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CRAVINGS FOR CIGARETTES AND COGNITIVE PERFORMANCE IN REGULAR AND OCCASIONAL SMOKERS.

GARETH MARK DAVIES

Research Thesis submitted in fulfilment of the requirements for the degree of PhD in Psychology

UNIVERSITY OF WALES, SWANSEA
2001
DECLARATION

This work has not previously been accepted in any substance for any degree and is not concurrently submitted in candidature for any other degree.

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STATEMENT 1

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DEDICATION

This thesis is dedicated to my parents Peter and Dorothy Davies, and to the memory of my Grandmother Sarah Madden.
ABSTRACT

Aim. The primary aim of this thesis was to investigate the reliability and validity of a multi-dimensional subjective measure of cravings for cigarettes - the Questionnaire of Smoking Urges (QSU - Tiffany & Drobes, 1991) in cigarette smokers. Another aim was to investigate the sensitivity and utility of objective, behavioural measures of the urge to smoke. Finally, an attempt was made to resolve the controversy as to whether the reported cognitive-enhancing effect of nicotine (e.g. Wesnes & Warburton, 1983) is a pharmacological effect or is instead merely the result of relief from withdrawal.

Design. A series of laboratory studies were conducted. Abstinence periods, smoking-related cues, and in one study, pre-treatment with placebo or nicotine gum, were manipulated as independent variables. Two participant groups were used. Participants used in the first four experimental chapters were all regular smokers whereas those used in the final two experimental chapters were all occasional, non-dependant, smokers or tobacco “chippers”.

Findings. Evidence was found for both the reliability and the validity of the QSU. The QSU was shown to be sensitive to both periods of abstinence and exposure to smoking-related cues. In addition, the QSU was shown to have a reliable two-factor structure and that these two factors were measuring different aspects of cigarette craving. The PR was demonstrated to be an unreliable subjective measure of craving, and attempts to use two alternative measures were unsuccessful. Further, no evidence was found for the cognitive-enhancing effects of nicotine in chippers.

Conclusions. The results support the multi-dimensional view of craving, and suggest that the multi-dimensional QSU is a valid and reliable measure of cravings for cigarettes.
Publications arising from this thesis:


CONTENTS

Acknowledgements ......................................................... i

Dedication ................................................................. ii

Abstract .................................................................. iii

Publications ............................................................... iv

Contents ........................................................................ v

Chapter 1 ................................................................ 1
Literature Review

Chapter 2 ................................................................ 36
Influence of nicotine gum on acute cravings for cigarettes

Chapter 3 ................................................................ 50
The sensitivity of the QSU to cigarette abstinence, and smoking-related cues

Chapter 4 ................................................................ 67
Replication of the two-factor structure of the QSU

Chapter 5 ................................................................ 80
Development of new objective measure of craving

Chapter 6 ................................................................ 91
Validation of the two-factor structure of the QSU

Chapter 7 ................................................................ 101
Cognitive effects of nicotine in non-dependent smokers

Chapter 8 ................................................................ 116
General Discussion

References ................................................................ 135

Appendices

v
Chapter 1: Literature Review

CHAPTER 1

LITERATURE REVIEW

1.1 The Problematic Definition of “Craving”

It is believed by some scientists and lay-people that drug craving causes drug addiction, and indeed the assumption that craving is responsible for compulsive drug use is the cornerstone of many scientific and popular conceptualisations of addictive behaviour (Tiffany and Carter, 1998; Tiffany, 1990, 1992, 1997). The concept of “drug craving” has been prominent in the drug addiction literature since the 1950s. The World Health Organization held an Expert Committee meeting in 1954, in an attempt to define and clarify the concept of craving. This committee suggested that the term craving be excluded from scientific use because it has several everyday connotations which could lead to confusion (Jellinek et al., 1955). Despite this recommendation, and the continued expression of concern about the utility of the term craving in scientific explanations of addiction (e.g., Hughes, 1987; Marlatt, 1977; Wise, 1988) the use of the term in the scientific literature continued, and so did the debates concerning its definition. Nearly forty years on, in 1992, an Expert Committee of the World Health Organization (WHO) and the United Nations International Drug Control Programme (UNDCP) met again to discuss the concept of “craving”, and to review the current scientific knowledge on this hypothetical construct (Markou et al., 1993). Despite the inherent problems of accurately defining a subjective concept, the WHO/UNDCP committee defined drug craving as “the desire to experience the effect(s) of a previously experienced psychoactive substance” (UNDCP & WHO, 1992). Despite the intuitive appeal of this definition, it does not easily
lend itself to the empirical investigation of the phenomenon of craving without further clarification of the scientific term “craving” as opposed to the popular generic understanding of the word. Further, many investigators employ the term “craving” without defining it precisely. Thus, there can be no guarantee of heterogeneity of the construct of craving across investigators, a fact that limits its utility (Kozlowski and Wilkinson, 1987; Merikle, 1999). Although the use of the term craving can be thought of as ambiguous for empirical research, the concept remains clinically useful. DSM-IV lists urges and cravings as part of the symptoms characteristic of some drug dependencies (American Psychiatric Association, 1994). The diagnostic usefulness of urges and cravings indicate that the behavioural manifestations of these constructs are important features of addictive disorders (Baker, Sherman and Morse 1987). As Tiffany (1990) states, “given the ubiquity of urge responding among addicts (particularly during periods of abstinence), a truly comprehensive theory of addictive disorders can ill afford to overlook this salient feature of addictive behaviour”. Concepts of craving will now be considered.

1.2 The Conceptualisation of “Craving”

1.2.1 Withdrawal Based Models

Withdrawal based models assume that the main motivating influence in compulsive drug use is the avoidance of withdrawal symptoms, indeed most drugs that support compulsive use will produce a physiological dependence syndrome when the drug is withdrawn (Tiffany, 1990). Although these dependence syndromes are different
across differing classes of drugs (Tiffany, 1990), it is a logical step to assume that urges and cravings are intimately related to drug withdrawal.

The earliest approaches to craving assumed that urges and cravings are caused by the physiological symptoms of withdrawal. Jellinek (1955), for example, suggested that craving for alcohol represented the anticipation of relief from the negative affect of withdrawal, and that it is this sort of craving which leads to compulsive alcohol consumption. Another approach suggests that urges and cravings are nothing more than a component of drug withdrawal. Such approaches are however purely descriptive in that they recognise that people withdrawing from drugs often report urges and cravings. This idea can be observed in the work of Shiftman and Jarvik (1976). These authors looked at trends in smoking withdrawal symptoms, and developed a 27-item questionnaire that was administered four times daily for 2 weeks to 35 participants in a smoking cessation clinic. A variety of symptoms were dealt with in the questionnaire. On the basis of a factor analysis, these authors identified a craving sub-scale as accounting for the largest share of the variance. Their findings suggest that urges are the primary manifestation of nicotine withdrawal in abstinent smokers.

However, people often report urges and cravings long after withdrawal symptoms have abated, and they have ceased using a particular drug. Fletcher and Doll (1969) for example, reported that over 20% of ex-smokers still report experiencing desire to smoke over 10 years after giving up. This is clearly inconsistent with the premise that cravings are a consequence of withdrawal, however one explanation for this could be that cravings
and urges could be conditioned effects, and that some sort of learning has taken place. Wikler (1948) developed a classical conditioning model of drug withdrawal, and proposed that environmental stimuli paired with drug withdrawal became conditioned stimuli capable of eliciting conditioned withdrawal reactions. In other words, if abstinent addicts are exposed to situations in which they had previously suffered drug withdrawal, they should experience conditioned withdrawal symptoms that will lead to urges and cravings to take the drug. Wikler described craving as nothing more than one aspect of the unconditioned withdrawal syndrome that, like other aspects of the withdrawal syndrome, could become conditioned to environmental stimuli (Wikler 1948; Wikler & Pescor, 1967). This view was later slightly amended when Ludwig and Wikler (1974) described craving as a “psychological or cognitive correlate of a sub-clinical, conditioned withdrawal syndrome”, and that craving was a desire for relief from withdrawal that was a necessary condition for relapse, but by itself was insufficient for relapse in abstinent addicts. However, a number of flaws exist with this model. Marlatt (1985), for example, pointed out that if Wikler’s model is correct, then alcoholics would experience the most craving in treatment centers where they had undergone withdrawal, yet clinical experience has shown that cravings tend to be reported as low or non-existent by patients in re-habilitation centers. McAuliffe (1982) examined Wikler’s theory of relapse in human opiate addicts. Forty addicts took part in structured interviews; the addicts had all had at least one period of abstinence outside of an institution. Only 11 of the addicts reported having experienced conditioned withdrawal by taking drugs, and only 1 relapsed as a result. The most common reason given for relapse (even for those who had reported experiencing conditioned withdrawal symptoms) was the desire for euphoria. In the same
year, Chaney and colleagues reported that only 16% of relapse episodes reported by their sample of opiate addicts could be attributed to conditioned withdrawal (Chaney et al., 1982).

A similar conditioning model to that of Wikler’s is Siegal’s (1975) theory of drug tolerance. The theory states that stimuli reliably paired with taking a drug elicit conditioned responses opposite in direction to the direct effects of the drug. These compensatory responses are believed to be responsible for conditioned tolerance effects when the addict is taking the drug and the withdrawal symptoms when the addict is abstinent. An abstinent addict exposed to cues previously associated with drug administration will have conditioned compensatory responses that are experienced as withdrawal and craving, which would increase the likelihood of relapse. Siegal (1983) argues that compensatory responses constitute the basis of urges or craving, which are major components of the drug withdrawal syndrome. The compensatory withdrawal model (Siegal, 1983) differs from Wikler’s conditioned withdrawal model in that it states that withdrawal symptoms are elicited by the presence of cues associated with the administration of the drug, and not with drug withdrawal. This distinction is not, however, a practical way of distinguishing these models, since in reality cues paired with drug withdrawal and cues paired with drug administration overlap in the environment of an addict (Tiffany, 1990).

Subsequent models of withdrawal-based urges integrated conditioning theories of drug withdrawal tolerance with social-cognitive concepts. These theories suggest that
physiological responses, produced by conditioned compensatory responses or conditioned withdrawal, are interpreted by the addict as desires to use the drug. Hence, these theories suggest that urges reflect the operation of attributional process, thus the combination of conditioned physiological arousal with a particular attribution for the source of that arousal is necessary for the production of urges and cravings to use a drug (Melchoir & Tabakoff, 1984; West & Schneider, 1987). By implication, physiological responses other than withdrawal may be incorrectly attributed to a desire to use a drug, or conversely under some circumstances some withdrawal responses, may not be attributed by the addict as urges and cravings (West & Schneider, 1987).

Problems exist with theories of conditioned withdrawal. Childress and colleagues (1988) found that in opiate addicts, at least a third deny that they experience conditioned withdrawal symptoms when they are exposed to drug-related cues, and that there is a poor correlation between craving and withdrawal signs. Ehrman and colleagues (1992) found that withdrawal-like physiological symptoms (e.g., skin resistance, temperature, heart rate) induced by drug-related cues are not highly correlated with reports of subjective state. More telling, many researchers have reported that self reported craving for some drugs (e.g., cocaine) is highest immediately after drug use, when a subjective “high” is being experienced, and withdrawal symptoms are eliminated or at their weakest (Childress et al., 1988; Ehrman et al., 1992; Fischman et al., 1990; Foltin & Fischman 1991; Jaffe et al., 1989; Meyer, 1988). Therefore, if cravings for drugs were due to a desire to alleviate negative withdrawal symptoms, cravings should decrease or cease with the administration of the drug. It is largely for these reasons that the negative reinforcing
effects of drugs, by themselves are not sufficient for the development and maintenance of addiction (Robinson & Berridge, 1993).

1.2.1 Appetitively based models

Partly due to the limitations of models of urges that concentrated on negative reinforcement, some theorists associated urges and cravings with the positive reinforcing, appetitive or excitatory effects of drugs of abuse. McAuliffe & Gordon (1974) for example suggested that craving in opiate addicts reflects the desire for, and the anticipation of the euphoric effects of the drug. Many studies have shown that animals will self-administer drugs of abuse (e.g. opiates, alcohol, amphetamines or cocaine) at high rates, sometimes to the point of intoxication or dependence (Stewart, de Wit & Eikelboom, 1984). Wise and Bozarth (1987) developed a psychomotor stimulant theory of addiction. They stated that for all addictive drugs, “a common mechanism, or at least elements of a common mechanism, mediates both psychomotor stimulant actions and reinforcing actions”. They also suggested that the strength of the reinforcing action of a drug could be predicted by the strength of the psychomotor stimulant properties of that particular drug. Many of the stimulating effects of abused drugs were equated with their appetitive or positively reinforcing properties and these, they argued, are all mediated by a common neural pathway located in the middle forebrain bundle. That drugs classified as stimulants (e.g. cocaine, nicotine and amphetamines) should have stimulating or excitatory effects is obvious, but excitatory effects have often been observed in drugs classified as depressants such as alcohol (Pohorecky, 1977; Tabakoff & Kiiianmaa, 1982) and opiates (Zelman et al., 1985).
Marlatt (1985) proposed a social learning model of addictive behaviour that elaborated on the role of drugs as positive reinforcers. According to Marlatt three interlocking cognitive factors play significant roles in the relapse process. The first is self-efficacy; this refers to how the individual perceives their ability to cope with prospective high-risk situations. This is a cognitive process as it deals with perceived judgements or evaluations. The second mediator is outcome expectancies; positive outcome expectancies increase the temptation to take the addictive substance. The third factor is also a cognitive process and is attribution of causality; if the individual does succumb to their urges then the attribution of causality is important in determining whether the first relapse will lead to a full relapse. Outcome expectancies, as stated above, play an important role in the relapse process; these are based on the anticipated effects of engaging in a particular behaviour. It must be pointed out that the expected effects of taking a drug may not be the same as the actual effect of taking the drug. As Marlatt (1985) writes, “the expectations one holds about the effects (perceived outcome) often exert greater influence than the actual or ‘real’ effects of taking the drug”. Marlatt (1985) defines craving as a subjective state motivated by the incentive properties of positive outcome expectancies. Although positive outcome expectancies may reflect the anticipation of relief from the negative effects of withdrawal, Marlatt’s model points out that the main determinant of craving in addicts is the anticipation of euphoria or stimulation. In other words, “craving is a motivational state associated with a strong desire for an expected positive outcome” (Marlatt, 1985). It should be noted, that Marlatt (1985) makes a distinction between “urges” and “cravings”, suggesting that urges reflect an intention to use a drug that is motivated by a craving for the drug.
There are a number of problems associated with the view that urges and cravings are associated with the positive reinforcing, appetitive or excitatory effects of drugs of abuse. Firstly, Robinson and Berridge (1993) point out that if the positive reinforcing effects of drugs are primarily due their ability to produce pleasurable affective states in addicts, these subjective pleasurable effects must be enormous. Nicotine for example is highly addictive yet does not produce strong euphoric states. As Robinson and Pritchard (1992) state, "there is no evidence that nicotine absorbed from cigarette smoke produces euphoria". Secondly, the positive reinforcement view of addiction fails to explain how cravings or relapse are elicited by drug-related cues. Wise and Bozarth (1987) and Stewart and colleagues (1984) suggest that drug-related cues can stimulate drug-like effects that motivate the addict to engage in further drug-seeking and drug-taking behaviour. But, as Robinson and Berridge (1992) ask, "what exactly is this drug-like process?" One possibility is that it reflects the positive state induced by the drug, and as such reflects a conditioned high. Stewart and colleagues (1984), in their conditioned incentive model of addiction, state that "Conditioned drug effects that mimic the unconditioned drug effects, as are conditioned positive affective states, are elicited by the environment where these drugs are experienced." In other words, drug-related cues trigger conditioned pleasure, which reminds the drug addict of the pleasurable aspects of using the particular drug, and motivates them to use the drug again. Stewart and colleagues presented considerable evidence for the positive incentive effects of addictive drugs motivate drug use, the strongest of this being that animals will self-administer drugs of abuse. However, human studies have found that subjective reports of conditioned highs occur far less frequently than subjective reports of conditioned
cravings, or conditioned withdrawal signs (Childress et al., 1988; O'Brien et al., 1992).

By implication, conditioned highs must be dissociated from conditioned craving, so how can the former be explained in the context of the latter (Robinson and Berridge, 1993)? Thirdly, studies have demonstrated the maintenance of drug taking in the absence of any pleasurable effects. Lamb and colleagues (1991) found that opiate users would work for a low dose of morphine, but not a placebo, despite the fact that four out of five of them could not distinguish between the subjective effects of the morphine and a placebo. Such evidence suggests that “drug ‘wanting’ is not equivalent to drug ‘liking’.” (Robinson & Berridge, 1993).

1.2.2 Dual Affect Model

Considering the evidence for and against withdrawal based models and appetitively based models, the logical compromise would be to present a model which saw cravings as arising from both positive and negative reinforcement mechanisms. Baker, Morse and Sherman (1987) suggested that affective processing systems control the reactivity to drug-related stimuli. These affective processing systems can be indexed by physiological, behavioural and subjective measures, and can be either appetitively or withdrawal based. Positive affect urges are hypothesized to be closely associated to an appetitive motivational system directly stimulated by drug use. Activation of this system could be through, for example, positive mood, drug-use-related cues, availability of the drug and small doses of the drug, and should produce urge reports, positive affect, physiological responses akin to the stimulating effects of the drug, and drug-seeking behaviour. Negative affective urges are hypothesized to be tied closely with withdrawal,
and activated by negative mood, withdrawal-related cues, unavailability of the drug, and withdrawal itself. In this instance, the urge system should produce urge reports, negative affect, symptoms of withdrawal and drug-seeking behaviour. In addition, this model hypothesizes that the two types of urges are mutually inhibitory, and that activation of one system will increase the threshold for activation of the other.

