passed on to the patients or patients paid less attention to the learning tasks, thus they showed the worse excitatory and inhibitory learning performance. Moreover, the demonstration of CI deficit on the summation test specifically demonstrates that such inhibitory stimuli will not transfer, i.e. suppress excitation to a new stimuli with which they have not previously been paired. Thus, impaired CI learning ability will result in inappropriate responding to a variety of stimulus constellations that do not predict an outcome. The dysfunctional inhibitory processes in schizophrenia may result from other processing impairments associated with the patients, such as sensory flooding (Bleuler, 1911; McGhie & Chapman, 1961; Venables, 1960) or general executive dysfunction (Cheung, Mitsis & Halperin, 2004). In consequence, the schizophrenic patients showed reduced excitatory and CI learning performance.

The absence of the CI effect in forensic PD reflects a selective effect on associative learning that could potentially be relevant to both the symptom profile and the inability to control unwanted behaviours. Stimuli provided by environmental events are recognised to trigger associations that generate habitual thoughts and feelings (Ferguson & Cassaday, 1999; Lishman, 1987; Siegel, 1977; Stewart, Wit & Eikelboom, 1984; Watson, 1924). In forensic PD patients, precisely where the need to inhibit such associations is greater, impaired inhibition of S-S associations may leave some individuals less able to inhibit the unwanted thoughts and associations that can lead to unwanted actions. Therefore, therapeutic

interventions to improve learning by inhibiting antecedent S-S associations could be an effective behavioural approach to symptom control.

To sum up CI learning in clinical groups, the current PhD research explored CI learning in schizophrenia and PD forensic settings. The results showed a reduced CI effect in schizophrenia and an abolished CI effect in PD forensic settings, which supported the experimental hypothesis.

6.4 Limitations and future directions

Due to strict a inclusion criteria (e.g. schizophrenic patients and patients with PD did not have co-morbidity with other mental illnesses, participants who did not pass the pre-training stage were excluded from the study) and the limited time allowed for the completion of the PhD, the clinical sample size was relatively small, which might have increased the possibility of a Type II error, and also limited statistical power to detect significant difference between the groups, particularly for correlational analyses. For example, the lack of an association between impulsive and CI learning measures in PD samples and their matched controls, which might also be due to a lack of statistical power in the current study (power: $0.11<r<0.35$).

The controls in the current study were matched as far as possible with the clinical groups in terms of age, ethnic, general factors; including educational levels and socio-economic status, but differences in general intelligence or motivational factors between the control group and clinical groups (schizophrenia, PD and psychopathy) - which would result in non-specific performance differences - cannot be ruled out. Similarly, the majority of the schizophrenic patients and PD samples were on

antipsychotic medications. It was unlikely to withdraw treatments, but the possible influence of antipsychotic medication on impulsivity and inhibition measures cannot be overlooked. Therefore the present study may only be relevant to medicated patients with schizophrenia, personality disorder and psychopathy.

The present study also cannot exclude the possibility that confounded factors contributed to the observed difference in CI in the clinical samples and control groups, such as the fact that the controls were not matched for substance abuse history. It is very common that schizophrenic patients and PD offenders have a history of substance use/abuse (Collins, 1986, 1993; Smith & Hucker, 1994), which may bias the present experimental findings. For example, elevated impulsivity scores are often associated with past substance abuse or dependent (Dervaux et al., 2001), and severe cognitive impairment were associated with alcohol abuse in schizophrenic and PD patients (Allen, Goldstein & Aldarondo, 1999; Allen & Remy, 2001; Bowie, Serper, Riggio & Harvey, 2005).