Baker et al's (1987) model was based on a bioinformation-processing approach (e.g., Lang, 1984), where urges are assumed to be organized at a cognitive level within a propositional network that encodes information on eliciting stimuli, drug-related responses, and the interpretation or meaning of stimuli and responses. They proposed that these networks, are mobilised to the extent that the prevailing cue configurations are adequately matched for the encoded prototypical stimulus complex, and as the stimulus conditions become closer to the prototype, the magnitude of the responses within a given urge network will become greater. One feature of this model is that partial activation of the urge systems should lower the threshold for additional activation of the urge network. For example, drinking alcohol will produce a partial pharmacological priming of the appetitive motivational systems and so should lead to enhanced urge reactivity to smoking-related stimuli in dependent smokers (Tiffany, 1995). Baker and colleagues summarised the evidence for this dual affect model (see Baker et al., 1987 for full review) such as the facilitative effect of priming doses of drugs on subsequent self-administration (Stewart et al., 1984), the influence of signals of drug availability on eliciting urges (Meyer & Mirin, 1979), and the potential inhibitory relationship positive affect urges and negative affect urges (Baker & Morse, 1985; Zinser et al., 1992). More
recent research has, however, challenged the dual affect model. Firstly, as pointed out by Tiffany (1995), a review of the literature shows that induction of positive mood generally has little or no impact on urge elicitation in the absence of explicit drug-related cues. Multi-item craving questionnaires which reflect both the anticipation of positive mood and relief of negative withdrawal (e.g., Tiffany and Drobes, 1991 – see section 1.3.1) generally show a high correlation between the two factors suggesting that they are not mutually inhibitory (Tiffany, 1995). Thirdly, partial activation of urge systems through pharmacological manipulations or withdrawal does not necessarily prime reactivity to urge-relevant stimuli (Drobes & Tiffany, 1997; Maude-Griffin & Tiffany, 1996). Finally, an examination of the two major classes of cue reactions, subjective reports of urges and physiological activation, reveals little evidence of a relationship between the two, suggesting that there is little evidence that the coherence of various responses to urge-eliciting stimuli becomes greater as more urge-related stimuli are presented (Tiffany, 1988, 1990, 1995). In addition, Elash and colleagues (1995) found that craving imagery augmented the negative affect and Weinstein and colleagues (1997) found that drug-related imagery resulted in non-significant trends towards increased anxiety and decreased positive affect. The latter authors argued that dual affect model would predict that the induction of craving should result in an increase in positive affect rather than negative affect and not the other way around as observed (Weinstein et al., 1997).
1.2.3 Incentive Sensitisation

Some authors have argued that craving is independent of reinforcement mechanisms. Robinson and Berridge (1993) proposed an incentive-sensitisation theory of addiction. They argued that an adequate theory of addiction must be able to explain: “1) What accounts for drug craving elicited by drug-associated stimuli, if craving is not causally related to conditioned withdrawal signs, conditioned ‘highs’ or the explicit memory of past pleasure? 2) Why is craving sometimes highest immediately after drug administration, when subjective pleasurable effects are still predominant? 3) Why does obsessive craving for drugs persist in the face of enormous negative consequences associated with continued drug use, and relatively modest subjective pleasurable effects? 4) How can low doses of drugs, which do not produce discernible subjective pleasure or physical dependence, maintain drug-seeking and drug-taking behaviour? 5) Why is relapse such a prevalent and persistent feature of addiction, even in ‘recovered’ addicts? 6) Why can relapse be precipitated by so many different stimuli (drugs, environmental stimuli associated with drugs, mood changes)?” (Robinson & Berridge, 1993). These authors argued that traditional negative and positive reinforcement theories of addiction fail to provide adequate answers to these points, and proposed a neural basis for drug craving. They suggested that all addictive drugs have the ability to enhance mesotelencephalic dopamine transmission. One psychological function of this neural system, they suggested, was to attribute “incentive salience” to the perception, and mental representations of events associated with the activation of the system (e.g. drug taking, drug-related cues). Robinson and Berridge (1993) proposed that incentive salience transforms the perception of stimuli making that stimuli attractive “wanted” incentive
stimuli. Repeated use of an addictive drug produces ever-increasing neuroadaptations in this system which eventually render it (perhaps permanently) sensitised to the drug and all stimuli associated with it. Excessive incentive salience is attached to the act of drug taking and drug-associated stimuli, and ordinary drug "wanting" becomes excessive drug craving. Further, these authors suggested that these changes in the neural systems for drug wanting occur independently of the neural systems for drug liking and for withdrawal. Thus, this theory proposes that drug craving can occur, even when the drug is no longer pleasurable, and the withdrawal effects have diminished.

Robinson and Berridge (1993) argued experimental evidence existed that repeated exposure to addictive drugs can produce neuroadaptations in order to meet the necessary requirements for the theory to be true. Firstly they pointed out that there is a whole body of evidence that addictive drugs all share the ability to enhance the mesotelencephalic dopamine system, and that "Although it cannot be said that there is a single neural system that is affected by all addictive drugs, dopamine systems and their associated structures are affected by most". Secondly, they presented what they claimed to be considerable evidence that the repeated administration of many types of addictive drugs produce behavioural sensitisation, which is associated with hypertensive mesotelencephalic dopamine systems. Thirdly, they presented evidence that the neuroadaptations underlying behavioural sensitisation are persistent and long lasting. Next they presented evidence that the expression of sensitisation is subject to conditioned stimulus control. Further, they presented evidence that the mesotelencephalic dopamine system plays a role in incentive motivation. Finally, they presented evidence that the effects of dopamine are on
incentive salience and not on pleasure. For a full review see Robinson and Berridge (1993).

However, the incentive-sensitisation model has not proved to be useful in the measurement of urges and cravings, and it is difficult to assess whether this model truly does provide an account of craving that is independent of reinforcement mechanisms, due to its reliance on the positive incentive-motivational aspects of drug use. There is evidence to suggest that a more cognitive approach to craving, as opposed to a psychobiological approach may be more appropriate (Tiffany, 1990, 1992).

1.2.4 Cognitive Automatic Theory

In 1990, Stephen Tiffany stated that one notable feature of the studies that he had reviewed (Tiffany, 1988) in which dependent smokers or alcoholics were exposed to drug-related or neutral stimuli while their physiological responses and self-reported urges were monitored, was that many of the correlations between physiological responses and urges were not reported. In his review two years earlier, Tiffany had reported that out of the 13 studies he reviewed only 17 of the approximately 48 possible correlation coefficients were reported, suggesting that those not reported were not significant (Tiffany, 1988). Those reported were mostly positive (e.g., 13 out of 17 of all reported coefficients and 8 out of 10 of the significant ones), suggesting that subjective urges tended to be associated with physiological activation or arousal (Tiffany, 1990). However, the magnitudes of the significant correlations were small, accounting for, on average, only 15% of the variance. Tiffany (1990) suggested that these low or non-
significant correlations would seem to be scant evidence to support theories (e.g., Ludwig & Wikler, 1974; Poulos et al., 1981; Siegal, 1983; Wikler, 1972) which claim that conditioned physiological responses are the basis for drug urges and cravings. Indeed, such data suggests that the psychological processes involved in drug use behaviour may be only loosely associated with the processes involved in verbal reports of urges and cravings. In addition to this, Tiffany (1990) stated that the available evidence did not support the notion that cravings and urges are necessary for the initiation or maintenance of drug-use behaviour. For example, Marlatt and Gordon (1980), found that only 7% of a cross section of relapsed heroin, nicotine and alcohol addicts, described urges as major factors in their relapse. As Tiffany (1990) states, “data are revealing in that they indicate that addicts typically do not spontaneously identify urges and cravings as an important component of their relapse”. Tiffany (1990) suggested that the data allowed the hypothesis that the psychological processes involved in drug-use behaviour operate independently of those processes that control subjective urge responding.

Tiffany’s (1990) cognitive model of drug urges and drug use rejects the assumption that craving reflects the central motivational process responsible for drug use behaviour. According to this model, craving is assumed to play a prominent role in relapse mechanisms, rather than in the day to day maintenance of the drug use behaviours. Tiffany suggests that as a result of long-term drug use, drug use behaviour becomes automatic in the addict. In other words, like other learned skills, drug use behaviour becomes efficient, stimulus orientated, difficult to control, and most importantly cognitively effortless and capable of being initiated and completed without
intention. Tiffany suggests that these automated skills are stored as action schema in the long-term memory. These action schemas are unitised, self-sufficient memory systems containing the necessary information for the initiation and coordination of complicated drug-use behaviour sequences. Urges and cravings are conceptualised as constellations of verbal, somatovisceral, and behavioural responses supported by non-automatic cognitive processes, which are utilised in situations in which automatic processes cannot be invoked to produce the appropriate responses (e.g. when the individual is attempting to over-ride the execution of an automated sequence). The non-automatic cognitive processes are cognitively effortful, slow and dependent upon intention, and according to the model, would be activated in parallel with drug use action schemata either in support of it (e.g. when a smoker runs out of cigarettes), or against it (e.g. when a smoker is deliberately attempting to quit). According to this model, the mechanisms involved in linking substance-related stimuli to substance use operate relatively independently of the processes involved in controlling craving (see figure 1.1).

Research by Sayette and colleagues supports Tiffany’s cognitive processing theory. The reaction times of dependent alcoholics and smokers to auditory probes were greater in the presence of drug-related cues than in the presence of drug-neutral cues (Sayette et al 1994; Sayette & Hufford 1994). Since the drug-related cues presented in these studies activated craving processes, Sayette and colleagues findings support the idea that craving is associated with the activation of non-automatic cognitive processes. Cepeda-Benito and Tiffany (1996) provided further evidence for this theory. Smokers were asked to imagine sentences that incorporated urge or no-urge descriptors. Imagery
of urge sentences produced slower probe reaction times, increased heart rate and skin conductance, and higher urge ratings. These authors suggested that the drug craving disrupts cognitive performance, and as such, "provides support for the conceptualization of craving as an effortful, nonautomatic cognitive process" (Cepeda-Benito and Tiffany, 1996).

**Figure 1.1:** Cognitive Processing Model of Drug Urges and Drug-Use behaviour (from: Tiffany, 1995)

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<thead>
<tr>
<th>AUTOMATIC FUNCTIONING</th>
<th>NON-AUTOMATIC FUNCTIONING</th>
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<td>ELICITING STIMULUS CONDITIONS</td>
<td>OVERT BEHAVIOURS: ACTIONS TO NEUTRALIZE OBSTACLE</td>
</tr>
<tr>
<td>DRUG-USE ACTION SCHEMA</td>
<td>VERBAL REPORTS: DESIRE, INTENTION, FRUSTRATION, ANGER, PROBLEM SOLVING DESCRIPTIONS</td>
</tr>
<tr>
<td>STIMULUS CONFIGURATIONS: ACTION PROCEDURES, ACTION COORDINATION, ALTERNATIVE SEQUENCES, SUPPORT PHYSIOLOGY, DRUG-ANTICIPATORY PHYSIOLOGY</td>
<td>SOMATOVISUAL RESPONSES: PROBLEM SOLVING PHYSIOLOGY SUPPORT PHYSIOLOGY</td>
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1.3 The Assessment of Craving

1.3.1 Subjective Assessment of Craving

As stated above, earlier models of addiction commonly suggest that cravings or urges are subjective states that reflect the primary motivation responsible for drug use in addicts (Tiffany, 1995). However, there has been considerable debate about how to measure cravings. In the past, craving has been evaluated using a simple one or two item Likert scale or visual analogue scale on the assumption that cigarette cravings are unidimensional in nature. Some investigators believed that such cravings reflected positive reinforcing (incentive) properties (Marlatt, 1985; Niaura et al. 1988; Wise, 1988), others that they reflected negative reinforcing properties (Ludwig and Wikler, 1974; Poulos et al. 1981; West and Schneider, 1987), but not both. For example, Behm and Rose (1994) assessed craving using a modification of the Shiffman-Jarvik questionnaire (Shiffman & Jarvik, 1976) which is based in the DSM-IIIR criteria for nicotine withdrawal. Participants were required to respond “not at all” (1) to “extremely” (7) to items inquiring how much they had “craved a cigarette”, “missed a cigarette”, “thought of a cigarette”, “had urges to smoke”, and (negatively scored) “would have refused a cigarette”. The mean of these four items constituted the participants “craving” score. A questionnaire routinely used in the Maudsley smokers clinic in London (West et al., 1989) similarly asks participants how much they had been craving, and also contains questions relating to time spent with urges to smoke, strength of urges, and difficulty not smoking. More recently, however, Tiffany and Drobes (1991) have argued that such ways of assessing craving are unreliable since they have small validation samples, an absence of information on their psychometric properties (e.g. reliability), and are
inherently limited by their assumption that urges and cravings are a manifestation of a unidimensional motivational state. Tiffany and Drobes (1991) have argued that urges and cravings should not be assumed to be reflective of the motivational processes central to drug use. These authors suggested that one consequence of this assertion is that cravings and urges should have a multi-dimensional nature.

The multi-dimensional Questionnaire of Smoking Urges (QSU) was intended to provide a measure of self-reported urge to smoke that was both reliable, and sufficient in content to address the many conceptualisations of cravings to smoke cigarettes (Tiffany and Drobes, 1991). A 32-item questionnaire was presented to 230 dependent smokers assigned to one of 3 levels of cigarette deprivation (0, 1 or 6 hours). Factor analysis of the data led Tiffany and Drobes (1991) to conclude that a two-factor structure best described the subjective experience of cravings for cigarettes. Items relating to factor 1 were mainly concerned with intention and desire to smoke and anticipation of positive outcomes, whereas items relating to factor 2 were mainly concerned with an overwhelming desire to smoke, and anticipation of relief from negative affect and withdrawal. Hence factor 1 items may be considered primarily to reflect the operation of positive reinforcement, and factor 2 items may be considered to reflect the operation of negative reinforcement.

This approach to the development of psychometric instruments have been applied by several research groups in the development of instruments to measure alcohol cravings (Clark, 1994; Singleton et al., 1994a; Bohn et al., 1995) cocaine cravings (Tiffany et al., 1993), and Heroin cravings (Tiffany et al., unpublished). The Alcohol Craving
Questionnaire (ACQ: Singleton et al., 1994a) and the Desires for Alcohol Questionnaire (DAQ: Clark, 1994) both used the QSU as their starting point, and as such have similarities both to each other and the QSU. A comparison of the two questionnaires by Love and colleagues (1998) revealed that both questionnaires yielded a three factor structure with two of the factors ("Positive and Negative Reinforcement" and "Strong desires and intentions") similar on both questionnaires. The third factor on Love and colleagues factor analysis of the DAQ revealed a "Mild desires and intentions" factor. On the ACQ, these authors found a third "No desire to drink" factor, although they suggested that this factor was unstable and was wholly comprised of "reverse-keyed" items which are logically more difficult to answer, and thus could just be a statistical artifact (Love et al., 1998). These authors argued that the factor structure of the DAQ in particular has important implications. Firstly, the "Positive and Negative Reinforcement" factor argues against accounts of craving based upon one or other of these processes, and supports the concept of the involvement of them both (Baker et al., 1987). Secondly, the presence of a "Strong Desires and Intentions" factor which includes no items related to reinforcement, provides support for theories which suggest that urges to take drugs are dissociated from reinforcement processes (Tiffany, 1990; Robinson & Berridge, 1993). Finally, Love and colleagues (1998) argued that the presence of a single higher order factor suggested that the three lower order factors were all representations of a single higher order construct, namely "craving". Tiffany and colleagues (1993) constructed two cocaine-craving questionnaire on the basis of the QSU, with one version asking questions on current craving for cocaine (Now version), and one version asking questions on average craving over the week (General). These authors also found that a multi-dimensional factor
solution best described the factor structure of both questionnaires, and the presence of a single higher-order “craving” factor.

However, not all authors have endorsed the multi-factorial approach to the subjective assessment of cravings and urges. Kozlowski and colleagues (1996) factor-analyzed the 26 items that contribute to the scoring of the QSU, and failed to replicate the original factor structure. They were, able to extract a two-factor structure, but only when they restricted the analysis to the 12 items that had the highest factor loadings in the original study by Tiffany and Drobes (1991). Four of the six items, which contributed to their factor 1 scale, were negatively worded. This led Kozlowski and colleagues (1996) to conclude that the two-factor structure of the QSU may be an artifact that reflects the use of negatively worded items. They suggested that multi-dimensional scales and factor-analytical approaches may be unnecessarily complicated, and that a simple 2 or 3 item “desire” scale is adequate to measure urges to smoke (Kozlowski et al. 1996).

1.3.2 Objective Assessment of Craving

Operant techniques have been employed for many years to measure the motivation to respond in animals. Behavioural economic analyses of motivated behaviour assume that a lawful trade-off exists between the value of a commodity, and the effort that will be expended to obtain it (Willner et al., 1995). For example, progressive-ratio (PR) schedules have been demonstrated to be useful measures of motivational strength to use drugs of abuse in animals (Markou et al., 1993; Risner & Goldberg, 1983). It is only in recent years, however, that investigators have attempted to employ a progressive ratio
procedure in human behavioural pharmacological research. A human PR procedure was developed at the University of Wales Swansea to provide a behavioural measure of the urge to smoke (Willner et al., 1995; Willner & Jones, 1996). The task requires participants to respond, by pressing a key on a computer, to earn puffs on a cigarette, on a progressive ratio basis. Reports from this laboratory (Willner et al., 1995; Willner & Jones, 1996), and others (Rusted et al., 1998), suggest that this PR task can differentiate between the urge to smoke in non-abstinent smokers and those who are abstinent for 6-8 hours on average.

Previous studies have reported significant correlations between PR performance maintained by a variety of reinforcers (cigarettes, chocolate, beer), and questionnaire measures of craving for these reinforcers (Willner et al., 1995, 1998a, 1998b). Additionally, induction of a depressed mood state has been shown to increase both questionnaire measures of craving for each of their reinforcers and performance under a PR schedule (Willner & Jones 1996; Willner et al., 1998a, 1998b). This suggests that PR performance may provide an alternative means of measuring craving in human participants, which has the advantage of being directly comparable to the same procedure in non-human subjects (Willner, 1996).

1.4 The Influence of Abstinence on Craving

There are only a few reports of the utility of multi-dimensional measures of craving. It is vital to the validity of any craving questionnaire that it demonstrates sensitivity to periods of drug abstinence since such acute periods of abstinence will
inevitably lead to an increase in craving for the drug (although it should be noted that abstinence from drug use is not always necessary to induce drug craving – Tiffany & Drobes, 1991; Tiffany et al., 1993). All of the limited number of studies that have examined the influence of abstinence on the QSU suggest that it is sensitive to short periods of cigarette abstinence, and is thus a valid tool for measuring cigarette craving. For example, Tiffany & Drobes (1991) found the QSU to be differentially sensitive to 1, 2 and 6 hours of abstinence. In addition, Willner and colleagues have demonstrated that the QSU is sensitive to periods of abstinence of at least 4 hours (Willner et al., 1995; Willner & Jones, 1996).

1.5 The Influence of Cues on Craving

There are numerous other variables, apart from abstinence, which may stimulate subjective cravings, and enhance the reinforcing value of the drug. As considered above, a major determinant of drug-use behaviour in the natural environment is likely to be the presence of exteroceptive, drug-related, stimuli or “cues”, such as a lit cigarette, or another person smoking. Tiffany (1990) suggests that such stimuli may elicit automatic action schemata and drug-use behaviour. Situational cues have been shown to be an important factor in the determination of cravings for a variety of drugs, such as alcohol (Rankin et al., 1983), and opiates (Robins et al., 1974). In addition, it has been suggested that such cues may play an important role in stimulating the urge to smoke cigarettes in abstinent individuals (Niaura et al., 1988), and in non-abstinent individuals (Rickard-Figueroa & Zeicher, 1992). Drobes and Tiffany (1997) reported that cue exposure resulted in large changes in subjective reports of craving compared with slight changes in
the physiological responses of participants. Maude-Griffin & Tiffany (1996) found clear evidence of an effect of content-specific imagery on the subjective urge to smoke. In addition, Burton & Tiffany (1997) reported that both imaginal and, *in vivo*, smoking cues enhanced craving for a cigarette. The magnitude of the effect of exteroceptive, smoking-related, cues has been found to vary for smokers. Hutchison and colleagues (1999) report that the urge response to cue exposure can be reduced by the administration of naltrexone to abstinent smokers maintained with transdermal nicotine replacement. However, it is important to note that with the exception of Maude-Griffin & Tiffany (1996), none of the latter studies of the effects of smoking-related cues on self-reported urge to smoke have used the multi-dimensional QSU. Carter and Tiffany (1999) concluded from a meta-analysis of cue-reactivity, that drug-related cues increase subjective reports of craving, compared to neutral cues, for all classes of drugs of abuse. Weinstein and colleagues (1997) used the multi-dimensional, but as yet unpublished, Heroin Craving Questionnaire (Tiffany, Fields, Singleton, Haertzen, Henningfield), and found evidence that imagery is powerful in eliciting craving for opiates, supporting similar findings reviewed by Childress et al., (1988) which suggested that opioid-related stimuli are powerful in eliciting autonomic conditioned responses. More recently, Robbins and colleagues (2000) found that drug-related stimuli produced increases in physiological arousal, self-reports of high, craving, and withdrawal in a sample of cocaine-dependent outpatients.
1.6 The Influence of Mood on Craving

Marlatt and Gordon (1980) reported that retrospective studies and anecdotal evidence suggest that negative moods are one of the most important precipitants of relapse in recovered alcoholics. It has often been assumed that negative moods increase the risk of relapse by eliciting cravings, and there is some evidence for a relationship between negative affect and craving. Greeley and colleagues (1992) reported that desire for alcohol in the presence of alcohol-related cues were predicted by scores on the depression adjective checklist. This evidence has been further supported by studies which experimentally manipulated mood. Cooney and colleagues have reported that hypnotic induction of a negative mood (Litt et al., 1990), and induction of negative mood by guided verbal imagery (Cooney et al., 1997) and musical mood induction (Willner et al., 1998b) elicited or increased desires for alcohol. Negative mood induced by means of a stressful task (Payne et al., 1992) guided imagery (Tiffany and Drobes, 1990) and musical mood induction (Willner and Jones, 1996) has also been shown to increase desire to smoke. Childress and colleagues (1994) reported increased craving for heroin following hypnotic induction of negative mood in opiate users.