The present study was also limited by an unknown capacity for participants to accurately self-report impulsiveness. It is unexpected that a failure to detect an association between the measures of impulsivity and inhibitory learning performance in clinical groups and matched controls; although some studies suggested low correlations between the questionnaire and behavioural measures of impulsivity (Claes et al., 2006; Helmers et al. 1995; Milich & Kramer, 1984; Paulsen & Johnson, 1980). Helmers et al., (1997) offered an explanation: laboratory testing this correlation under low arousal conditions which made impulsive participants restrain their impulsive behaviours. Besides, it cannot confirm whether long term

incarceration would impact on the measures of impulsivity; especially some of the PD participants that have been locked up for several decades.

6.5 Conclusions

The current research used a novel conditioned inhibition task, and tried to rule out the attention and generalisation decrement arguments in Pavlovian associative learning performance. The measure of excitatory and inhibitory learning was examined within the same learning procedure, and the CI effect was confirmed by the results of the summation test (Rescorla, 1969). The present study demonstrated correlations between excitatory learning performance and individual differences, as well as CI learning performance and established measures of individual differences. The results confirmed that healthy individuals with higher BAS and UPPS urgency (indicate higher impulsivity), neuroticism and O-LIFE scores, performed worse on the excitatory learning task; furthermore these people with high O-LIFE and neuroticism scores performed worse on the CI learning task. The findings of the present study supported the hypothesis that individual differences (in general populations) predicted differences in conditioned inhibition learning performance. However, there was no clear evidence that the different CI learning performance related to levels of impulsivity (was measured by questionnaires). It was unable to rule out this finding possibly due to shortcomings of self-report measurement of impulsivity.

The present study also confirmed schizophrenic patients, patients with personality disorder, and psychopaths showed reduced or even abolished CI effect. For CI learning in schizophrenic participants, the results provided evidence that the patients showed a clear reduction in their excitatory and inhibitory learning. Within the samples used in the present study, it was

unable to demonstrate any relationship between the level of CI shown and medication. However, the PANSS negative (but not positive) scores were negatively associated with the expression of inhibitory (but not excitatory) learning. It can be concluded that in schizophrenia, the contextual information provided by conditioned inhibitors has a reduced effect on pre-potent associations, particularly in those individuals displaying a high level of negative symptoms. This impairment in inhibitory learning will result in inappropriate respones to a variety of stimulus constellations that do not predict an outcome.

For CI learning in the forensic PD group, the CI effect was clearly demonstrated in the controls, but it was abolished in the PD group, which was recruited from a high security psychiatric hospital. These 'forensic PD' participants showed a striking and statistically significant change in their inhibitory learning in a highly controlled discrimination learning procedure: the contextual information provided by conditioned inhibitors had virtually no effect on their pre-potent associations. In terms of implications for forensic PD, impaired CI would reduce the ability to learn to control associative triggers. There was also a significant difference in CI effect between patients in the PD and the DSPD units. Specifically participants from the DSPD unit showed less inhibitory learning than those in the PD unit, while levels of excitatory learning were relatively unaffected. The two groups ruled out some general limitations of some typical clinical studies (eg. they have a similar pattern of substance abuse history and all have medications in both units). Therefore, this was an important finding for understanding patients with PD and/or co-morbidity with psychopathy in forensic settings.

In conclusion, the findings of the present study were consistent with the viewpoint from which the study was conceived, schizophrenic patients and patients with personality disorders may show the CI learning deficits, which is either through dysfunctions in the inhibition of further procession of unwanted material, or a failure to inhibit at a preconscious level. These dysfunctional inhibitory processes may help us to understand cognitive dysfunctions in schizophrenia and PD, which may provide an explanation of some types of abnormal or offending behaviours in patients. The study also suggested a possible CI learning procedure for investigating the cognitive behavioural therapy of schizophrenia and PD; however, the specific nature of this impairment (i.e. slower inhibitory learning processes or impaired triggering of inhibitory performance processes) is complicated and remains unclear, and further explorations are warranted.