O'Connell and Martin (1987) suggested that it is easier for smokers to successfully resist an urge to relapse if smoking-related cues are present than if negative affect is present. This implies that a negative affective state is a more powerful stimulus than physical cues alone. Marlatt and Gordon (1985) suggested that a combination of negative affect and the presence of drug-related cues would result in greater craving for the drug than when either factor is present alone. However, Payne et al., (1987)
manipulated negative affect as well as smoking-related cues and found that, although both factors increased puff duration on a cigarette, there was no interaction between cues and affect, and no effect of either on self-reported urge to smoke.

A number of studies have reported that negative moods enhance cue-induced craving state in smokers (Elash et al., 1995; Maude-Griffin & Tiffany, 1996), alcoholics (Cooney et al., 1997) and recreational drinkers (Greeley et al., 1992; Willner et al., 1998b). However, other investigators have failed to find that negative moods enhance cue-induced craving states in alcoholics (Litt et al., 1990), smokers (Tiffany and Drobes, 1990; Shadel et al., 1998) and opiate users (Childress et al., 1994).

From the literature, it is apparent that the precise nature of the relationship between mood and craving remains unclear. There is evidence that cravings can be elicited or enhanced by cue exposure and depressed mood, but the evidence is inconsistent with respect to the extent to which these two factors interact (e.g. Willner et al., 1998b). Further, there is paradoxical evidence of the nature of the increases in cravings elicited by depressive mood induction. Willner and colleagues have reported that depressive mood induction also causes a decrease in subjective reports of hedonic capacity (Willner and Healy, 1994; Willner et al., 1998a; Willner et al., 1998b). This is consistent with the view that anhedonia is a central feature of depression (American Psychiatric Association, 1994). Although it would be reasonable to assume that more valued rewards would be more highly craved, and that unwanted rewards would be little valued, evidence such as that from Willner and his colleagues suggests that drug wanting
and liking are not necessarily the same thing. The clarification of this issue is important to theories of addiction which state that the psychological processes involved in drug-use behaviour operate independently of those processes that control subjective urge responding (Tiffany, 1990).

1.7 **Non-dependent drug users ("Chippers")**

Theories of drug dependence tend to assume that dependence is a necessary consequence of repeated exposure to an addictive drug. Despite this, however, a small number of drug users seem able to regularly self-administer particular addictive drugs such as heroin, without exhibiting dependency (Zinberg and Jacobsen, 1976; Harding et al, 1980; Powell, 1973). Such users are referred to as "chippers", and are primarily social drug users, whose usage is determined by social, rather than pharmacological, stimuli (Harding et al, 1980).

Tobacco dependence is far more common in society than opiate addiction, yet despite this, some smokers are able to sustain regular long-term tobacco smoking without becoming dependent (Shiffman, 1989). Shiffman (1989) compared dependent 20 – 40 cigarettes per day smokers to "tobacco chippers" who regularly smoked 5 or fewer cigarettes per day. Unlike the dependent smokers, chippers seemed unaffected by overnight cigarette abstinence, and showed no signs of withdrawal. In addition, chippers obtained low Fagerström dependency scores (Fagerström, 1978) and reported being able to abstain from smoking for days at a time. However, it was not the case that these chippers could be classified simply as "social smokers", since when Shiffman (1989)
controlled for the amount smoke, the chippers were just as likely as dependent smokers to smoke when alone. Shiffman and colleagues have reported a number of comparisons between tobacco chippers and dependent smokers. They have reported that chippers are regularly exposed to nicotine, and absorb the same amount of nicotine from each cigarette as dependent smokers and that chippers' per-cigarette nicotine exposure resembles that of free-smoking dependent smokers (Shiffman et al., 1990). In addition, they have reported that chippers eliminate nicotine at comparable rates, and show similar cardiovascular responses to smoking as dependent smokers (Shiffman et al., 1992), and show no differences in their smoking topography (Brauer et al., 1996). Such evidence suggests that the smoking behaviour of chippers could be maintained by nicotine’s pharmacological effects, and Shiffman and colleagues (1990), suggest that nicotine may have direct motivating reinforcing effects, besides its ability to relieve withdrawal. Shiffman and colleagues (1994) examined the smoking typology profiles of chippers and regular smokers and found that chippers’ profiles de-emphasised dependence-related motives, and emphasised appetitive and sensory motives such as handling and pleasure from smoking. Such evidence is consistent with multi-dimensional theories of craving (Baker et al., 1987; Tiffany, 1990).

1.8 Nicotine Replacement Therapies (NRTs)

Nicotine replacement therapies are widely available over the counter, as a method of aiding smokers attempting to quit. They function by replacing plasma nicotine that would normally have been derived from smoking a cigarette, on the assumption that this should reduce the severity of withdrawal, and so allow the smoker to abstain from
Chapter 1: Literature Review

smoking more easily. The two most commonly used nicotine replacement therapies are transdermal nicotine patches, which deliver nicotine through the skin, and nicotine chewing polacrilex gum, which delivers nicotine through the mouth and stomach. Such therapies are designed to deliver nicotine at a constant rate in order to achieve stable plasma nicotine concentrations.

Research generally suggests that nicotine replacement therapies improve cessation rates among smokers. For example, Lam and colleagues (1987) meta-analysis of 14 randomised, placebo controlled trials of the efficacy of nicotine gum in smoking cessation, reported cessation rates of 27% after 6 months with nicotine gum, compared to 18% with placebo gum. Similarly, Palmer and colleagues (1992) in their review of the pharmacodynamic and pharmacokinetic properties of transdermal nicotine have reported improved cessation rates with nicotine patches when compared to placebo patches. For example, Abelin and colleagues (1989) reported 22% cessation rates with nicotine patches after 6 months compared to 12.2% cessation with placebo patches.

However, it is clear from the meta-analyses of Abelin and colleagues (1989) and Lam and colleagues (1987), that nicotine replacement therapies are by no means completely successful. This suggests that craving is a far more complex phenomenon than simply being the result of withdrawal from a given substance, and that the nature of craving and its relationship to relapse is not a simple one.
1.9 Cognitive-Enhancing Effects of Nicotine

The effects of nicotine on the Central Nervous System are complicated, but it is well established that nicotine acts on nicotinic acetylcholine receptors (NAChr’s) initially as an agonist, and as a depolarising nicotinic-receptor blocker following initial excitation (Kruk & Pycock, 1991). It is thus more appropriate to think of nicotine as both a stimulant and a blocker of cholinergic transmission, rather than its traditional classification as just a stimulant. In addition to its effects on the cholinergic system, nicotine also promotes the release of endogenous opiates, catecholamines, numerous hormones, and stimulates the reticular activating system causing arousal. Nicotine also causes direct and indirect stimulation of the medullary respiration centres (McKim, 1991). It is therefore of no surprise that numerous studies have investigated the cognitive effects of nicotine. Research into the cognitive effects of nicotine has yielded some compelling yet also conflicting results. Some studies have reported that nicotine makes no difference, or may even impair performance on some cognitive tasks, whereas others have found nicotine-induced improvement on cognitive tasks (see Wesnes & Warburton, 1983).

The most consistent evidence of nicotine-enhanced performance has been found with tasks of attention and vigilance. Attention can be considered to be a conglomeration of alertness, selectivity and processing capacity (Posner & Boies, 1971; Kinchla, 1980). Kinchla (1980) proposed that attention could be measured using three types of tasks: 1) a sustained attention task; 2) an attentional switching task; 3) a selective attention task. On the basis of this, Warburton (1992) reviewed studies that had investigated the effects of
nicotine on attention using the three tasks suggested by Kinchila (1980). Wesnes and colleagues (1983) utilized a version of the Mackworth Clock Task (Mackworth, 1950) as a measure of sustained attention. Participants had to detect brief pauses in the movement of the minute hand on a clock. This task produces a reliable vigilance decrement over time, but Wesnes and colleagues reported that nicotine tablets reduced this decrement. In another test of sustained attention, participants were required to detect sequences of odd and even numbers in a series of rapidly changing (100 per minute) digits on a computer screen (Rapid Visual Information Processing Task – RVIPT). Improvements in speed and accuracy on this task after administration of nicotine have been reported (Wesnes & Warburton 1984ab; Parrott & Craig, 1992). Attentional switching has been assessed using a task in which participants must attend to more than one source of information at a time. The task was based on the RVIPT (Wesnes & Warburton 1984a), with stimuli being presented at the rate of 50 per minute in both the visual and auditory modality. Detection in both modalities improved by 7% when smokers deprived for 10 hours were allowed to smoke (Warburton & Walters 1989). Finally, selective attention was assessed using the stroop test by Wesnes and Warburton (1978). They reported that doses of 1mg and 2mg of nicotine enhanced selective attention for relevant material, and suppressed attention for irrelevant material in both deprived smokers and non-smokers. More recently, Warburton and Mancuso (1998) reported that nicotine administration, via a nicotine patch, improved attentional processing.

The issue of whether or not nicotine improves memory is more ambiguous. The literature is inconsistent, and reports of nicotine improving learning can often be
attributed to state dependent learning rather than to the enhancing effects of nicotine *per se* (See Wesnes & Warburton, 1983; Warburton, 1992). It initially seemed that any enhancement was indirect, and due to nicotine’s effects on attention. This idea was supported by a study by Anderson and Hockey (1977), who reported improvements in information storage, but only when that information was intentionally encoded for recall. Further, Rusted and colleagues reported that ingestion of a nicotine tablet improved free recall of a 30-word, but not a 10-word, list suggesting an attentional component. However, some studies have investigated the possibility that nicotine could facilitate pure memory improvements (Rusted & Warburton, 1992; Warburton et al, 1992). Peeke and Peeke (1984) found that nicotine improved immediate recall of a 50-word list in two hour deprived smokers when the cigarettes were high in nicotine, but not when they were low in nicotine. Warburton and colleagues (1986) reported that long-term recall was improved when nicotine had been taken prior to learning, but it made no difference when taken prior to recall alone. These authors concluded that nicotine facilitates the input of information into storage, but has no direct effect on retrieval. Mangnan and colleague have reported that smoking facilitates long-term memory, but not short-term memory (Mangnan, 1983; Mangnan & Golding, 1983). More recently, Warburton and Mancuso (1998) have reported that nicotine improves verbal memory. Warburton and colleagues (1992) conducted a study designed to specifically test if nicotine aided memory, or if improvements were attentional in their basis. Participants were presented with 32 words broken down into 8 blocks, each made up of 4 words. Participants were allowed to rehearse the words and puff on a cigarette after each block. Once the list of 32 items had been presented participants performed a filler task for 10 minutes, and were then given 5
Chapter 1: Literature Review

minutes to recall words. Warburton and colleagues suggested that if nicotine was producing an indirect improvement in memory via attention, then better recall for items in the later block (when attention lapses would be expected) should be observed. If nicotine enhanced memory consolidation directly, the earlier blocks should be recalled better when full attention is being paid. These authors reported significant improvements for words in the earlier blocks, supporting the suggestion that nicotine produces a direct improvement on memory consolidation.

1.10 Aims and Objectives

The primary aim of this research program was to further investigate the nature of craving by concentrating on cigarette smokers. It was intended to begin by examining the acute efficacy of nicotine replacement therapies using the largely under-utilised multi-dimensional Questionnaire of Smoking Urges (Tiffany & Drobes, 1991), and the Progressive Ratio task. This study is reported in chapter 2 of this thesis. The ambiguous nature of the outcome of this study, led to a re-examination of the validity of the factor structure of the QSU, and the utility of the PR task in humans. It was decided to investigate the influence of brief periods of abstinence, and smoking-related cues, on the scores derived from the two factors of the QSU. These are reported in chapter 3. Chapter 3 also presents evidence concerning the sensitivity of two variants of the PR procedure (Willner et al., 1995; Willner & Jones 1996; Rusted et al., 1998) to the same manipulations, and the extent to which performance on these behavioural measures of the urge to smoke cross-validated the subjective QSU measures. Since the PR procedure did not give strong behavioural validation to the QSU, the aim of the studies presented in
Chapter 1: Literature Review

Chapter 4 was to investigate the validity of the multi-factorial structure of the QSU, and was divided into 2 phases. In the first phase, the QSU was first administered to a large sample of dependent smokers and the data were factor analysed using the same methodology as Tiffany and Drobos (1991). The next phase was to investigate the effects of cigarette abstinence and smoking-related cues on old and new factor 1 and factor 2 measures in dependent smokers. Having replicated the original factor structure of the QSU, it was decided to attempt to find alternative objective correlates of QSU scores other than the unreliable PR procedure. This attempt is reported in chapter 5. In chapter 6, the validated factor structure of the QSU was employed to investigate the construct validity of the two-factor QSU, and the effects of exposure to smoking-related cues on cravings, in non-dependent smokers are reported. Finally, in chapter 7, a change of direction was adopted on the basis of the findings reported in chapter 6 that non-dependent smokers exhibit minimal withdrawal-based craving. It was decided to investigate whether studies demonstrating the cognitive enhancing effects of nicotine (e.g. Wesnes and Warburton., 1983) could be attributed to relief of withdrawal rather than nicotine per se, in a sample of non-dependent smokers.

Implications for the area of craving research, on the basis of evidence supporting the multi-dimensional nature of the Questionnaire of Smoking Urges, as well as methodological shortcomings and future areas of research are discussed in depth in chapter 8.
CHAPTER 2

INFLUENCE OF NICOTINE GUM ON ACUTE CRAVINGS FOR CIGARETTES

2.1 INTRODUCTION

Smoking cessation programs often include ways of effectively modifying smoking behaviour by replacing it with some acceptable substitute. Reviews of nicotine gum trials generally confirm the efficacy of this substitute in smoking cessation, (Fagerström et al., 1988; Sachs and Leischow, 1991). It has been suggested that nicotine gum increases the success rates by between 15 and 30%, a doubling of the success rates, in smoking cessation clinics (Fagerström et al., 1991).

While research has generally considered the efficacy of nicotine gum in aiding smoking cessation, little research has considered the efficacy of nicotine gum as a method for alleviating acute cravings in situations where smokers are not permitted to smoke (e.g. on an airplane). Cohen and colleagues (1997) asked regular smokers to smoke a cigarette at the beginning of a test session, and then asked them not to smoke again until after the session had ended. Half of the participants were given nicotine gum, and half were not. Participants then watched a film of their choice. Craving and withdrawal measures were taken immediately after smoking, immediately after watching the film and 30 minutes after watching the film using the Tobacco Withdrawal Symptom Checklist (WSC; Hughes and Hatsukami, 1986). The WSC is a 12-item self-report measure that assesses specific withdrawal symptoms (including craving) and the severity of each
symptom. The results suggested that chewing nicotine gum reduced craving and helped, but did not completely alleviate, withdrawal symptoms in situations when a nicotine dependent person is not allowed to smoke. However, these authors did not use a placebo gum, hence the possibility exists that the results may have been an artifact of participants expectations.

The aim of the present chapter was to evaluate the efficacy of nicotine gum in alleviating acute cravings. Three groups of regular smokers were required to stop smoking for 4 hours. Participants in the first group were given nicotine gum to chew during their abstinence period. Participants in the second group were given a placebo gum to chew during abstinence. Participants in the third group were not given any abstinence aides. It was decided to utilise the multi-dimensional Questionnaire of Smoking Urges (Tiffany and Drobes, 1991) to assess craving, since this measure has been demonstrated to be sensitive to acute periods of cigarette abstinence (Tiffany and Drobes, 1991; Willner et al., 1995). The Progressive Ratio procedure (Willner et al 1995) was used to provide an objective behavioural measure of desire to smoke, since it too has been demonstrated to be sensitive to acute periods of cigarette abstinence (Willner et al 1995).
2.2 METHODS AND MATERIALS

2.2.1 Participants

A total of 45 paid participants (21 male and 24 female) were recruited through posters on the University of Wales Swansea campus, and through advertisements in the local evening newspaper “The Evening Post”. All participants were pre-screened to ensure that they all smoked at least 15 cigarettes a day, had smoked regularly for at least 3 years, had not attempted to quit smoking in the 6 months prior to testing, and were not currently suffering from any major illnesses. In addition, participants were required not to have ever used nicotine replacement therapies so that they would not be familiar with the taste or effects of nicotine gum. The participants were randomly assigned to one of three groups: gum “A”, gum “B” or no gum control. The average participant was 33.07 (± 1.71) years old, smoked 21.41 (± 0.96) cigarettes per day, first smoked at 14.00 (± 0.45) years of age, had smoked regularly for 17.07 (± 1.77) years and had attempted to quit smoking 1.26 (± 0.24) times. Participants gave informed consent to participate and were required to abstain from smoking for exactly four hours prior to testing. The study received approval from the Ethics Committee of the Department of Psychology.

2.2.2 Design

The experiment was a double-blind placebo controlled design. An independent 3rd party labeled the gum as gum “A” or gum “B” and then kept the code locked away until completion of the experiment. Opening of the code revealed that gum “A” contained nicotine, and that gum “B” was the placebo.
2.2.3 Questionnaire of Smoking Urges

The Questionnaire of Smoking Urges ("QSU"-Tiffany & Drobes, 1991) was presented on an IBM 3/486 PC. The QSU is a 32-item questionnaire containing 8 questions in each of four categories representing four “distinct conceptualisations of drug urges”(Tiffany & Drobes, 1991): desire to smoke; anticipation of immediate positive outcome from smoking; anticipation of immediate relief from nicotine withdrawal or relief from negative affect; intention to smoke. Participants responded by using the left and right cursor keys on the PC keyboard to move a cross from the central box to the desired box (or leaving it in the central box) between ‘strongly agree’ and ‘strongly disagree’ under each of the statements. Each item is scored on a 7-point scale (1-7). The scoring of the QSU is based on Tiffany & Drobes’ (1991) factor analysis of scores from a group of 230 smokers. Fifteen items contribute to scores on factor 1, which reflects the desire to smoke and the anticipation of positive outcomes and intention to smoke, and 11 items contribute to factor 2, which reflects anticipation of relief and a strong urge to smoke. The remaining six items do not contribute to the scoring.