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Appendix

Appendix 1. Selected IAPS pictures in the experiments

25 positive pictures

1440*Δ▲○	2040*Δ▲	5480○	7200	8190
1610*Δ▲○	2154*Δ▲	5600	7270	8210
1750*Δ▲○	2160*Δ▲	5700	7330○	8370*Δ▲○
1811	2216	5780	7502○	8380*Δ▲○
1920*Δ▲○	2395○	5833	7580	8496*Δ▲

25 neutral pictures

2038	5471	7006*Δ▲○	8160	3550.2
2393*Δ▲○	5510	7010*Δ	8232	
2396*Δ▲○	5532	7055*Δ▲○	8466	6150*Δ▲○
2512▲○	5740	7175*Δ▲○		
2516	5920	7182		9070
2704		7185*Δ▲○		
2890*Δ▲○		7187*Δ▲○		

25 negative pictures

2095*	3005.1	6022	9040
2205	3102*	6212*	9405
2352.2	3120*	6313	9410*
2703	3170*	6350	9433*
2800	3301*	6560	9570*
2811	3350	6570	9635.1*
	3530		

Notes:

1. Seventy-five pictures were selected from IAPS for pilot study, after data analysis, 30 pictures (*) were chosen from pilot study.
2. Twenty pictures (Δ) were used as USs for experiment 1.
3. Picture no. 7010 was replaced by no. 2512. Twenty pictures (▲) were used as USs for experiment 2, 3, 4, 5, 6, 7, 8 and 9.
4. Excluded all children images: picture no.2040, 2154, 2160, and 8496. Twenty pictures (○) were used as USs for experiment 10 (forensic settings).

Appendix 2. Consent form for non-clinical participants.

CONSENT FORM

Title of Project: Conditioned inhibition

Researcher: Zhimin He
Supervisors: Dr. Charlotte Bonardi & Dr. Helen Cassaday

Please complete the whole of this sheet, and please cross out as necessary.

- Have you read and understood the participant information sheet YES/NO
- Have you had the opportunity to ask questions and discuss the study YES/NO
- Have all the questions been answered satisfactorily YES/NO
- Have you received enough information about the study YES/NO
- Do you understand that you are free to withdraw from the study:
  at any time YES/NO

  without having to give a reason YES/NO
- Do you agree to take part in the study YES/NO

"This study has been explained to me to my satisfaction, and I agree to take part. I understand that I am free to withdraw at any time."

Signature of the Participant: Date:

Nationality of the Participant:

Name (in block capitals)

I have explained the study to the above participant and he/she has agreed to take part.

Signature of researcher: Date:

Appendix 3. Information sheet for CI experiments (E1-5).

Subject Number: _____

Session Number: _____

Behavioural Neuroscience
School of Psychology
University of Nottingham
University Park
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NG7 2RD

INFORMATION TO PARTICIPANTS

You are being invited to take part in a research study on learning. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Please ask ZHIMIN HE if there is anything you do not understand or if you would like further information.

There is a magic cat "Mogwai", and she will bring you either a nice picture or a neutral, boring picture, depending on what kind of magical Lego blocks she finds in her basket. You will see one or two blocks and predict how likely the cat will give you a nice picture or a neutral picture. For example, the assessments will ask you to give a number from 1 to 9. Number 1 as neutral picture, 5 as not sure, 9 as nice picture. All information obtained during the study will be confidential.

We hope that you feel able to help us with this study. If at any time you decide that you do not want to continue to take part in the study, you are free to withdraw. If you would like to discuss anything further, please contact me at the above address or e-mail me lpxzh@nottingham.ac.uk or on 0115-8467281.

Yours sincerely

Researcher: ZHIMIN HE

Supervisors: Dr. CHARLOTTE BONARDI & Dr. HELEN CASSADAY

Appendix 4. Information sheet for EC Experiments (E6-8)

Subject Number: _____

Session Number: _____

Behavioural Neuroscience
School of Psychology
University of Nottingham
University Park
Nottingham
NG7 2RD

INFORMATION TO PARTICIPANTS

You are being invited to take part in a research study on learning. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Please ask ZHIMIN HE if there is anything you do not understand or if you would like further information.

The experiment included two parts, one is questionnaires, and another is computer-based experiment. The computer-based experiment will show you a magic cat "Mogwai". She will bring you various images, and your task is to pay close attention to the images on the screen and then answer any questions about them. All information obtained during the study will be confidential.

We hope that you feel able to help us with this study. If at any time you decide that you do not want to continue to take part in the study, you are free to withdraw. If you would like to discuss anything further, please contact me at the above address or e-mail me lpxzh@nottingham.ac.uk or on 0115-8467281.

Yours sincerely

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Appendix 5. Introductions were showed on computer screen during experiment 8

Pre-test stage

1. Here is the magical cat, Mogwai. She will bring you either a nice picture or a neutral picture, depending on what kind of magical Lego block(s) she finds in her basket.

   Click any button on the mouse to continue

2. You will be shown either one or two Lego blocks. Please GUESS how likely it is that Mogwai would give you a nice picture or a neutral picture if she were to find these blocks in her basket and how much you like or dislike these block(s).

You will not see any pictures in this phase. Please use the mouse to click on a number from 1 to 9. At first rating scale, number 9 means a nice picture, 5 means not sure, 1 means a neutral picture. At second rating scale, number 9 means you like the block(s), 5 means neither like nor dislike, 1 means you dislike the block(s).

Click any button on the mouse to continue

Pre-training and training stages

Now it is time to PREDICT what type of picture Mogwai will bring. According to the block(s) you are shown, please guess what type of picture will follow and please rate how much you like or dislike these block(s). Depending on the blocks she finds, the cat will give you a nice picture or a neutral picture.

Please use the mouse to click on a number from 1 to 9. At first rating scale, number 9 means a nice picture, 5 means not sure, 1 means a neutral picture. At second rating scale, number 9 means you like the block(s), 5 means neither like nor dislike, 1 means you dislike the block(s).

Click any button on the mouse to continue

Test stage

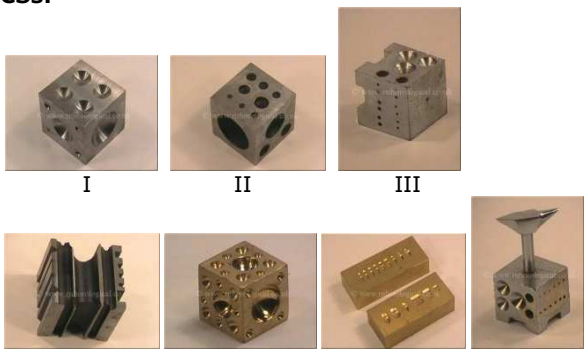
Now it is your turn to use what you have learned. Again you will be shown one or two Lego blocks, and you will be asked to PREDICT what type of picture Mogwai would bring if she found them in her basket and how much you like or dislike these block(s). You will not see any pictures in this phase.

Please use the mouse to click on a number from 1 to 9. At first rating scale, number 9 means a nice picture, 5 means not sure, 1 means a neutral picture. At second rating scale, number 9 means you like the block(s), 5 means neither like nor dislike, 1 means you dislike the block(s).

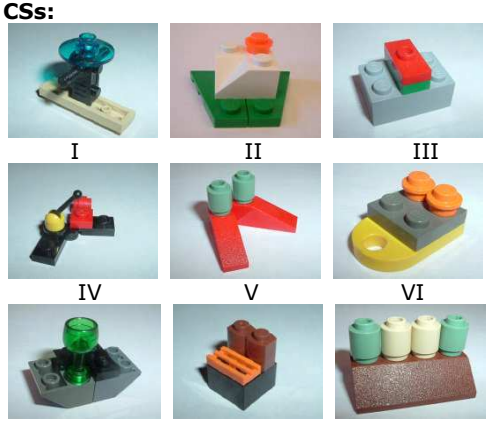
Click any button on the mouse to continue