2.2.4 Progressive Ratio Task

The Progressive Ratio (PR) procedure was similar to that employed by Willner and colleagues (1995). The PR schedule was presented on a PC programmed in TurboPascal. Participants were told that they would be able to obtain rewards by pressing the space bar on the computer, and that the number of responses required would increase; they could stop responding and restart at any time, provided that not more than a minute had elapsed since their previous response, in which case the session would terminate; and
that they should only work if they felt an urge to smoke. To earn the first reinforcer, the participant was required to press the space bar on the computer keyboard four times. To earn another reinforcer, the participant had to produce eight such responses. The number of responses required for each subsequent reinforcer continued to double until the task was terminated by either a delay in responding for 60 s, or on request of the participant.

Two measures of PR performance were used: total number of responses, and total number of reinforcers earned. Feedback about various aspects of the performance was presented on a monitor to the experimenter, but not to the participant. Responses emitted with an inter-response interval of less than 0.25 s were not recorded, and feedback for successful responses was provided by a brief low-pitched tone. A longer, high-pitched, tone was used to signal that a reinforcer had been earned.

2.2.5 Mood Scale

A set of nine 7-point mood scales labeled from “Not at all” (=0) to “Extremely Much” (=6) was used. Four of the scales (happy, joyful, pleased and enjoyment/fun) were averaged to give a composite “positive” mood score and five scales (depressed/blue, unhappy, frustrated, worried/anxious, and angry/hostile) were averaged to give a composite “negative mood” score (Tiffany and Drobes, 1991).

2.2.6 State/Trait Anxiety Inventory (STAI)

The state/trait anxiety expression inventory (Spielberger, 1977) was used. This questionnaire consists of a set of 40 questions. The first 20 questions relate to state anxiety and ask how the participant feels right now. They are answered on a 4-point
scale: Not at all (1), Somewhat (2), Moderately so (3) and Very Much So (4). The last 20 questions relate to trait anxiety and ask how the participant generally feels. They are answered on a 4-point scale: Almost Never (1), Sometimes (2), Often (3) and Almost Always (4). The minimum score on each scale is 20 and the maximum 80 with higher scores indicating higher levels of state or trait anxiety.

2.2.7 Nicotine Replacement Gum and Placebo Gum

Nicorette® 4mg nicotine gum (Pharmacia & Upjohn) was used as the active gum. In order to disguise its taste, each piece was dipped in tobasco sauce, and then wrapped in Wrigley’s spearmint gum. The placebo gum was made by dipping a rolled piece of cinnamon chewing gum in tobasco sauce, and then wrapping it in Wrigley’s spearmint gum. Tobasco sauce was used to insure that a spicy dominant taste would mask the distinctive taste of the nicotine gum. Wrapping the active and placebo gum in spearmint gum insured that both types of gum looked the same.

2.2.8 Carbon Monoxide Reading

Participants’ carbon monoxide readings (in particles per million – ppm) were taken using a Smokerlyser (UK) CO monitor. Participants were led to believe that this measure would be able to detect a fraudulent claim of 4 hours abstinence.

2.2.9 Procedure

Participants were tested individually, either in a plain room at the University of Wales Swansea, or in their own home. All participants were instructed to smoke a
cigarette exactly 4 hours before testing and then to not smoke again until after the session had ended. Participants in the two gum conditions were provided with instructions on the correct way to chew the gum in accordance with manufacturer instructions. They were instructed to not chew the gum for 30 minutes, then to chew for 30 minutes, then to not chew for 30 minutes and so on until their testing time. Hence, each participant chewed four pieces of gum, finishing the last piece immediately prior to testing (see fig 2.1).

**Figure 2.1** Time line of gum chewing schedule prior to testing.

<table>
<thead>
<tr>
<th>Finish Cig.</th>
<th>Start</th>
<th>Finish</th>
<th>Start</th>
<th>Finish</th>
<th>Start</th>
<th>Finish</th>
<th>Start</th>
<th>Finish/Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gum1</td>
<td>Gum1</td>
<td>Gum2</td>
<td>Gum2</td>
<td>Gum3</td>
<td>Gum3</td>
<td>Gum4</td>
<td>Gum4</td>
</tr>
<tr>
<td>0</td>
<td>30</td>
<td>60</td>
<td>90</td>
<td>120</td>
<td>150</td>
<td>180</td>
<td>210</td>
<td>240 (Minutes)</td>
</tr>
</tbody>
</table>

Participants were given a personal details questionnaire, and the state half of the STAI to complete immediately after their last cigarette. During the testing stage, participants were first given a Carbon Monoxide reading, and then completed the trait half of the STAI and the mood questionnaire. They were then presented with the QSU. Immediately following this, participants completed the PR procedure. It was explained, that they would be able to obtain puffs on a cigarette by pressing the space bar on the computer, and that the number of responses required would increase. They were told that they could stop responding and restart at any time, provided that no more than 60 seconds had elapsed since their previous response, in which case the session would terminate. During the session, the experimenter held a lit cigarette out of sight of the participants so as to minimise its impact as a cue, and made a 4-mm mark on it each time the computer...
tone indicated that a reward had been earned. The cigarette was handed to the participant who was allowed to smoke down as far as the mark before handing back the cigarette and continuing with the PR task if they so desired. The session terminated when the participant failed to respond for 60 seconds, or when they indicated that they no longer wished to continue. The PR was immediately followed by a second QSU. Participants were then thanked for their time and paid £2 for participating.

2.2.10 Analysis

Participant details, mood and anxiety scores, and PR performance were analysed using one way ANOVA with the between participants factor of gum type (3 levels: active, placebo, control). The Questionnaire of Smoking Urges was analysed using two-way mixed design ANOVAs with the repeated measure of time point (2-levels: pre PR and post PR) and the between participants factor of gum type (3 levels: active, placebo, control). Scheffé post-hoc comparisons were employed where necessary. Partial correlations, controlling for the effects of gum type were employed to investigate the relationship between behavioural and subjective measures.

2.3 RESULTS

2.3.1 Participant Characteristics

One-way ANOVA revealed that there were no significant differences between experimental groups for age, number of cigarettes smoked per day, age first smoked, number of years smoked and number of quit attempts (F(2,42)<2.94, p> 0.05). In
addition, there was no significant difference (F(2,42)= 0.13, p>0.05) between experimental groups for Carbon Monoxide readings after 4 hours of abstinence (mean 14.67 ± 0.60 ppm in the active gum group, 14.87 ± 1.33 ppm in the placebo gum group, 15.60 ± 1.82 ppm in the control group).

2.3.2 Mood and Anxiety

One-way ANOVA revealed no significant differences between groups for trait anxiety scores (F(2,42)=0.48, p>0.05), state anxiety scores (F(2,42)=0.146, p>0.05), positive mood scores (F(2,42)=0.65, p>0.05) or negative mood scores (F(2,42)=0.37, p>0.05). See table 2.1.

Table 2.1 Mood and anxiety scores (Mean, SEM) by experimental groups.

<table>
<thead>
<tr>
<th></th>
<th>Nicotine Gum</th>
<th>Placebo Gum</th>
<th>No Gum Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trait anxiety</td>
<td>40.73 (2.55)</td>
<td>41.33 (2.82)</td>
<td>40.27 (1.81)</td>
</tr>
<tr>
<td>State anxiety</td>
<td>36.60 (2.16)</td>
<td>35.73 (2.39)</td>
<td>37.40 (1.99)</td>
</tr>
<tr>
<td>Positive Mood</td>
<td>3.13 (0.43)</td>
<td>2.82 (0.39)</td>
<td>2.55 (0.24)</td>
</tr>
<tr>
<td>Negative Mood</td>
<td>0.91 (0.34)</td>
<td>0.80 (0.27)</td>
<td>0.59 (0.17)</td>
</tr>
</tbody>
</table>

Two-way ANOVA revealed a significant main effect of condition on QSU factor 1 scores (F(1,42)= 10.55, p<0.001). Scheffé post-hoc comparisons revealed that participants who did not chew any type of gum scored significantly higher on factor 1 than participants who did chew, irrespective of whether it was nicotine gum or placebo. Two-way ANOVA also revealed a significant main effect of time point (F(1,42)=37.62, p<0.001) such that participants factor 1 scores were significantly lower after the PR
procedure (and consequently after smoking). There was no significant interaction between time point and condition \((F(1,42)=0.97, p>0.05)\) on factor 1 scores. See figure 2.1.

Similarly, two-way ANOVA revealed a significant main effect of condition on QSU factor 2 scores \((F(1,42)=7.18, p<0.01)\). Scheffé post-hoc comparisons revealed that participants who did not chew any type of gum scored significantly higher on factor 2 than participants who did chew, irrespective of whether it was nicotine gum or placebo. Two-way ANOVA also revealed a significant main effect of time point \((F(1,42)=23.31, p<0.001)\) such that participants factor 2 scores were significantly lower after the PR procedure (and consequently after smoking). There was no significant interaction between time point and gum condition \((F(1,42)=0.97, p>0.05)\) on factor 2 scores. See figure 2.2.

2.3.4 Progressive Ratio

Participants in the nicotine gum condition earned an average of \(4.20 \pm 0.62\) reinforcers from an average of \(171.53 \pm 42.24\) responses. Participants in the placebo gum condition earned an average of \(4.27 \pm 0.64\) reinforcers from an average of \(260.33 \pm 132.76\) responses. Participants in the no gum control condition earned an average of \(4.40 \pm 0.71\) reinforcers from an average of \(335.13 \pm 143.90\) responses. One-way ANOVA revealed that neither of these between groups differences was significant \((F(2,42)=0.02, p>0.05, F(2,42)=0.50, p>0.05\) respectively).
2.3.5 Correlation between QSU and PR

Partial correlations controlling for the effects of gum type, revealed a significant positive correlation between the number of reinforcers earned in the PR procedure and pre PR QSU factor 1 \((r=0.57, p<0.001)\) and factor 2 \((r=0.30, p<0.05)\) scores.

2.4 DISCUSSION

The main finding of the present study was that chewing nicotine gum and a placebo gum both reduced self-reported levels of craving after 4 hours of abstinence relative to a control group who did not chew gum. QSU factor 1 and factor 2 scores were significantly lower after 4 hours of abstinence in both active and placebo gum groups compared to the control group. These findings are similar to those of Cohen and colleagues (1997), although the present results suggest that acute craving may be alleviated by the action of chewing gum, rather than through the administration of a nicotine substitute. This suggestion has implications for placebo-controlled trials (e.g. Vickers and de Craen, 2000), and begs the question “to what extent are the observed benefits of nicotine replacement therapies attributable to placebo effect, and to actual therapeutic effect?” The present findings suggest that while nicotine gum appears to be effective in reducing acute cravings for cigarettes, most of this effect is largely “placebo” in nature.

Contrary to the subjective responses to the QSU, the objective PR measure did not demonstrate differential responding between experimental groups, although a significant positive partial correlation between the QSU and number of reinforcers earned was
observed when the effect of experimental groups was controlled for. This was an unexpected finding, since previous research has demonstrated the sensitivity of the Progressive Ratio Procedure to periods of cigarette abstinence (Willner et al., 1995) and induced mood state (Willner and Jones, 1996). Hence, it was expected that reduced subjective craving reports, as observed with the QSU, should be mirrored by reduced responding to the objective Progressive Ratio. A number of explanations for this may be offered. Firstly, it is possible that the action of chewing gum was enough to satisfy the automatic process of drug taking (Tiffany 1990, see section 1.2.4), but that when a cigarette was actually available under the PR procedure urge responding was activated. Secondly, it is possible that this result may be an artefact due to the fact that participants had ceased chewing gum just prior to performing the PR. However, neither of these explanations satisfactorily accounts for why reduced craving scores were observed with the QSU. The third possibility is that the PR was not differentially sensitive enough. A final possibility is that the PR was sensitive, but that the difference observed in the QSU was an experimental artefact.

On the basis of the present findings, and considering previous reports that have utilised the QSU and the PR (Willner et al., 1995; Willner and Jones, 1996), it is difficult to draw a definite conclusion, due to the contrary nature of the findings from the QSU and the PR. The findings from the QSU appears to suggest that both nicotine and placebo gum are equally effective at reducing acute cravings for cigarettes. The findings from the Progressive Ratio task appear to dispute this. It is clear that further investigation is needed to clarify the sensitivity and the usefulness of the QSU and PR in assessing acute
cravings and urges for cigarettes. This issue was addressed in chapters 3, 4, 5 and 6 of the present thesis. In chapter 2, the validity of the QSU was assessed by considering its sensitivity to two variables that should influence subjective craving, namely drug-related cues and drug-abstinence. Further, chapter 2 considers an attempt to cross-validate the subjective QSU with the objective PR measure of craving.
Figure 2.2: QSU Factor 1 and Factor 2 scores by Experimental Conditions before and after the PR procedure.
3.1 INTRODUCTION

As discussed in section 1.3.1, until recently the measurement of subjective craving for cigarettes was questionable. The typical method of evaluating craving was to administer one or two questionnaire items that elicited ratings on either a Likert scale or a visual analogue scale. This practice appears to have been based on preconceptions that cigarette cravings comprise only one component which arises either from positive reinforcing (incentive) properties (Marlatt, 1985; Niaura et al., 1988; Wise, 1988) or from their negative reinforcing properties (Ludwig & Wikler, 1974; Poulos et al., 1981; West & Schneider, 1987), but not both.

In the early 1990s Tiffany & Drobes sought to remedy this situation by developing a multi-dimensional subjective measure of cigarette cravings - the Questionnaire of Smoking Urges (QSU, Tiffany & Drobes, 1991). As discussed in section 1.3, there are only a few reports of the utility of the QSU, but these suggest that it is sensitive to short periods of cigarette abstinence, and is a valid tool for measuring cigarette craving (Tiffany & Drobes 1991; Willner et al., 1995; Willner & Jones, 1996).

However, as discussed in section 1.5, there are numerous other variables, apart
from abstinence, which may stimulate subjective cravings for cigarettes, and enhance the reinforcing value of cigarette smoking. Another major determinant of smoking behaviour in the natural environment is likely to be the presence of exteroceptive, smoking-related, stimuli or “cues”, such as a lit cigarette, or another person smoking, and is covered in detail in section 1.5 (Carter and Tiffany 1999). However, with the exception of Maude-Griffin & Tiffany (1996), none of the studies of the effects of smoking-related cues on self-reported urge to smoke have used the QSU.

In recent years, however, investigators have attempted to employ a progressive ratio procedure in human behavioural pharmacological research (see section 1.3.2). Reports (Willner et al., 1995; Willner & Jones, 1996, Rusted et al., 1998), suggest that the PR task can differentiate between the urge to smoke in non-abstinent smokers and those who are abstinent for 6-8 hours on average, and that PR performance may provide an alternative means of measuring craving in human participants, which has the advantage of being directly comparable to the same procedure in non-human subjects (Willner et al., 1995, 1998a, 1998b; Willner, 1996).

The purpose of the present chapter, therefore, was to investigate the influence of brief periods of abstinence, and smoking-related cues, on the scores derived from the two factors of the QSU. The study also investigated the sensitivity of two variants of the PR procedure (Willner et al., 1995; Willner & Jones 1996; Rusted et al., 1998) to the same manipulations, and the extent to which performance on these behavioural measures of the
urge to smoke cross-validated the subjective QSU measures. A repeated-measures design was employed, with cue exposure as a within-participants factor, and abstinence as a between-participants factor.

3.2 METHODS

3.2.1 Participants

A total of 101 paid participants (41 male and 60 female) were recruited through posters on the University of Wales Swansea campus. Participants gave informed consent to participate and were then randomly assigned to one of three abstinence conditions: non-abstinence, 2 hours abstinence and 4 hours abstinence. All participants were pre-screened to ensure that they met the following criteria: they all smoked at least 15 cigarettes a day, all had smoked for at least 3 years, and none had attempted to quit within the last 6 months. Each participant agreed to attend for two sessions on two different days. The Psychology department research ethics committee approved the study.

3.2.2 Questionnaire of Smoking Urges

The Questionnaire of Smoking Urges ("QSU"-Tiffany & Drobes, 1991) as described in section 2.2.1.2 was presented on an IBM 486 PC.

3.2.3 Progressive Ratio Task

The Progressive Ratio (PR) procedure as described in section 2.2.1.3 was used.
3.2.4 Carbon Monoxide Monitor

Participants’ carbon monoxide readings were taken using a Smokerlyser (UK) CO monitor as described in section 2.2.1.7. Participants were led to believe that this measure would be able to detect a fraudulent claim of 2 or 4 hours abstinence.

3.2.5 Cue / No Cue Room

Two different rooms were used. Both were of approximately the same size and layout, with no windows. Both rooms contained a 3/486 PC. One room was deemed the “Cue” room and contained smoking-related cues such as cigarette smoke, cigarette packets and ashtrays containing cigarette butts. There were no smoking-related cues in the “No Cue” room.

3.3 EXPERIMENT 1

Before arrival, the 48 participants (16 in each condition) were randomly assigned to the cue room, or the no-cue room, for their first day of testing. On the second day of testing, they were allocated to the other room. Participants attended for testing on the two separate days under the same deprivation condition. On each day, all participants arrived for an initial session in the cue room, in which their CO readings were taken, and then completed a personal details questionnaire while smoking their usual brand of cigarette. This session always took place in the cue room, because the no-cue room was smoke free.
Participants in the two abstinence conditions were then requested to leave and return 2 or 4 hours later, whereas non-abstinent participants remained in the room. Next, or after the return of abstinent participants, a second CO reading was taken (to ensure compliance in abstinent participants).

Participants who were in the cue condition returned to the cue room, where they were asked to complete the QSU followed by the PR task. While doing so, they were required to hold a lit cigarette. The QSU was given exactly 10 minutes after non-abstinent participants had finished their cigarette, and exactly 2 or 4 hours after participants in the 2 hour and 4 hour abstinent conditions had finished their cigarettes respectively. During the PR procedure, participants were given a secondary reinforcer (paper clip) at each reinforcement point. They were informed that each paper clip represented one puff on a cigarette that they could smoke after completion of the PR task. At the end of the experiment they were allowed to smoke the number of puffs corresponding to the number of paper clips they had earned. Each "puff" was defined as a 4mm draw on a cigarette, as indicated by a line marked on the cigarette by the experimenter. In the no-cue room condition, participants underwent a similar procedure to that in the cue room, except that they completed the QSU and the PR task in the no-cue room, returning to the cue room to smoke their final cigarette, and they did not hold a lit cigarette as they completed the QSU, and the PR task.
3.4 EXPERIMENT 2

Due to the lack of effect of cues, or abstinence, on PR measures in the first experiment, another 53 participants (21 non-abstinent, 16 two hours abstinent, 16 four hours abstinent) were tested with a modified PR procedure. In this experiment, a more standard progressive ratio procedure was adopted (Willner et al., 1995; Willner & Jones 1996), in which participants were rewarded immediately after they completed each reinforcement point by smoking a puff on a cigarette. Since this required participants to smoke in the “no cue” room, it was necessary to minimise the olfactory, and visual, cues generated by smoking. This was achieved by constructing a smoke extraction device behind the participant. Between puffs, the lit cigarette was held underneath a cup, out of sight of the participant, which was in turn connected to the room’s ventilation unit. In all other respects, this experiment exactly replicated experiment 1.

3.5 Analysis

Participant details and QSU data, from both experiments, were combined for analysis. Data were analysed by repeated-measures 4-way analysis of variance (ANOVA), with cue (2 levels) as a within-participant factor, and abstinence condition, gender, and experiment, as between-participant factors. PR data were analysed separately for each experiment, using the same design with the omission of the factor “experiment”.
Simple main effects, Scheffé post-hoc comparison and one-way ANOVA (for participant details) were employed where appropriate. Partial correlations, controlling for the effects of abstinence and gender, were employed to investigate the relationship between behavioural and subjective measures.