Appendix 6. The main differences of experiments

<table>
<tr><th></th><th>Stimuli</th><th>Experimental design</th><th>Results & solutions</th></tr>
<tr>
<td>E1

Condition inhibitory learning task - summation test</td>
<td>CSs:
 
I II III IV V VI VII
USs: Ten neutral pictures and 10 positive pictures from IAPS (selected by pilot study)</td>
<td>
<table>
<tr><th colspan="6">Phase</th></tr>
<tr><th colspan="2">Pre-test</th><th colspan="2">Training</th><th colspan="2">Test</th></tr>
<tr><th>CSs</th><th>No. trials</th><th>CSs +/- outcome</th><th>No. trials</th><th>CSs</th><th>No. trials</th></tr>
<tr><td>AZ</td><td>2</td><td>AZ +</td><td>8</td><td>AZ</td><td>2</td></tr>
<tr><td>AP</td><td>2</td><td>AP –</td><td>8</td><td>AP</td><td>2</td></tr>
<tr><td>BX</td><td>2</td><td>BX –</td><td>8</td><td>BX</td><td>2</td></tr>
<tr><td>CY</td><td>2</td><td>CY +</td><td>8</td><td>CY</td><td>2</td></tr>
<tr><td>CP</td><td>2</td><td></td><td></td><td>CP</td><td>2</td></tr>
<tr><td>YP</td><td>2</td><td></td><td></td><td>YP</td><td>2</td></tr>
<tr><td>CX</td><td>2</td><td></td><td></td><td>CX</td><td>2</td></tr>
<tr><td>YX</td><td>2</td><td></td><td></td><td>YX</td><td>2</td></tr>
</table>
Note: The conditioned stimuli pictures were as shown on left. A was picture I or II; B was II or I; P was IV or V; X was V or IV; C was III; Y was VI, and Z was VII. With respect to US presentations, '+' represents positive pictures and '-' represents neutral IAPS pictures (selected by pilot study).
</td>
<td>During the test stage C/Y, P v. C/Y, X) was not significant, F (1, 15)=1.17, p=0.30, suggesting no evidence of a putative inhibitor P had become a conditioned inhibitor.

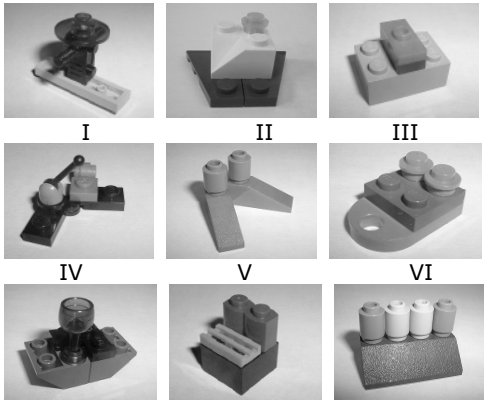
Solutions:
1. Add pre-training stage.
2. Delete YP and YX trials.
3. Increase CP, CX trials in testing stage</td>
</tr>
<tr>
<td>E2

Condition inhibitory learning task - summation test</td>
<td>CSs:
 