3.6 RESULTS

3.6.1 Participant details (Table 3.1)

There were no significant differences between abstinence groups for age, number of cigarettes smoked per day, number of years that the participants had smoked, number of quit attempts, or their confidence that they would be able to quit smoking for one month.

3.6.2 Questionnaire of Smoking Urges (Fig. 3.1)

QSU factor 1 scores were significantly higher in women than in men [F(1,89)=5.57, p<0.05], but gender did not interact significantly with abstinence or cues. There were significant effects of abstinence [F(2,89)=30.61, p<0.001], smoking-related cues [F(1,89)=10.88, p<0.001] and a significant abstinence by cues interaction [F(2,89)=5.53, p<0.01]. Simple main effects of cues at the 3 levels of abstinence indicated that factor 1 scores were significantly elevated by smoking-related cues in the 0 hr abstinence group [F (1,98)=26.14, p<0.001], but not in the 2- or 4-h, abstinence groups. Simple main effects of abstinence, at the 2 levels of cue exposure, indicated that factor 1 scores were significantly elevated by abstinence in both the cues condition [F
Chapter 3: The sensitivity of the QSU to cigarette abstinence, and smoking-related cues.

(2.89)=12.41, p<0.001], and the no-cues condition [F (2,89)=36.47, p<0.001]. Scheffé post-hoc comparisons indicated that, in both conditions, factor 1 scores were significantly elevated in both abstinence groups, compared to the non-abstinence group.

For QSU factor 2 scores, there was no significant effect of gender, but there were significant effects of abstinence [F (2,89)=6.92, p<0.005], smoking-related cues [F (1,89)=11.48, p<0.005], and an abstinence by cues interaction [F(2,89)=5.32, p<0.01], were found. Simple main effects of cues, at the 3 levels of abstinence, indicated that factor 2 scores were significantly elevated by smoking-related cues in the 0-h [F (1,98)=17.55, p<0.001], and 2-h [F (1,98)=4.33, p<0.05], abstinence groups, but not in the 4-h abstinence group. Simple main effects of abstinence, at the 2 levels of cue conditions, suggested that factor 2 scores were significantly elevated by abstinence in both the smoking-related cues condition [F (2,89)=3.22, p<0.05], and the no-cues condition [F (2,89)=10.19, p<0.001]. Scheffé post-hoc comparisons indicated that, compared to the 0-h abstinence group, in the smoking-related cues condition, factor 2 scores were significantly elevated in the 2-h, but not in the 4-h, abstinence group. In the no-cues condition, however, factor 2 scores were significantly elevated in both the 2-h and 4-h abstinence groups.

3.6.3 Progressive Ratio (PR) performance.

There were no significant effects of smoking-related cues, gender, or abstinence, and no interaction between cues and abstinence, on the number of reinforcers earned in...
the PR task in either experiment. Similarly, there were no significant effects of smoking-related cues, or abstinence, and no interaction between cues and abstinence, on the number of responses made in the PR task in either experiment (Table 3.2). However, in experiment 2 (primary reinforcement) there was a significant gender by abstinence interaction for number of reinforcers earned \[F(2,47)=6.73, p<0.01\] and number of responses made \[F(2,47)=4.52, p<0.05\]. Simple main effects of abstinence on each gender revealed a significant effect of abstinence in females for number of reinforcers earned \[F(2,48)=5.52, p<0.01\] and number of responses made \[F(2,48)=4.12, p<0.05\]. Females worked harder for puffs on a cigarette when not abstinent, than when deprived from smoking cigarettes (figure 3.2). Although not statistically significant, the opposite tended to be true for males.

Notwithstanding the overall lack of effect of abstinence on PR performance, significant correlations were found between behavioural and subjective measures of cigarette craving (Table 3.3). However, these were dependent on a complex interaction between the presence/absence of smoking-related cues and the type of reinforcer used. In participants responding under primary reinforcement (puffs on a cigarette), both measures of PR performance correlated significantly with both QSU measures in the presence of smoking-related cues, but not in their absence. In participants responding under secondary reinforcement (paper clips), both measures of PR performance correlated significantly with QSU factor 2 scores, but only in the absence of smoking-related cues.
3.7 DISCUSSION

The main finding was that the Questionnaire of Smoking Urges (QSU) was sensitive to both brief periods of abstinence from cigarette smoking, and exposure to smoking-related cues. The effect of abstinence on QSU scores was significant at both 2 and 4 hours, but the QSU scores after 4 hours of abstinence were not significantly elevated compared to those after 2 hours. The effect of smoking-related cues on QSU scores was maximal in non-abstinent smokers. These results support the claims by other investigators that the QSU is sensitive to longer periods of abstinence (Tiffany & Drobes, 1991; Willner et al., 1995; Willner & Jones, 1996), and also provide the first evidence that the QSU is sensitive to smoking-related cues.

Generally, abstinence, and smoking related cues, appeared to have similar, non-additive effects on both factor 1, and factor 2, scores. Scores on both factors were sensitive to the effects of abstinence from smoking, although females scored higher than males on factor 1 scores. For both genders, the factor 1 scores of participants in both the 2 hr, and 4 hr abstinence groups were elevated compared to those of the 0 hr group, but the factor 1 scores of the 4 hr group were not elevated compared to those of the 2 hr group. This suggests that factor 1 scores had reached "ceiling" after only two hours of abstinence. A similar, but less obvious, ceiling effect was observed with factor 2 scores. For both genders, factor 2 scores were elevated after 2, and 4 hours, of abstinence, in the condition in which smoking related cues were not present, but were only elevated after 2
hours of abstinence when such cues were present. It would also appear that the QSU is only sensitive to the additional influence of smoking-related cues if cravings to smoke are relatively mild, and participants' scores are in the middle of the range. Factor 1 scores were only elevated by smoking-related cues in the non-abstinent group, whereas, factor 2 scores were elevated by smoking-related cues in both the 2 hour abstinent group, and the non-abstinent group.

Levels of PR performance in the present study were comparable to those observed, under baseline conditions, in earlier studies (Willner et al., 1995; Willner & Jones, 1996; Rusted et al., 1998). However, in the present study, neither abstinence nor smoking-related cue exposure significantly influenced the number of reinforcers earned, or the number of responses made, in the PR task (both of these factors did, however, influence responses to the QSU). The lack of effect of abstinence on PR performance in the present study appears to be inconsistent with earlier reports (Willner et al., 1995; Willner & Jones, 1996; Rusted et al., 1998), but all of the latter studies required participants to abstain from smoking for 6-8 hours on average, compared to 2 or 4 hours in the present study. Thus, it is likely that this PR task is inherently less sensitive to subtle influences on the urge to smoke than the QSU, and can only discriminate the effects of periods of abstinence of more than 4 hours. This conforms to the known insensitivity of human operant behaviour to changes in contingencies (Catania et al., 1990).

Despite the overall insensitivity of the PR measures, there was a significant
interaction between gender and abstinence under primary reinforcement, both in the presence and the absence of smoking-related cues. Male participants exhibited a non-significant trend towards lawful operant behaviour – they tended to work harder for access to puffs on a cigarette as the period of abstinence from smoking increased. Females, however, showed a significant trend towards unlawful operant behaviour – the number of responses they made declined as the period of abstinence from smoking increased. A similar interaction between gender and abstinence under primary reinforcement was reported by Willner et al., 1995. However, in that case, although males responded significantly more than females after an average of 7 hours of abstinence, both genders exhibited lawful behaviour. Thus, although PR performance does not appear to provide sensitive measures of the urges to smoke elicited by periods of abstinence of less than 4 hours, this appears to be partially attributable to the gender of participants. More work is needed to clarify these relationships.

Although there was no effect of abstinence on PR performance in the present study, some correlations were observed between QSU scores and PR measures. The significance of these correlations was determined by a complex relationship between the presence/absence of smoking-related cues, and the type of reinforcer maintaining behaviour under the PR schedule. Significant correlations between behavioural and subjective measures were observed in the presence of cues in participants responding under primary reinforcement, and in the absence of cues in participants responding under secondary reinforcement. Although presently it is not possible to provide a complete
Chapter 3: The sensitivity of the QSU to cigarette abstinence, and smoking-related cues.

explanation of these relationships which, while significant, account for a relatively small proportion of the variance, the existence of these correlations confirm earlier observations of similar relationships in non-deprived smokers (Willner et al., 1995). Significant correlations have also observed between subjective measures of craving, and PR performance reinforced by chocolate (significantly correlated with scores on the Chocolate Craving Questionnaire: Willner et al., 1998a), and by alcohol (significantly correlated with scores on the Desires for Alcohol Questionnaire: Willner et al., 1998b). However, the present findings provide only cursory support for the validity of performance under a PR schedule as a behavioural measure of cravings in human participants.

In conclusion, the results of the present study suggest that the QSU is sensitive to both brief periods of abstinence from cigarette smoking and the effects of exposure to smoking-related cues, and as such is a useful tool for the investigation of mild cravings for cigarettes. In contrast the PR task appears to be less sensitive to both of these manipulations. However, further research is required in order to assess the validity of the QSU’s 2-factor structure. This issue was addressed in chapter 4.
Table 3.1  Participant Characteristics ¹

<table>
<thead>
<tr>
<th>Hours abstinent</th>
<th>0</th>
<th>2</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>37</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Gender breakdown:</td>
<td>m=16 f=21</td>
<td>m=12 f=20</td>
<td>m=13 f=19</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>23.11 (1.21)</td>
<td>25.19 (1.99)</td>
<td>22.25 (0.96)</td>
</tr>
<tr>
<td>Years Smoked</td>
<td>6.92 (0.97)</td>
<td>8.75 (1.87)</td>
<td>6.19 (1.10)</td>
</tr>
<tr>
<td>No. of Quit Attempts</td>
<td>1.47 (0.41)</td>
<td>1.26 (0.28)</td>
<td>0.84 (0.20)</td>
</tr>
<tr>
<td>Cigarettes Per Day</td>
<td>20.26 (0.90)</td>
<td>21.34 (1.05)</td>
<td>19.30 (0.79)</td>
</tr>
<tr>
<td>Quit Confidence²</td>
<td>2.22 (0.19)</td>
<td>1.84 (0.15)</td>
<td>1.75 (0.17)</td>
</tr>
</tbody>
</table>

¹ Values are means (+ SEM)
² "If you tried to give up smoking now, how confident are you that you could go for more than a month without smoking?". Participants responded by ticking one of 5 boxes ranging from "Not confident"(1) to "Extremely confident"(5).

Table 3.2  PR performance measures (Mean, SEM)

<table>
<thead>
<tr>
<th>Hours abstinent</th>
<th>0</th>
<th>2</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Reinforcers Experiment 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cue</td>
<td>6.48 (0.51)</td>
<td>5.94 (0.42)</td>
<td>6.06 (0.47)</td>
</tr>
<tr>
<td>No Cue</td>
<td>6.52 (0.41)</td>
<td>5.88 (0.46)</td>
<td>5.75 (0.54)</td>
</tr>
<tr>
<td>Experiment 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cue</td>
<td>5.94 (0.53)</td>
<td>6.63 (0.34)</td>
<td>6.25 (0.40)</td>
</tr>
<tr>
<td>No Cue</td>
<td>5.94 (0.50)</td>
<td>6.56 (0.32)</td>
<td>6.13 (0.30)</td>
</tr>
<tr>
<td>Total Responses Experiment 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cue</td>
<td>812.33 (164.2)</td>
<td>448.63 (110.4)</td>
<td>597.13 (195.8)</td>
</tr>
<tr>
<td>No Cue</td>
<td>789.86 (220.4)</td>
<td>528.25 (176.7)</td>
<td>602.38 (263.4)</td>
</tr>
<tr>
<td>Experiment 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cue</td>
<td>551.94 (143.1)</td>
<td>580.00 (118.9)</td>
<td>564.13 (162.5)</td>
</tr>
<tr>
<td>No Cue</td>
<td>537.50 (153.8)</td>
<td>637.19 (148.7)</td>
<td>484.50 (126.5)</td>
</tr>
</tbody>
</table>
Chapter 3: The sensitivity of the QSU to cigarette abstinence, and smoking-related cues.

Table 3.3  Correlations between behavioural and subjective measures

<table>
<thead>
<tr>
<th></th>
<th>Cue present</th>
<th></th>
<th>Cue absent</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Factor 1</td>
<td>Factor 2</td>
<td>Factor 1</td>
<td>Factor 2</td>
</tr>
<tr>
<td><strong>Primary reinforcement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reinforcers</td>
<td>.47***</td>
<td>.46***</td>
<td>.09</td>
<td>.04</td>
</tr>
<tr>
<td>Responses</td>
<td>.32*</td>
<td>.31*</td>
<td>.06</td>
<td>.03</td>
</tr>
<tr>
<td><strong>Secondary reinforcement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reinforcers</td>
<td>-.03</td>
<td>.20</td>
<td>.10</td>
<td>.49***</td>
</tr>
<tr>
<td>Responses</td>
<td>-.09</td>
<td>.05</td>
<td>.15</td>
<td>.44**</td>
</tr>
</tbody>
</table>

1 The table shows Pearson product-moment correlations between measures of PR performance (reinforcers earned and responses emitted) and QSU factor 1 and factor 2 scores, in the presence or absence of smoking-related cues. All values are partial correlations, controlling for the effects of abstinence and gender. *p<0.05, **p<0.01, ***p<0.001
Chapter 3: The sensitivity of the QSU to cigarette abstinence, and smoking-related cues.

Figure 3.1 Scores on the two factors of the Questionnaire of Smoking Urges (QSU) in the presence or absence of smoking-related cues, and following 0, 2, or 4 hours of abstinence. Values are means ± S.E.M.
Figure 3.2 Number of reinforcers earned in the PR task under primary reinforcement in the presence or absence of smoking-related cues, and following 0, 2 or 4 hours of abstinence for males and females. Values are means ± S.E.M.
CHAPTER 4

REPLICATION OF THE TWO-FACTOR STRUCTURE OF THE QSU

4.1 INTRODUCTION

The findings of chapter 3 suggest that the QSU is sensitive to periods of abstinence, and smoking-related cues. The multi-dimensional Questionnaire of Smoking Urges (QSU) was intended to provide a measure of self-reported urge to smoke that was both reliable, and sufficient in content to address the many conceptualisations of cravings to smoke cigarettes (Tiffany and Drobes, 1991). However, as discussed in section 1.3.1, some authors have questioned the validity of the QSU's factor structure. Kozlowski and colleagues (1996) concluded that the two factor structure of the QSU may be an artifact that reflects the use of negatively worded items, and that a simple 2 or 3 item “desire” scale is adequate to measure urges to smoke.

The aim of the present study was to investigate the validity of the multifactorial structure of the QSU, and was divided into 2 phases. In the first phase, the QSU was first administered to a large sample of dependent smokers and the data were factor analyzed using the same methodology as Tiffany and Drobes (1991). The next phase was to investigate the effects of cigarette abstinence and smoking-related cues on old and new factor 1 and factor 2 measures in regular smokers.
4.2 EXPERIMENT 1 - FACTOR ANALYSIS

4.2.1 METHODS AND MATERIALS

4.2.1.1 Participants

The factor-analysis was conducted on data from 271 regular smokers (152 males, 119 females) integrated from eight separate but similar studies that investigated the cognitive and behavioural effects of cigarette smoking and environmental influences on cigarette craving. Each study was similar in that the Questionnaire of Smoking Urges (Tiffany & Drobes, 1991) had been used at an early point in the procedure. The average participant was 21.63 (± 0.25) years old (range 17-59), smoked 16.46 (± 0.32) cigarettes per day (range 10-45), had smoked regularly for 6.03 (± 0.26) years (range 1-35), first smoked at 14.07 (± 0.16) years of age (range 6-24) and had attempted to give up smoking 2.42 (± 0.28) times (range 0-50). Participants were excluded from the factor-analysis if they smoked less than 10 cigarettes per day, had not smoked regularly for at least one year or had attempted to give up smoking within the last 6 months.

4.2.1.2 Design

A between participants factorial design with two factors, abstinence and cue condition, was employed for the purposes of the analysis. Abstinence had three levels, non-abstinent (n=141), 2 hours abstinent (n=70), and between 4 to 10 hours abstinent (n=60). Cue had two levels, no-cue and cue.
4.2.1.3 The Questionnaire of Smoking Urges

All of the eight contributing studies employed the Questionnaire of Smoking Urges (Tiffany & Drobes, 1991) similar to that described in section 2.2.1.2, and an identical questionnaire of cigarette smoking history. The QSU was presented on paper, and participants responded by marking in one of seven boxes between 'strongly agree' and 'strongly disagree' under each of the statements.

4.2.1.4 Procedure

In four of the studies (n=130) participants in the abstinent conditions were asked not to smoke for 2, or at least 4 hours before they came to their session. Non abstinent participants were given a cigarette of their usual brand to smoke upon arrival. Participants then completed the smoking history questionnaire and the QSU as well as various other mood questionnaires before completing the rest of the session. In the other 4 studies (n=141) participants first smoked a cigarette of their usual brand, and completed a smoking history questionnaire. These participants then either completed questionnaires (non-abstinence) or returned 2 or 4 hours later. They then completed the QSU as well as various other mood questionnaires. Participants in the cue condition (n=125), completed the QSU with a lit cigarette held in front of them, or while they held a lit cigarette that they were not permitted to smoke. Participants in the no cue condition (n=146) had no sight of a cigarette or any other smoking-related cues.

4.2.1.5 Analysis

Participant characteristics were analyzed using one-way ANOVA and Tukey’s HSD. The QSU data were analyzed initially using factor analysis using a Promax...
Chapter 4: Replication of the two-factor structure of the QSU

rotation identical to that used by Tiffany and Drobes (1991) in order to investigate the reliability of their 2 factor structure. Principal-axis factor analysis was conducted, with squared multiple correlations as communality estimates. Factors were retained on the basis of scree tests and eigen-values greater than 1. Retained factors were then rotated to simple structure with the promax procedure. The factor structure was then further explored using analysis of variance (ANOVA), and is reported here as experiment 1.

4.2.2 RESULTS

4.2.2.1 Participant Characteristics

One-way ANOVA’s revealed no significant differences between abstinence conditions for the age that participants began smoking, number of attempts to quit smoking or confidence in their ability to quit smoking for one month. One-way ANOVA did show significant differences between abstinence conditions for age [p<0.05] and the number of years that participants had smoked [p<0.005]. In each of these cases, Tukey’s HSD revealed that age and number of years smoked were significantly higher in the non-abstinent condition compared to the two abstinence conditions. The number of cigarettes smoked per day also differed significantly [p<0.01], and Tukey’s HSD revealed that participants in the 4 to 10 hour abstinence conditions smoked significantly fewer cigarettes per day than those in the 0 hour and 2 hour abstinence conditions. The average age and the age at which participants in the present study began smoking were similar that of the participants studied by Tiffany and Drobes (1991). The mean number of cigarettes smoked per day by participants in the present study (14.65 – 17.26) was less than that of the participants in Tiffany and
Chapter 4: Replication of the two-factor structure of the QSU

Drobes study (21.28 - 23.30). However, participants in the present study had smoked for a longer period of time (5.10 - 6.85 years compared to 4.58 - 5.55 years). The characteristics of participants in each of the abstinence conditions are summarised in Table 4.1 below.