I II III IV V VI VII VIII IX
USs: One neutral picture (no 7010) was replaced by no. 2512.</td>
<td>
<table>
<tr><th colspan="8">E2 Phase</th></tr>
<tr><th colspan="2">Pre-testing</th><th colspan="2">Pre-training</th><th colspan="2">Training</th><th colspan="2">Testing</th></tr>
<tr><th>CSs</th><th>No. trials</th><th>CSs</th><th>No. trials</th><th>CSs and outcome</th><th>No. trials</th><th>CSs</th><th>No. trials</th></tr>
<tr><td>A</td><td>2</td><td>A +</td><td>12</td><td>AZ +</td><td>8</td><td>A</td><td>2</td></tr>
<tr><td>C</td><td>2</td><td>U –</td><td>12</td><td>AP –</td><td>8</td><td>C</td><td>2</td></tr>
<tr><td>AZ</td><td>2</td><td>V –</td><td>12</td><td>BX –</td><td>8</td><td>AZ</td><td>2</td></tr>
<tr><td>AP</td><td>2</td><td>C +</td><td>12</td><td>CY +</td><td>8</td><td>AP</td><td>2</td></tr>
<tr><td>BX</td><td>2</td><td></td><td></td><td></td><td></td><td>BX</td><td>2</td></tr>
<tr><td>CY</td><td>2</td><td></td><td></td><td></td><td></td><td>CY</td><td>2</td></tr>
<tr><td>CP</td><td>2</td><td></td><td></td><td></td><td></td><td>CP</td><td>4</td></tr>
<tr><td>CX</td><td>2</td><td></td><td></td><td></td><td></td><td>CX</td><td>4</td></tr>
</table>
Note: The conditioned stimuli pictures were as shown on left. A was picture I or II; B was II or I; P was IV or V; X was V or IV; C was III; Z was VII; V was IX; and U was VIII. With respect to US presentations, '+' represents positive pictures and '-' represents neutral IAPS pictures (selected by pilot study).
</td>
<td>Pre-testing:
Rating scores of CP lower than CX, showed some pre-existing biases.
(CP v. CX, t (39)=1.93, p=0.06)

Testing:
Interaction between CP and CX during the two stages (Pre-testing stage and Testing stage) was not significant, F<1.

Solutions:
CSs changed to black and white.</td>
</tr>
</table>

<table>
<tr><th></th><th>Conditioned Stimuli</th><th>Experimental design and number of participants</th><th>Results & solutions</th></tr>
<tr>
<td>E3

Condition inhibitory learning task - summation test</td>
<td>CSs:
 
I II III
IV V VI
VII VIII IX

USs: same as E2</td>
<td>Same as E2</td>
<td>Pre-testing: CP v. CX, t <1, suggesting no pre-existing biases.

Testing:
Interaction between CP and CX during the two stages (Pre-testing stage and Testing stage) was not significant, but numerically the difference was in the correct direction, suggesting a weak inhibition effect.

Solutions:
Increasing the proportion of non-reinforced trials.</td>
</tr>
<tr>
<td>E4

Condition inhibitory learning task - summation test</td>
<td>CSs and USs were same as E3.</td>
<td>E4 Phase
<table>
<tr><th colspan="2">Pre-testing</th><th colspan="2">Pre-training</th><th colspan="2">Training</th><th colspan="2">Testing</th></tr>
<tr><th>CSs</th><th>No. trials</th><th>CSs</th><th>No. trials</th><th>CSs and outcome</th><th>No. trials</th><th>CSs</th><th>No. trials</th></tr>
<tr><td>A</td><td>2</td><td>A +</td><td>12</td><td>AZ +</td><td>8</td><td>A</td><td>2</td></tr>
<tr><td>C</td><td>2</td><td>U –</td><td>12</td><td>AP –</td><td>12</td><td>C</td><td>2</td></tr>
<tr><td>AZ</td><td>2</td><td>V –</td><td>12</td><td>BX –</td><td>12</td><td>AZ</td><td>2</td></tr>
<tr><td>AP</td><td>2</td><td>C +</td><td>12</td><td>CY +</td><td>8</td><td>AP</td><td>2</td></tr>
<tr><td>BX</td><td>2</td><td></td><td></td><td></td><td></td><td>BX</td><td>2</td></tr>
<tr><td>CY</td><td>2</td><td></td><td></td><td></td><td></td><td>CY</td><td>2</td></tr>
<tr><td>CP</td><td>2</td><td></td><td></td><td></td><td></td><td>CP</td><td>4</td></tr>
<tr><td>CX</td><td>2</td><td></td><td></td><td></td><td></td><td>CX</td><td>4</td></tr>
</table>
Note: CSs and USs were same as E3.</td>
<td>Pre-testing:
CP v. CX,
t (23)<1, suggesting no pre-existing biases.

Testing:
Interaction between CP and CX during the two stages was significant, F (1, 23) =7.70, p=0.01, suggesting evidence of a putative inhibitor P had become a conditioned inhibitor.

Next experiment:
Test evaluative condition - another form of classical condition</td>
</tr>
</table>

	Conditioned Stimuli	Experimental design and number of participants	Results & solutions
E5a and 5b **CI in both summation and retardation tests**	CSs and USs are same as E3.	Same as E4	E5a data was collected at university examination period (no CI effects). E5b data was collected during summer holidays (CI effects in summation test only). Anxiety level significantly correlated the CI learning performance.
E6 **Evaluative condition (EC) (Sequential)**	CSs and USs are same as E3. The CSs and USs were sequentially presented on computer screen.	Same as E4 Changed information sheet and experimental introductions	Experiment did not find evidence to support evaluative condition learning occurred.
E7 **EC (Simultaneous)**	CSs and USs are same as E3. The CSs and USs were simultaneously presented on computer screen.	Experimental design was same as E4 In order to match the number of training trials with previous experiment, during Pre-training stage: 8 trials presentation and 8 trials rating (6 cycles) →6×(2×A+, 2×U-, 2×V-. and 2×C+); during Training stage: 6 trials presentation and 6 trials rating (4 cycles)→4×(1×AZ+, 2×AP-, 2×BX-, and 1×CY+) 4 trials presentation and 4 trials rating (4 cycles)→ 4×(1×AZ+, 1×AP-, 1×BX-, and 1×CY+)	Experiment did not find evidence to support evaluative condition learning occurred. However, during the pre-training stage, participants improved EC learning performance.
E8 (E4+E6) **Added CI and EC ratings together**	CSs and USs are same as E3.	Experimental design was same as E4 Difference: 1. The presentation of US time increased from 1 sec. to 1.5 sec. 2. The colour of EC experimental rating buttons was blue which was different from CI experimental rating buttons (green).	Experiment did not find evidence to support the EC phenomena, but CI effects were significant.
E9 **CI in schizophrenia**	CSs and USs are same as E3.	Same as E4	Reduced CI effects in the schizophrenic patients.
E10 **CI in PD and/or psychopathy**	**USs:** excluded all children images (no.2040, 2154, 2160, and 8496), and replaced by no. 2395, 5480, 7330, and 7502.	Same as E4	Abolished CI effects in the patients with PD and/or psychopathy.

Appendix 7. Summary of experiments

Experiments (experimental type)	Participants	Participants number (exclusion no)	Individual differences' assessment	Main associative learning results
Pilot Study	University students	28	No assessments	
Experiment 1 (CI summation test)	University students	16	BIS/BAS O-LIFE (Short) STB EPQ-R (Short)	Weak CI effects
Experiment 2 (CI summation test)	University students	40 (3)		Weak CI effects, but found pre-existing biases
Experiment 3 (CI summation test)	University students	16 (3)		Weak CI effects
Experiment 4 (CI summation test)	University students	24 (2)		CI effects
Experiment 5a and 5b (CI summation test and retardation test)	University students	64 (6)	4 questionnaires, plus UPPS	E5b CI effects in summation test only
Experiment 6 (EC)	University students	16	No assessments	No EC effects
Experiment 7(EC)	University students	16	No assessments	No EC effects
Experiment 8 (CI summation test +EC)	University students	24 (3)	Same as E1-4	CI effects, but no EC effects
Experiment 9 (CI summation test)	Schizophrenic patients	25 (9)	PANSS	Reduced CI effects
	Matched control for Sch	25 (2)	Same as E 5	CI effects
Experiment 10 (CI summation test)	PD (Forensic settings)	24 (2)	UPPS, IPDE, PCL-R	Abolished CI effects
	Matched control for PD	24	Same as E 5	CI effects