### Table 4.1 Participant Characteristics (Mean, SEM) between smoking abstinence conditions.

<table>
<thead>
<tr>
<th>Abstinence Condition</th>
<th>0-hour (n=141)</th>
<th>2-hour (n=70)</th>
<th>4to10hour (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>22.34(0.44)</td>
<td>20.91(0.23)</td>
<td>20.80(0.17)</td>
</tr>
<tr>
<td>Male / female</td>
<td>82 / 59</td>
<td>43 / 27</td>
<td>45 / 55</td>
</tr>
<tr>
<td>Cigarettes / day</td>
<td>16.84(0.41)</td>
<td>17.26(0.58)</td>
<td>14.65(0.78)</td>
</tr>
<tr>
<td>Years regular smoker</td>
<td>6.85(0.46)</td>
<td>5.19(0.31)</td>
<td>5.10(0.29)</td>
</tr>
<tr>
<td>Age began smoking</td>
<td>13.96(0.22)</td>
<td>14.24(0.30)</td>
<td>14.10(0.34)</td>
</tr>
<tr>
<td>Quit attempts</td>
<td>2.72(0.35)</td>
<td>2.16(0.33)</td>
<td>2.00(0.86)</td>
</tr>
<tr>
<td>Quit confidence&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.91 (0.09)</td>
<td>1.97(0.13)</td>
<td>2.27(0.15)</td>
</tr>
</tbody>
</table>

<sup>a</sup> "How confident are you that you could go the next month without smoking?", rated on a 5-point scale with 1 = not at all confident and 5 = extremely confident

### 4.2.2.2 QSU Factor Analysis

Analysis of the QSU data from all three abstinence conditions revealed the presence of two non-trivial factors with eigen values of 13.71 and 1.91 accounting for 75 and 10% of the item variance respectively. These findings are strikingly similar to those of Tiffany and Drobes (1991) who found two non-trivial factors with eigen values of 15.50 and 1.97 accounting for 78 and 10% of the variance respectively. Promax rotation identical to that used by Tiffany and Drobes (1991) produced a
similar structure with an inter-factor correlation of 0.65, compared to an inter-factor correlation of 0.66 reported by Tiffany and Drobes (1991). Sub-scales for the factors were formed by assigning each item to a scale if it loaded at least 0.40 on one factor and less than 0.25 on the other (as indicated by the reference vector structure matrix), and if the difference in loading between the two factors differed by less than 0.20. These are the criteria used by Tiffany and Drobes (1991). The resultant factor loadings and a comparison with those reported by Tiffany and Drobes (1991) are presented in Table 4.2 below.

Factor 1 comprised 5 items from the “desire to smoke category”, 4 from the “anticipation of positive outcome” category, and 5 from the “intention to smoke”. With the exception of item 28 from the “intention to smoke” category, which narrowly failed to reach the criteria for loading, the first factor found here was identical to that found by Tiffany and Drobes (1991). This factor appears to primarily reflect intention and desire to smoke and anticipation of pleasure from smoking. Factor 2 comprised 1 item from the “desire to smoke” category, 2 items from the “anticipation of positive outcome” category, 5 items from the “relief of withdrawal or negative affect” category and 1 item from the “intention to smoke” category. With the exception of item 13 (“desire to smoke”) and item 12 (“relief of withdrawal or negative affect”), which both narrowly missed the criteria for inclusion, the items that comprised our second factor are identical to those described by Tiffany and Drobes (1991). These items appear to primarily reflect anticipation of the relief from negative affect associated with withdrawal as a result of smoking.
4.3 EXPERIMENT 1 - EFFECTS OF ABSTINENCE AND SMOKING-RELATED CUES ON THE FACTOR SCORES OF REGULAR SMOKERS

In the next phase, the effects of abstinence from smoking, and exposure to smoking-related cues on the QSU factor structure found in phase 1, and in the original factor structure, were investigated with 211 of the regular smokers whose data had provided the basis for the earlier factor analysis. Participants in the “4-10 hours abstinence” condition (n=60) were excluded from further analysis. This was primarily because their precise duration of abstinence was unknown, but also because despite smoking an average of 14.65 cigarettes a day, they smoked significantly fewer cigarettes than participants in the 0 or 2-hr abstinence groups (see above). The remaining 211 participants (125 males, 86 females) had an average age of 21.87 (± 0.31) years, smoked an average of 16.98 (± 0.34) cigarettes per day, and on average had smoked for 6.29 (± 0.32) years, began smoking aged 14.06 (± 0.18) years, and had attempted to quit smoking 2.54 (± 0.26) times. The effects of abstinence and cue exposure on the new QSU factor scores calculated from the present factor structure are shown in figure 4.1. Two-way ANOVA revealed that abstinence significantly elevated factor 1 scores \[ F(1,207)=34.05, p<0.001 \], and exposure to smoking-related cues also tended to elevate factor 1 scores, although this effect marginally failed to achieve statistical significance \[ F(1,207)=3.78, p=0.053 \]. Two-way ANOVA also revealed that abstinence did not significantly influence factor 2 scores, but that exposure to smoking-related cues did significantly elevate factor 2 scores \[ F(1,207)=5.52, p<0.05 \]. Identical analysis of the original factor structure yielded a similar outcome. Two-way ANOVA revealed that abstinence significantly elevated factor 1 scores \[ F(1,207)=34.44, p<0.001 \], and exposure to smoking-related cues also tended to elevate factor 1 scores, although this effect marginally failed to achieve
statistical significance \[F(1,207)=3.49, \ p=0.063\]. Two-way ANOVA also revealed that abstinence did not significantly influence factor 2 scores, but that exposure to smoking-related cues did significantly elevate factor 2 \[F(1,207)=4.93, \ p<0.05\].

4.4 DISCUSSION

The results of the present factor analysis of the Questionnaire of Smoking Urges (QSU), based on data from 271 regular smokers, support the reliability of the two-factor structure of this measure of cravings to smoke cigarettes (Tiffany and Drobes, 1991). The factor structure derived from the present data set was strikingly similar to that presented by Tiffany and Drobes (1991). Only one item for the original factor one was not included in the present factor 1, and only two items from the original factor 2 were not included in the present factor 2. Furthermore, all three of these items only narrowly failed to meet the loading criteria for inclusion.

The present findings are in contrast with those of Kozlowski and colleagues (1996). The latter investigators had difficulty replicating the two-factor structure of the QSU, and only achieved this when their factor analysis was restricted to the 12 items with the highest factor loadings in the original study by Tiffany and Drobes (1991). However, although it remains theoretically possible that cravings can be assessed using single dimensional scales, the failure of Kozlowski and colleagues to produce a reliable two-factor structure from 26 items of the QSU may simple reflect methodological inadequacies. Firstly, their sample of 116 smokers was significantly smaller than the sample of 271 investigated in the present study and 230 reported by Tiffany and Drobes (1991). Secondly, participants were included in Kozlowski and colleagues’ study if they smoked more than 5 cigarettes a day. The present inclusion
criteria for regular smokers was that participants should smoke more than 10 cigarettes a day, and the average number of cigarettes smoked a day in the original study by Tiffany and Drobes (1991) was over 20. Thus, it is likely that some of the participants in the study conducted by Kozlowski and colleagues were less dependent than any of the participants in the present study. A third discrepancy was that the participants in the study conducted by Kozlowski and colleagues were instructed to observe their normal smoking patterns before the study. This is in contrast to the fact that the majority of participants in the first phase of the present study, and in the study conducted by Tiffany and Drobes (1991), were required to be abstinent for specific periods before assessment. Thus, it is likely that the majority of participants in the study conducted by Kozlowski and colleagues were not in a state of significant nicotine withdrawal during assessment, and that items designed to assess subjective aspects of this experience were not meaningful to them at the time of testing. This explanation could also account for the findings from the same research group that positively and negatively worded counterparts to the items on the QSU are poorly correlated (Sweeney et al., 1996).

Having established the reliability of the two-factor structure of the QSU, both factor structures were then used to investigate the effects of a brief period of abstinence from smoking, and exposure to smoking related cues, in a subset of the same sample of regular smokers. The data from sixty participants in the “4-10 hours abstinence” condition were excluded from this analysis primarily because we did not have precise measures of their actual duration of abstinence. (These participants were not excluded from the factor analysis because they still smoked an average of 14.65
cigarettes a day, and the precise duration of their abstinence was not central to the factor analysis).

Analysis of the data for participants who had been abstinent for 0 and 2 hours indicated that only two hours of abstinence from smoking was sufficient to elevate factor 1 scores significantly, but not factor 2 scores, compared to the non-abstinent condition. Furthermore, exposure to smoking-related cues significantly elevated factor 2 scores and also tended to elevate factor 1 scores, although this effect marginally failed to achieve statistical significance. These results are generally consistent with the findings presented in Chapter 3.

The present lack of an effect of abstinence on QSU factor 2 scores is inconsistent with previous results from other investigators, and this laboratory (see Chapter 3; Tiffany and Drobes, 1991). However, this inconsistency may simply reflect the fact that the present analysis only investigated the effect of two hours of abstinence, compared to the effects of one and six hours, and two and four hours abstinence, respectively, in earlier studies (Tiffany and Drobes, 1991; see Chapter 3).

Another potential methodological shortcoming of the present study was that some of the data that were combined for the present analysis derived from studies that used a less salient form of exposure to smoking-related cues. Some participants completed the QSU with a lit cigarette held in front of them, instead of actually holding a lit cigarette while completing the QSU, as in the study presented in Chapter 3. Thus, the fact that exposure to smoking-related cues produced an only marginally-significant effect, in dependent smokers, on QSU factor 1 scores in the present study,
may be attributable to the lower salience of smoking-related cues in some of the studies combined for the purposes of the present analysis. Despite the lower salience of cues in the first phase of the present study, however, there was a significant effect of cues on factor 2 scores of the QSU (see Figure 4.1).

The findings of the present chapter and of chapter 3 suggest that the QSU is a reliable measure of craving and that, by implication from the findings of chapter 3; the PR is an unreliable measure of craving. Chapter 5 reports an attempt to develop an alternative objective measure of craving to the “bar-pressing” PR.

4.5 Acknowledgements

Many thanks to Guy Eaton, Sally Hardman, Matthew Crighton, Benjamin James, Catherine Jones, Jonathan Dunnett and Lisa Joslin for collecting some of the data used in this chapter, and for giving permission to use the data in a factor-analysis. In addition, many thanks to Professor Steve Tiffany of Purdue University for help in conducting the factor-analysis.
### Table 4.2 Factor loadings on QSU items grouped by content categories.

<table>
<thead>
<tr>
<th>Item</th>
<th>Present Loadings</th>
<th>Tiffany &amp; Drobes (1991)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>f1</td>
<td>f2</td>
</tr>
<tr>
<td><strong>Desire to smoke</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>I am not missing smoking right now</td>
<td>0.432</td>
</tr>
<tr>
<td>6.</td>
<td>I don't want to smoke now</td>
<td>0.629</td>
</tr>
<tr>
<td>13.</td>
<td>All I want right now is a cigarette</td>
<td>0.239</td>
</tr>
<tr>
<td>17.</td>
<td>I have no desire for a cigarette right now</td>
<td>0.655</td>
</tr>
<tr>
<td>18.</td>
<td>My desire to smoke seems overpowering</td>
<td>0.068</td>
</tr>
<tr>
<td>20.</td>
<td>I crave a cigarette right now</td>
<td>0.457</td>
</tr>
<tr>
<td>23.</td>
<td>I have an urge for a cigarette</td>
<td>0.533</td>
</tr>
<tr>
<td>31.</td>
<td>I need to smoke now</td>
<td>0.199</td>
</tr>
<tr>
<td><strong>Anticipation of positive outcome</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Smoking would make me feel very good right now</td>
<td>0.402</td>
</tr>
<tr>
<td>3.</td>
<td>Nothing would be better than smoking a cigarette right now</td>
<td>0.142</td>
</tr>
<tr>
<td>11.</td>
<td>Smoking a cigarette would not be pleasant</td>
<td>0.547</td>
</tr>
<tr>
<td>15.</td>
<td>Smoking would make me happier now</td>
<td>0.238</td>
</tr>
<tr>
<td>19.</td>
<td>Smoking would make things seem just perfect</td>
<td>0.062</td>
</tr>
<tr>
<td>21.</td>
<td>I would not enjoy a cigarette right now</td>
<td>0.533</td>
</tr>
<tr>
<td>22.</td>
<td>A cigarette would not taste good right now</td>
<td>0.539</td>
</tr>
<tr>
<td>27.</td>
<td>A cigarette would not be very satisfying now</td>
<td>0.548</td>
</tr>
<tr>
<td><strong>Relief of withdrawal or negative affect</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>I would be less irritable now if I could smoke</td>
<td>0.036</td>
</tr>
<tr>
<td>7.</td>
<td>Smoking would make me less depressed</td>
<td>-0.140</td>
</tr>
<tr>
<td>8.</td>
<td>Smoking would not help me calm down now</td>
<td>0.024</td>
</tr>
<tr>
<td>12.</td>
<td>If I were smoking this minute, I would feel less bored</td>
<td>-0.006</td>
</tr>
<tr>
<td>14.</td>
<td>Smoking right now would make me feel less tired</td>
<td>-0.044</td>
</tr>
<tr>
<td>24.</td>
<td>I could control things better right now if I could smoke</td>
<td>-0.057</td>
</tr>
<tr>
<td>26.</td>
<td>I would not feel better physically if I were smoking</td>
<td>0.142</td>
</tr>
<tr>
<td>29.</td>
<td>If I were smoking now I could think more clearly</td>
<td>-0.079</td>
</tr>
<tr>
<td><strong>Intention to smoke</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>I will smoke as soon as I get the chance</td>
<td>0.484</td>
</tr>
<tr>
<td>9.</td>
<td>If I were offered a cigarette I would smoke it immediately</td>
<td>0.581</td>
</tr>
<tr>
<td>10.</td>
<td>Starting now, I could go without smoking for a long time</td>
<td>0.236</td>
</tr>
<tr>
<td>16.</td>
<td>Even if it were possible, I probably wouldn't smoke now</td>
<td>0.630</td>
</tr>
<tr>
<td>25.</td>
<td>If I were going to smoke as soon as possible</td>
<td>0.519</td>
</tr>
<tr>
<td>28.</td>
<td>If I had a lit cigarette in my hand I probably wouldn't smoke it</td>
<td>0.331</td>
</tr>
<tr>
<td>30.</td>
<td>I would do almost anything for a cigarette now</td>
<td>0.086</td>
</tr>
<tr>
<td>32.</td>
<td>Right now, I am not making plans to smoke</td>
<td>0.480</td>
</tr>
</tbody>
</table>
Figure 4.1 Scores on the two new factors of the Questionnaire of Smoking Urges (QSU) in the presence or absence of smoking-related cues, and following 0 or 2 hours of abstinence, in regular smokers. Values are means ± S.E.M.
CHAPTER 5

DEVELOPMENT OF NEW OBJECTIVE MEASURE OF CRAVING

5.1 INTRODUCTION

An alternative to the subjective questionnaire based method of measuring craving is to adapt operant measures used in animal research for use with humans (see section 1.3.2). In a typical progressive ratio task, animals obtain a rewarding substance (e.g. nicotine or cocaine: Risner & Goldberg, 1983) at increasingly large reinforcement intervals. It was suggested by Perkins and colleagues (1994) that the reinforcing value of a cigarette could be determined by the effort used by a smoker to earn a puff on a cigarette. Indeed, behavioural economic analyses of motivated behaviour assume that a lawful trade-off exists between the value of a commodity, and the effort that will be expended to obtain it (Willner et al., 1995). Perkins and colleagues (1994) fitted a progressive ratio (PR) reinforcement schedule into a computer game, "Applepicker". Smokers earned a puff on a cigarette each time they obtained a progressively doubling (1, 2, 4, 8, 16, 32 etc.) score on the game. These authors demonstrated that smokers whom had been abstinent from cigarettes overnight, worked harder (i.e. achieved higher scores) than when they were non-deprived. In a similar human adaptation of an animal operant task, Willner and colleagues have developed a behavioural measure of the urge to smoke which requires participants to press a space bar on a computer keyboard on a progressive reinforcement schedule (Willner et al., 1995; Willner and Jones, 1996; Willner et al 1998a; Willner et al, 1998b; Rusted et al, 1998). Reports suggest that this PR task can differentiate between the urge to smoke in abstinent and non-abstinent smokers. In addition, the PR task has been shown to correlate with and mirror subjective...
measurements of craving obtained using the QSU. However, the results obtained in chapters 2 and 3 suggest that the sensitivity of the PR task is limited at cigarette abstinence periods which are less than or equal to 4 hours, despite scores on the QSU indicating that significantly elevated levels of craving are being experienced.

An alternative approach to assessing the reinforcing value of a drug was proposed by Griffiths and colleagues (1993). These authors utilised a multiple-choice questionnaire that consisted of 135 choices. For each of these choices, the participants were required to choose between two drug conditions (first three choices) or between drug condition 1 and money for the next 44 choices, drug condition 2 and money for the next 44 choices, and drug condition 3 and money for the final 44 choices. The three drug conditions were placebo, 200 and 400 mg/kg of pentobarbital. Participants were exposed to each of these prior to testing, but were unaware as to which drug condition was which. For each of the 44 sets of money/drug choices, the monetary value began at 50 cents and rose in increments of 1.1 times the previous value up to $30.12. After completing the questionnaire, participants randomly drew a number between 1 and 135. The chosen item corresponding to the randomly selected number was then delivered to the participant. If the chosen number corresponded to a choice of money, the appropriate monetary value was added to the participant’s earnings, but they received no drug. Griffiths and colleagues (1993) reported an orderly dose-related choice of drug over money and an orderly choice of higher drug doses over lower drug doses. They suggested that the multiple choice questionnaire paradigm was a useful, efficient and valid way of assessing the reinforcing value of a drug in drug abusers.
Despite offering the opportunity to directly assess the reinforcing value of a drug in monetary terms however, the multiple-choice paradigm does not yield an objective behavioural measure of drug craving. Since the PR procedure has been shown in Chapter 3 to be insensitive to abstinence periods of less than 4 hours, and to smoking-related cues, it was decided to design and test an alternative objective behavioural measure of craving, for abstinence periods of less than 4 hours. A key feature of the PR task is that it is not cognitively demanding. A reinforcement schedule dependent upon performance per se may not provide a measure of craving; since it is likely that heightened craving may worsen cognitive performance (Hughes 1991; Sherwood 1993). On the other-hand, a disadvantage of the PR task could be that acute craving levels might not be high enough to influence task performance. As a result, participants may simply take advantage of the simplistic nature of the task to obtain "free" reinforcement, even if they do not overly desire it. One solution may be to combine the advantageous aspects of both the PR and a cognitively demanding task. It was decided to utilise a cognitively demanding task (Rapid Visual Information Processing - RVIP), but to apply a progressive ratio reinforcement schedule that was dependent upon time spent doing the task rather than performance levels achieved on it. The Rapid Visual Information Processing Task was chosen since anecdotal reports from participants who have performed the procedure, often suggest that they find it tiring, frustrating and cognitively demanding (i.e. hard work).

The aim of the present chapter was to evaluate the sensitivity and reliability of an adaptation of the multiple-choice paradigm, and a cognitively demanding progressive ratio procedure in discriminating very acute (2 hours) abstinence periods. The QSU has been demonstrated to be sensitive to 2 hours of abstinence (see Chapters
3 and 4), but to date objective measures have failed to discriminate such an acute abstinence period. The present chapter also aimed to cross-validate measures from the cognitive PR procedure and the multiple-choice questionnaire with scores obtained on the Questionnaire of Smoking Urges.

5.2 MATERIALS AND METHODS

5.2.1 Participants

A total of 30 paid participants (7 male and 23 female) were recruited through posters on the University of Wales Swansea campus. Participants gave informed consent to participate and were then randomly assigned to one of two conditions: 2 hours abstinent or non-abstinent. All participants were pre-screened to ensure that they met the following criteria: they all smoked at least 15 cigarettes a day, all had smoked for at least 3 years, and none had attempted to quit within the last 6 months. The average participant was 23.13 (± 1.18) years old, smoked 20.67 (± 0.78) cigarettes per day, had smoked regularly for 7.77 (± 1.12) years, and had attempted to give up smoking 1.64 (± 0.45) times. Participants agreed to abstain from smoking for 2 hours prior to testing. The study received approval from the Ethics Committee of the Department of Psychology.

5.2.2 Design

Each participant completed only one session, in one of 2 conditions: 2 hours abstinent or non-abstinent. All participants were instructed not to smoke for exactly 2 hours prior to testing. Participants assigned to the non-abstinent condition were asked to smoke a cigarette of their usual brand upon arrival at the laboratory. Cigarette-
related cues were not prevalent in the laboratory. Informed written consent was obtained from each participant.

5.2.3 The Questionnaire of Smoking Urges

The Questionnaire of Smoking Urges ("QSU"-Tiffany & Drobes, 1991) as described in section 2.2.3 was presented on an IBM 3/486 PC. Participants responded by moving a centrally located cursor to the desired position in response to each question.

5.2.4 Rapid Visual Information Processing Task (RVIPT)

The Rapid Visual Information Processing Task (Donohoe and Benton 1999) was presented on a desktop PC computer. Participants observed a rapidly changing series of numbers (from 1 to 7) presented at the rate of 100 per minute. Participants were required to concentrate on these numbers, and to press the space bar on the keyboard in front of them whenever they detected sequences of three consecutive odd, or three consecutive even digits. There were eight such sequences presented per minute. Actual performance on the task was not assessed, although participants were led to believe that their performance was being monitored. Participants were instructed that they could earn cigarettes, the number of which depended upon how long they were willing to endure the task for. They were instructed that they could end the task whenever they wished, but that they should maintain concentration on the task for its duration.
5.2.5 Monetary Incentive Questionnaire (MIQ)

The monetary Incentive Questionnaire (MIQ) was a modification of a multiple-choice questionnaire devised by Griffiths and colleagues (1993) designed to assess drug reinforcement in humans. The present version consisted of 25 numbered choices. For each number, the participant had to choose between a cigarette and money. The money began at 10 pence for choice 1 and rose in whole number increments of 1.1 times the previous value up to £1 for choice number 25. Later in the procedure, the participant randomly drew a number between 1 and 25 from a bag. Participants were rewarded with their choice corresponding to the drawn number at the end of the session.

5.2.6 Carbon Monoxide Monitor

Participants' carbon monoxide readings were taken using a smokerlyser (UK) CO monitor as described in section 2.2.8. Participants were led to believe that this measure would be able to detect a fraudulent claim of 2 hours abstinence.

5.2.7 Procedure

Participants were tested individually in one session, and were previously instructed to abstain from smoking for 2 hours prior to the experiment. Participants in the non-abstinence condition were then instructed to smoke a cigarette of their preferred brand. This cigarette was not provided by the experimenter, and was smoked outside the laboratory so as to avoid the build up of smoke. Participants then had their CO readings taken, and then completed a personal details and smoking history questionnaire. Participants then completed the QSU followed by the Monetary Incentive Questionnaire. Next participants completed the Rapid Information
Processing Task (RV1PT). Participants were instructed that they could perform the RV1PT for as long as they wished, but that the longer they performed it for the more cigarettes they would earn. Cigarette rewards were given on a progressive ratio with the first earned after 1 minute, the second after 3 minutes, the third after 6 minutes the fourth after 10 minutes up to a maximum of 8 after 36 minutes. Participants were unaware of the exact nature of the reinforcement schedule, or the maximum reinforcement limit. Participants were verbally informed when each cigarette had been earned, and the total number of cigarettes earned was given to the participants at the end of the procedure. A thirty-second practise run was given to participants to familiarise themselves with the task, during which no rewards were given, and participants were required to successfully identify one sequence of odd or even numbers. Upon successful completion of the practise session, the test session began. After the RV1PT, participants then randomly drew a number between 1 and 25, and the reward corresponding to their choice for that number on the MIQ added to their total of money or cigarettes. The number was drawn after the RV1PT rather than immediately after completion of the MIQ, to avoid the outcome of the MIQ influencing performance on the RV1PT. Finally, participants were thanked for their time and paid £2 plus any additional money and / or cigarettes that they had earned.

5.3 RESULTS

5.3.1 Participant details

There were no significant differences between abstinence conditions for age, number of cigarettes smoked per day, number of years that the participants had smoked, number of quit attempts.
5.3.2 Questionnaire of Smoking Urges

QSU factor 1 and factor 2 scores were significantly higher in abstinent participants compared to non-abstinent participants \( F(1,28)=20.57 \ p<0.001 \) \( F(1,28)=15.06, \ p=0.001 \) respectively. See Figure 5.1.

Fig 5.1 Scores on the two factors of the QSU following 0 or 2 hours abstinence.
Values are means ± S.E.M.

5.3.3 Monetary Incentive Questionnaire

Participants in the 2 hour abstinent condition gave a cigarette an average value of 65.47 ± 7.44 pence. Participants in the non-abstinence condition gave a cigarette an average value of 70.13 ± 7.86 pence. The difference between the two conditions was not statistically significant \( F(1,28)=0.186, \ P>0.05 \).

5.3.4 RVIPT

Participants in the abstinence condition earned an average of 2.20 ± 0.55 cigarettes in 382.33 ± 140.02 seconds compared to 2.47 ± 0.34 cigarettes in 355.33 ± 72.85 seconds for participants in the non-abstinent condition. Neither of these
differences was statistically significant (F(1,28)=0.17, p>0.05; F(1,28)=0.29, p>0.05 respectively).

5.3.5 Correlation between Subjective and Objective Measures.

Partial correlations, controlling for abstinence condition, between the objective measures of the MIQ (value of a cigarette) and RVIPT (cigarettes earned and time) and the subjective QSU factor scores revealed a significant positive correlation between the MIQ score and QSU factor 2 scores (r=0.43, p=0.021) but not factor 1 scores (r=0.28, p>0.05). In addition, partial correlations revealed a significant positive relationship between the average number of cigarettes smoked per day by each participant, and the number of cigarettes that they earned on the RVIPT (r=0.44, p=0.017), and the amount of time that they were prepared to invest in performing the RVIPT (r=0.54, p=0.003).

5.4 DISCUSSION

The main finding was the replication of the sensitivity of the Questionnaire of Smoking Urges to a brief period of abstinence from cigarette smoking. Scores on both factor 1 and factor 2 were significantly elevated after 2 hours of abstinence compared to participants who were not cigarette abstinent. This finding is in line with previous research (Tiffany & Drobes, 1991; Willner et al, 1995; Willner & Jones, 1996), and the findings of chapters 3 and 4.

In the present study, brief cigarette abstinence did not significantly influence, the number of reinforcers earned on the RVIPT task, or the amount of time that participants spent doing the task. The lack of effect of abstinence on progressive ratio
RV IPT performance in the present study is inconsistent with previous reports that utilized a bar-pressing PR task (Willner et al., 1995; Willner & Jones, 1996; Rusted et al., 1998), although each of these employed a longer period of abstinence. The present finding is consistent with reports of the lack of sensitivity of progressive ratio based measures of craving to very brief periods of abstinence as reported in chapter 3. The reward schedule differed slightly from that used in chapter 3, in that participants worked for cigarettes in the present study rather than puffs on a cigarette as reported in chapter 3. This methodological issue may account for the failure of the progressive ratio task employed in the present study to successfully discriminate an acute period of abstinence. However, the present study did find a significant positive relationship between average number of cigarettes smoked per day, and time spent performing the RV IPT, and the number of cigarettes earned, when abstinence condition was controlled for. This finding may suggest that the higher the motivation to smoke, the higher the daily consumption, although this suggestion can only be speculative on the basis of the present data.

Brief abstinence periods did not influence the monetary value that participants ascribed to a cigarette. This finding is contrary to the suggestion by Griffiths and colleagues (1993) that the multiple choice questionnaire paradigm is a useful, efficient and valid way of assessing the reinforcing value of a drug in drug abusers. It is likely that this finding was due to the acute nature of the abstinence period used, and also to the fact that since cigarettes are a readily available, legal form of drug abuse, smokers have pre-conceived ideas concerning the monetary value of their drug of choice. However, a significant positive relationship between MIQ score and QSU factor 2 but not QSU factor 1 was observed, when abstinence was controlled for. This finding
Chapter 5: Development of New Objective Measure of Craving

adds plausibility to the suggestion that factors 1 and 2 of the QSU reflect different aspects of cigarette craving (see chapter 6), and that craving is multi-dimensional in nature (Tiffany, 1990; Tiffany & Drobes, 1991). The present findings suggest that the value that smokers assign to a cigarette is related to the negative withdrawal based aspects of craving and not the positive pleasurable aspects of smoking. This could be seen as evidence for the role of withdrawal based craving in the motivation to use drugs (see 1.2.1) or even as evidence for the role of withdrawal based craving in relapse (e.g. Tiffany 1990). However, the precise nature of the correlation, or indeed the reliability of the MIQ, is too uncertain to be strong evidence in either case.

In summary, the findings of the present chapter provide further evidence for the sensitivity of the QSU to brief periods of abstinence. The progressive ratio rapid information processing task, and the monetary incentive questionnaire did not prove to be useful for discriminating the behavioural effects of brief abstinence periods in regular smokers. However, the present findings do provide tentative evidence for the multi-dimensional nature of craving. The issue of the multi-dimensional nature of craving, and the discriminative validity of the 2 factors of the QSU was considered further in chapter 6.
CHAPTER 6

EFFECT OF SMOKING-RELATED CUES ON CRAVING IN NON-DEPENDENT SMOKERS: VALIDATION OF THE TWO FACTOR STRUCTURE OF THE QSU

6.1 INTRODUCTION

Stolerman (1997) suggests that craving is the consequence of multiple factors operating upon the individual, and that these factors are more or less important at different phases of drug dependence: acquisition, maintenance, extinction and relapse. This would imply that multi-dimensional measures of craving are necessary, and that the influence of drug abstinence and cue-exposure should be investigated in both dependent and non-dependent smokers. Cigarette “chippers” are especially light, non-dependent smokers who smoke less than 5 cigarettes a day on average and do not exhibit nicotine dependence despite often having smoked for a number of years (Shiffman et al. 1992). Any craving experienced by “chippers” should, by definition, be unrelated to the period of abstinence before smoking and should be restricted to aspects of positive reinforcement. Furthermore, the factor 1 and factor 2 scores of “chippers” should be differentially sensitive to exposure to smoking related cues if this elicits any changes in craving. This provides an empirical opportunity to assess the construct validity of the factor structure of the QSU and is examined in the present chapter.

Tobacco “chippers” are interesting to addiction researchers for many reasons because their behaviour is inconsistent with theories that predict that frequent
exposure to nicotine should lead to dependence (Shiftman, 1989). Since tobacco chippers are not dependent upon cigarettes, it is reasonable to assume that they do not smoke in order to obtain relief from the negative affect associated with withdrawal. It is also reasonable to assume that they are primarily motivated to smoke because they find smoking pleasurable. Previous work has demonstrated that exposure to smoking-related cues increases cravings for cigarettes in dependent smokers, and that this effect is most striking in non-deprived smokers (see Chapter 3). The aim of the present study was to investigate the construct validity of the two-factor QSU, and the effects of exposure to smoking-related cues, in non-dependent smokers.

It was therefore predicted that if the two factors of the QSU primarily reflect positive and negative reinforcement aspects of craving, respectively, then tobacco chippers exposed to smoking-related cues should exhibit elevated scores on QSU factor 1 (positive reinforcement) items compared to those who are not exposed to smoking-related cues. Furthermore, exposure to smoking-related cues should have no effect on the responses of tobacco chippers to QSU factor 2 (negative reinforcement) items.

6.2 MATERIALS AND METHODS

6.2.1 Participants

A total of 32 paid participants (12 male and 20 female) were recruited through posters on the University of Wales Swansea campus. Participants gave informed consent to participate and were then randomly assigned to one of two smoking-related cue conditions: smoking-related cues present or absent. All participants were pre-
screened to ensure that they all smoked cigarettes, did not smoke every day, and had smoked occasionally for at least 1 year. The average participant was 20.59 (± 0.38) years old, smoked 8.29 (± 1.25) cigarettes per week, and had smoked for 3.15 (± 0.32) years. Each participant agreed to abstain from smoking for at least 24 hours prior to testing. The study received approval from the Ethics Committee of the Department of Psychology.

6.2.2 Design

Each participant completed only one session, in one of 2 rooms. The 2 rooms used were identical to those outlined in section 3.2.5. Both were of approximately the same size and layout, with no windows. Both rooms contained a 3/486 PC. One room was deemed the “Cue” room and contained smoking-related cues such as cigarette smoke, cigarette packets and ashtrays containing cigarette butts. There were no smoking-related cues in the “No Cue” room.

All participants were instructed to not smoke for at least 24 hours prior to testing. Informed written consent and breath carbon monoxide samples were obtained upon arrival at the appropriate room.

6.2.3 The Questionnaire of Smoking Urges

The Questionnaire of Smoking Urges (“QSU”-Tiffany & Drobes, 1991) as described in section 2.2.1.2 was presented on an IBM 3/486 PC. Participants responded by moving a centrally located cursor to the desired position in response to each question.
6.2.4 Carbon Monoxide Monitor

Participants' carbon monoxide readings were taken using a smokerlyser (UK) CO monitor as described in section 2.2.1.7. Participants were led to believe that this measure would be able to detect a fraudulent claim of 24 hours abstinence.

6.2.5 Procedure

Participants arrived at the laboratory and were immediately placed in either the cue room, or the no-cue room. Each participant then completed a consent form, followed by a participant-details questionnaire. Participant’s carbon monoxide readings were then taken to confirm that they were not regular smokers (by providing an exhaled CO reading of less than 10 ppm). Participants in the cue room were then given a lit cigarette to hold and were instructed to not smoke it. These participants then completed the QSU. Participants in the no-cue room underwent an identical procedure, except that they were not required to hold a lit cigarette.

6.2.6 Analysis

Participant details and QSU factor and raw scores were analysed using one-way ANOVA. QSU factor 1 and factor 2 scores were compared to QSU factor 1 and 2 scores in chapter 3 using independent samples t-tests.

6.3 RESULTS

6.3.1 Participant characteristics

One-way analysis of variance revealed that there were no significant differences between cue groups for age, number of cigarettes smoked per week or
number of years that the participants had smoked occasionally. In addition, one-way analysis of variance revealed that there was no significant difference between cue groups for exhaled CO readings (3.75 ± 0.27 ppm in the cue condition, 3.13 ± 1.15 ppm in the no-cue condition).

### 6.3.2 Questionnaire of Smoking Urges – factor 1 and 2 scores

The original factor 1 and 2 scores derived according to Tiffany and Drobes (1991) were analyzed using one-way analysis of variance. Factor 1 scores were significantly elevated in participants in the cue room compared to those in the no-cue room [F(1,30)=10.25 P<0.005). Factor 2 scores did not differ significantly between participants in the cue room and participants in the no cue room (see Figure 6.1, left panel).

### 6.3.3 Questionnaire of Smoking Urges – Item by item analysis

One-way analysis of variance was then applied to each of the 32 items to assess which items were elevated by the presence of smoking-related cues. None of the responses to any of the 32 items were elevated in the no-cue condition compared to the cue condition. Responses to eleven items were elevated in the cue condition compared to the no-cue condition (Max F(1,30)=4.36, p=0.05; Min F(1,30)=13.24, p<0.001). Only one of these eleven items (item 13) loaded on the original factor 2 scale derived by Tiffany and Drobes (1991). Eight of the items loaded on the original factor 1 scale (items 6, 16, 17, 20, 21, 22, 25 and 32) and two items did not load on either factor (items 1 and 31). None of these items derived from the “Relief of withdrawal or negative affect” category. Four derived from the “Desire to smoke”
category, two derived from the “Anticipation of positive outcome” category and three derived from the “Intention to smoke” category (See Table 4.2).

6.3.4 Questionnaire of Smoking Urges – Comparison to regular smokers

Finally, the QSU factor 1 and 2 scores from the present study (Fig 6.1, left panel) were compared to those found in regular non-abstinent smokers in Chapter 3 (Fig 6.1, right panel). In the no-smoking cues present condition, t-tests revealed that factor 1 and factor 2 scores of tobacco chippers were significantly lower than the corresponding factor 1 and factor 2 scores of non-abstinent, regular smokers ($t_{(5)}= 4.76, p<0.001; t_{(5)}= 3.20, p<0.01$ respectively). Exposure to smoking-related cues in chippers elevated factor 1 scores such that they did not differ significantly from factor 1 scores found in non-abstinent regular smokers who were not exposed to smoking related cues ($t_{(5)}= 1.44, p>0.1$). However, exposure to smoking-related cues in chippers did not significantly elevate factor 2 scores; therefore, the factor 2 scores of cue-exposed chippers remained significantly lower than the factor 2 scores of non-abstinent, regular smokers who were not exposed to smoking related cues ($t_{(5)}= 2.36, p<0.05$).

6.4 DISCUSSION

The main finding from the present study was that the two factors of the QSU are differentially sensitive to exposure to smoking-related cues in tobacco “chippers”. Factor 2 items, which are thought to reflect negative reinforcement aspects of craving, were insensitive to the influence of smoking-related cues, while ratings of craving on factor 1 items, which are thought to reflect positive reinforcement, were elevated by the presence of smoking-related cues. Furthermore, an item by item analysis revealed
that none of the items, for which responding was elevated by exposure to smoking-related cues, derived from the "Relief of withdrawal or negative affect" content category. These findings support the view that there are two qualitatively distinct components of the urge to smoke cigarettes, which reflect the influences of positive and negative reinforcement, and contradict earlier criticisms (Kozlowski et al. 1996) of the validity of the two-factor structure of the QSU.

Further, indirect support for the validity of the QSU is provided by a comparison of the QSU scores from the tobacco chippers in the present study with the scores obtained from regular smokers in Chapter 3 that employed identical salient cue and no-cue conditions (holding a lit cigarette). Factor 1 and 2 scores of chippers who were not exposed to smoking-related cues in the present study, were significantly lower than those of the non-abstinent regular smokers in the study reported in chapter 3. Exposure to smoking-related cues in the present study elevated the QSU factor 1, but not the factor 2 scores, nearer to the level found in non-abstinent regular smokers who were not exposed to smoking-related cues (see Fig 6.1). Thus, the present findings demonstrate that the QSU can distinguish between regular and non-regular smokers. Furthermore, the present findings demonstrate that while exposure to smoking-related cues acts upon positive reinforcement in tobacco chippers, exposure to such cues acts primarily on negative reinforcement-driven craving in regular smokers in whom smoking-related cues have an even greater influence than brief periods of abstinence.

Tiffany (1991) proposed that a questionnaire of smoking urges needs to be developed that is psychometrically sound and has a broad enough content to capture
various conceptualisations of the verbal aspects of urges to smoke. Most other methods of assessing urges to smoke rely on single item questionnaires of unknown reliability, or longer questionnaires with small validation samples, limited information on their psychometric properties, and founded on the assumption that urges reflect a uni-dimensional motivational state (e.g. Shiffman & Jarvik, 1976; West et al. 1984). The findings of the present study, and those presented in Chapter 3, suggest that the QSU is an easy to administer, psychometrically sound, instrument for the measurement of subjective cravings for cigarettes.

In their recent meta-analysis of cue-reactivity studies, Carter and Tiffany (1999) concluded that, compared to neutral cues, exposure to drug-related cues elevated subjective reports of craving for a variety of other substances of abuse including alcohol, heroin and cocaine, in dependent users. None of the latter investigations used multi-dimensional measures of craving however. Indeed, the present findings, and the findings presented in Chapters 3 and 4, are the first to employ a multi-factorial measure to demonstrate that exposure to cues elevates craving in regular smokers. Thus, further research is needed to determine if exposure to drug-related cues has more influence than brief periods of abstinence on multi-factorial measures of negative reinforcement-driven craving in dependent users of other substances of abuse.

One practical implication of the present findings is that future studies of the efficacy of craving reduction techniques in dependent smokers should employ multi-factorial measures, and assess the extent to which such interventions reduce the influence of smoking-related cues, as well as that of brief periods of abstinence, on
cravings for cigarettes. Furthermore, the present findings suggest that efforts to prevent non-smokers and non-dependent smokers from becoming dependent should concentrate on minimising exposure to smoking-related cues and the positive reinforcement properties of cigarettes.

Many investigators argue that subjective cravings for cigarettes are a strong predictor of relapse in dependent smokers (e.g. Swan et al. 1996). If this is true, the present findings, those presented in Chapter 3, suggest that individual differences in reactivity to smoking-related cues may be a better predictor of relapse, in dependent smokers, than the ability to remain abstinent from smoking for brief periods of time. This remains an empirical question for future research.

The findings of the present study suggest that cigarette chippers do not suffer from withdrawal symptoms. As such, they represent an ideal study group to address whether the reported cognitive enhancing effects of nicotine (e.g. Wesnes and Warburton, 1983), are due to relief from withdrawal, or the nootropic effects of nicotine. An implication of Tiffany’s (1990) cognitive automatic theory is that craving is cognitively effortful; therefore we would expect to observe decreased cognitive performance in participants who are craving. This issue was addressed in chapter 7.
Figure 6.1 Effect of smoking-related cue exposure on original QSU factor scores in “Chippers” and non-abstinent regular smokers. Values are means + S.E.M.

Non-regular Smokers (“Chippers”)  Non-abstinent regular smokers

\[ \text{Mean QSU score} \]

\begin{align*}
\text{Factor 1} & \quad \text{Factor 2} \\
\text{No Cues} & \quad \text{Cues} \\
\end{align*}

\( b \) from Chapter 3
CHAPTER 7

COGNITIVE EFFECTS OF NICOTINE IN NON-DEPENDENT SMOKERS

7.1 INTRODUCTION

As discussed in section 1.9, research into the cognitive effects of nicotine has yielded some compelling yet also conflicting results. If, however, nicotine does enhance cognitive performance, what exactly is causing these improvements? Initially, the most supported explanation was the idea of relief from withdrawal. Smokers who have been deprived from smoking are usually in a state of withdrawal, the symptoms of which affect their performance. Some of the effects of abstinence include irritability, anxiety, anger, difficulty concentrating, hunger, fatigue and somatic disturbances (Clark, 1987). In addition, Tiffany's (1990) cognitive automatic theory suggests that craving is cognitively effortful. A consequence of this is that cognitive performance under a state of withdrawal will be significantly impaired. Foulds and colleagues (1996) for example found that abstaining smokers performed significantly worse than never-smokers on cognitive tasks prior to subcutaneous administration of nicotine. Thus, it could be suggested that nicotine improves cognitive performance indirectly by relieving withdrawal symptoms (Hughes 1991; Sherwood 1993). More recently, Parrott and Kaye (1999) have stated that repetitive nicotine use does not lead to any real psychobiological advantages, and that "dependent smokers need regular hits of nicotine just to remain feeling normal."

The second set of explanations for observed improvements in cognitive function after nicotine administration is that nicotine produces neuropharmacological nootropic or cognitive enhancing effects, and are covered in section 1.9. The main
draw back of studies investigating the mechanisms underlying nicotine-induced improvements is their use of regular cigarette smokers as participants. This presents several problems, firstly, participants are usually nicotine deprived, which does not allow the researcher to distinguish between withdrawal relief, and neuropharmacological explanations for any improvement in performance. Secondly, smokers are a pre-selected population, and so results found may not be generalized to the population as a whole. In addition, since nicotine is chronically self-administered by smokers, this makes it difficult to find a true control condition since regular smokers will always be either under the influence of nicotine, or in a state of withdrawal to varying degrees. It is also impractical to use non-smokers in such experiments since nicotine often makes non-smokers feel nauseous.

Another consideration when assessing the cognitive effects of nicotine is the method of administration. Suitable low-nicotine cigarettes are ineffective since they are easily distinguishable from standard cigarettes by regular smokers (Rose 1988). The alternative method of sham smoking (e.g. Revell 1988) is also ineffective since it is not a blind procedure, and participants are well aware that they are not receiving nicotine. Transdermal delivery systems (i.e. nicotine patches) are a far more practical method of nicotine delivery, since they ensure steady states of plasma nicotine levels (Benowitz et al. 1991; Srivastava et al. 1991), can be readily incorporated into a double-blind design, and avoid any confounding influence of the sensory-motor effects of smoking (Warburton & Mancuso, 1998).

As discussed in section 1.7 and chapter 6, tobacco chippers are an anomalous group of smokers who maintain low-level cigarette use without becoming dependent.
Further, the findings of chapter 6 support the notion that cigarette chippers do not experience withdrawal-based craving. Cigarette chippers are thus an ideal population to study when wishing to address if the cognitive enhancing effects of nicotine result from cognitive enhancing neuropharmacological effects, or the relief of withdrawal, since they do not experience cigarette withdrawal like regular smokers, and in addition do not feel nauseous after smoking like non-smokers.

The present chapter used a population of non-regular smokers to investigate the effects of nicotine delivered via a nicotine patch on two measures of attention (reaction time and rapid information processing task), and a simple verbal memory task. As discussed in section 1.8, measures of attention have yielded the most robust findings in the literature concerning the enhancing effects of nicotine. Warburton and Mancuso (1998) have recently reported nicotine-induced improvements in attention and verbal memory in regular smokers wearing a nicotine patch. It was therefore predicted that if improved performance was observed in a group of chippers receiving nicotine, then the relief of withdrawal hypothesis would not be a viable explanation of nicotine-induced cognitive enhancement. In addition, measures of positive and negative mood were taken to assess if the administration of nicotine via a transdermal patch to non-regular smokers improved mood as has been reported for regular smokers by Warburton and Mancuso (1998).
7.2 MATERIALS AND METHODS

7.2.1 Participants

A total of 40 paid participants (9 male and 31 female) were recruited through posters on the University of Wales Swansea campus. Participants gave informed consent to participate and were then randomly assigned to one of two nicotine patch conditions: active or placebo patch. All participants were pre-screened to ensure that they all smoked cigarettes, did not smoke every day, and had smoked occasionally for at least 1 year. The average participant was 21.40 (± 0.35) years old, smoked 1.49 (± 0.17) times per week, and smoked 5.81 (± 0.82) cigarettes per session. Each participant agreed to abstain from smoking for at least 24 hours prior to testing. The study received approval from the Ethics Committee of the Department of Psychology.

7.2.2 Design

The experiment was a double-blind placebo controlled design. An independent 3rd party labeled the patches as “Patch A” or “Patch B” and then kept the code locked away until completion of the experiment. Opening of the code revealed that “Patch A” was the active patch, and that “Patch B” was the placebo.

7.2.3 Active and inactive (placebo) patches

Active patches were Nicotinell® (Novartis Consumer Health) large size (30cm²) patches each containing 52.5mg of nicotine, with an average absorption rate of 21mg of nicotine in 24 hours. This dose was selected as it was identical to that used by Warburton and Mancuso (1998). These patches have been reported to have few adverse effects yet after 6 hours, they produce average levels of nicotine similar to the
trough levels found in a smoker during the day, that is half of the peak levels achieved at the end of a cigarette (Warburton & Mancuso, 1998; Benowitz et al, 1991; Srivastava et al, 1991).

Placebo patches were constructed by placing a transparent, non-permeable, adhesive sheath over the nicotine-impregnated part of the Nicotinell® patch. Since the sheath was transparent, the placebo patches looked and smelt exactly like the active patches. All patches were initially removed from their packaging which was then replaced, re-sealed and given to an independent 3rd party who labelled the patches as “Patch A” or “Patch B”. The independent 3rd party revealed after completion of the experiment that “Patch A” was the active patch, and that “Patch B” was the placebo patch.

7.2.4 Reaction Time: Decision and Movement Time

Reaction time was measured using a technique proposed by Jensen (1982). The apparatus consisted of a 13 x 17 inch black panel tilted at a 30°angle. Eight orange lights were arranged in a semi-circle on the face of the panel. Half an inch below each light was a button, with each button being equidistant (6 inches) from the home key. The home key was a button situated at the bottom of the semi-circle of lights. Participants were instructed place the index finger of their preferred hand onto the home key. They were instructed that one of the lights would illuminate, and that they were to move their finger from the home key to the button corresponding to the lit lamp and back again as quickly as possible. The test session consisted of four sets of twenty illuminations. In the first set of twenty, only one of the lamps illuminated (simple reaction time). For the next 3 sets, two, four and eight of the lamps
illuminated respectively (choice reaction time). Participants were instructed as to the exact nature of each set, and performed a practice trial of 10 illuminations to ensure that they understood. Each trial was preceded by instructions presented on a PC monitor and a tone to indicate that the test was about to begin. Two measures were recorded by the PC in milliseconds: 1) Decision time – the period between the onset of the light and removal of the finger from the home key and 2) Movement time – the duration between releasing the home key and pressing the button corresponding to the illuminated lamp. Reaction times more than three standard deviations above or below the participant's own means were considered “outliers”, and automatically removed by the computer program. In addition, reaction times of less than 170 milliseconds were removed as a physiological impossibility and reaction times over 990 milliseconds were removed as they were considered to reflect a lack of attention rather than processing speed.

For the purposes of the present study, only median reaction times were analysed, rather than the means, because they provide a better measure of central tendency (Jensen, 1982). In addition, linear regressions of the median decision times for each set of twenty trials were used to calculate the intercept and the slope. The intercept represented the total time required for the processes of sensory and attentional registration, and the slope provided a measure of the time taken for discrimination (Jensen, 1982).

7.2.5 Rapid Visual Information Processing Task

The Rapid Visual Information Processing Task as described in section 5.2.4 was presented on a desktop PC. However, in the present study the RVIPT was
employed as a vigilance task rather than as a progressive reward task. Participants were required to perform the task for ten minutes, over which period the number of correct and incorrect responses was recorded at one-minute intervals. Responses that occurred more than 1500ms after the presentation of the third digit of a target sequence were recorded as errors.

7.2.6 Word Recall

A list of 15 words was used, these being identical to those used by Benton and Owens (1993) and Moss and Scholey (1996), each having six letters and two syllables, and being high in imagery, concreteness and frequency. The words were presented verbally at the rate of one per second, on a Mono cassette player.

7.2.7 Mood

Positive and negative mood scores were obtained using the mood scales described in section 2.2.5.

7.2.8 Carbon Monoxide Monitor

Participants’ carbon monoxide readings (in particles per million – ppm) were taken using a Smokerlyser (UK) CO monitor. Participants were led to believe that this measure would be able to detect a fraudulent claim of 24 hours abstinence prior to the experiment, and 6 hours abstinence while wearing the patch. Participants were required to have a CO reading of less than 10ppm.
7.2.9 Procedure

Participants were tested in groups of between 1 and 4 at a time. Participants arrived at an initial session at 9 a.m. having been instructed not to smoke for 24 hours prior to arrival at the laboratory. Participants then completed a mood questionnaire and had their CO levels taken. Participants were randomly assigned to patch A or patch B, and then had the appropriate patch fitted to their upper arm. They were then instructed not to smoke, drink alcohol or caffeine or engage in physical exercise while wearing the patch, and to return to the laboratory 6 hours later at 3 p.m.

Upon return to the laboratory CO readings were taken, then participants completed a personal details questionnaire. Next they were presented with the list of 15 words to remember followed by immediate recall for 60 seconds. Participants were then seated at a desktop PC where they completed the reaction time task, followed by the RVIPT. Finally, participants completed 60 seconds of delayed recall of the list of 15 words. Participants then had their patches removed, debriefed, and were paid £10 for their time.

7.3 RESULTS

7.3.1 Personal Details

One way ANOVA revealed no significant difference between groups for Age (F(1,38)=1.70, p>0.05), number of times smoked per week (F(1,38)=0.48, p>0.05) or number of cigarettes smoked per session (F(1,38)=0.93, p>0.05). See table 7.1.
Table 7.1 Participant characteristics and mood scores. Values are mean ± S.E.M.

<table>
<thead>
<tr>
<th></th>
<th>Active Patch</th>
<th>Placebo Patch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>20.95 (.42)</td>
<td>21.85 (0.55)</td>
</tr>
<tr>
<td># Times smoke per week</td>
<td>1.37 (0.15)</td>
<td>1.61 (0.31)</td>
</tr>
<tr>
<td># cigarettes per session</td>
<td>5.03 (0.86)</td>
<td>6.60 (1.39)</td>
</tr>
<tr>
<td>Pre Patch +ve Mood</td>
<td>2.59 (0.23)</td>
<td>2.31 (0.23)</td>
</tr>
<tr>
<td>Post Patch +ve Mood</td>
<td>2.30 (0.30)</td>
<td>2.29 (0.23)</td>
</tr>
<tr>
<td>Pre Patch -ve Mood</td>
<td>0.40 (0.12)</td>
<td>0.49 (0.13)</td>
</tr>
<tr>
<td>Post Patch -ve Mood</td>
<td>0.66 (0.20)</td>
<td>0.35 (0.15)</td>
</tr>
</tbody>
</table>

7.3.2 Mood

Two-way ANOVA revealed no difference in positive mood scores before and after wearing the patch ("Time" - $F(1,38)=0.93$, $p>0.05$), no positive mood difference between patch types ($F(1,38)=0.21$, $p>0.05$) and no interaction between Time and Patch type ($F(1,38)=0.66$, $p>0.05$). See Table 7.1.

Similarly, two-way ANOVA revealed no difference in negative mood scores before and after wearing the patch ("Time" - $F(1,38)=0.25$, $p>0.05$), no negative mood difference between patch types ($F(1,38)=0.36$, $p>0.05$) and no interaction between Time and Patch type ($F(1,38)=2.72$, $p>0.05$). See Table 7.1.

7.3.3 Immediate and Delayed Word Recall

For immediate word recall participants in the active patch condition recalled an average of 7.30 (± 0.42) words compared to 6.85 (± 0.43) words in the placebo patch condition. One way-ANOVA revealed that this difference was not significant ($F(1,38)=0.56$, $p>0.05$).
Similarly, for delayed word recall participants in the active patch condition recalled an average of 5.50 (± 0.52) words compared to 5.80 (± 0.56) words in the placebo patch condition. One way-ANOVA revealed that this difference was not significant (F(1,38)=0.16, p>0.05).

### 7.3.4 Rapid Visual Information Processing Task

Repeated measures ANOVA revealed that there were no significant difference between patch groups for the number of correct responses on the task (F(1,38)=0.12, p>0.05). The number of correct responses altered significantly across the 10 minutes of the task (F(9,342)=4.52, p<0.001), however there was no interaction between patch groups and duration of task for number of correct responses (F(9,342)=0.55, p>0.05) See table 7.2.

Repeated measures ANOVA revealed that there were no significant difference between patch groups for the number of incorrect responses on the task (F(1,38)=0.19, p>0.05). The number of incorrect responses altered significantly across the 10 minutes of the task (F(9,342)=2.32, p=0.015), however there was no interaction between patch groups and duration of task for number of in correct responses (F(9,342)=0.85, p>0.05) See table 7.2.

Repeated measures ANOVA revealed that there were no significant difference between patch groups for the reaction time to correct responses on the task (F(1,38)=0.91, p>0.05). The reaction times to correct responses altered significantly across the 10 minutes of the task (F(9,342)=3.79, p<0.001), however there was no
interaction between patch groups and duration of task for the reaction time to correct responses ($F(9,342)=0.78$, $p>0.05$) See table 7.2.

### 7.3.5 Reaction Time (Table 7.3)

One way ANOVAs revealed no significant difference between patch groups for simple decision time or any of the three choice decision times (Min $F(1,38)=0.034$, Max $F(1,38)=0.72$, $p>0.05$).

One way ANOVAs revealed no significant difference between patch groups for simple movement time or any of the three choice movement times (Min $F(1,38)=0.29$, Max $F(1,38)=1.06$, $p>0.05$).

In addition one way ANOVAs revealed no significant difference between patch groups for slope (discrimination time – $F(1,38)=3.90$, $p>0.05$) or Intercept (sensory and attentional registration – $F(1,38)=0.33$, $p>0.05$).

### 7.4 DISCUSSION

The present findings found no evidence of nicotine-induced improvement in attentional and verbal memory tasks using a population of non-regular smokers. These findings are contrary to previous research. Warburton and Mancuso (1998), for example, state that the transdermal nicotine patch can improve attentional performance by 10.8% and 4% respectively for correct detections and reaction times. Further they suggest that transdermal nicotine patches can improve performance on immediate and delayed recall tasks, and that these cognitive improvements are similar
in magnitude to those found using cigarette smoke administered nicotine (e.g. Wesnes and Warburton 1983; Wesnes et al., 1983).

The present findings suggest that nicotine-induced improvements in cognitive performance are based on the relief of withdrawal in regular smokers (Hughes 1991; Sherwood 1993). However, Wesnes and Warburton (1983) stated that, “smoking has a marked effect on mental efficiency, and thus it is probable that studies which have failed to demonstrate any effects have been methodologically inadequate”, and further that “nicotine is the agent in tobacco smoke responsible for the improvements in mental efficiency”. It is thus apparent that the present findings either refute these claims, or arose as the consequence of methodological inadequacies. The present study was methodologically similar to that of Warburton and Mancuso (1998). In both studies, participants were required to wear a placebo or a 21 mg nicotine transdermal patch for 6 hours prior to testing. Participants were not permitted take alcohol or caffeine during, or 12 hours prior to, the experiment, nor where they permitted to engage in strenuous exercise or to smoke while wearing the patch. In addition, the rapid information processing task used in the present study was identical to that used by Warburton and Mancuso (1998). While the verbal memory task, differed in the number of words, the present verbal memory task has been successfully used in studies assessing the cognitive effects of glucose (e.g. Benton & Owens, 1993a) and oxygen (e.g. Moss & Scholey 1996) administration.

The present study did differ to that of Warburton and Mancuso (1998) in two respects. Firstly, the present study did not employ training sessions on the experimental tasks prior to the test session, nor were baseline measures taken before
the patch was fitted. This was not deemed necessary since the RIPT and reaction time tasks have been successfully employed without training in the assessment of the cognitive effects of glucose administration (e.g. Donohoe and Benton, 1999). In addition, differences from baseline measures were taken, but not used in Warburton and Mancuso’s (1998) analysis. Secondly, the Warburton and Mancuso study was a repeated measures design with participants completing both active and placebo patch conditions. It could thus be argued that nicotine-induced cognitive enhancement only occurs in familiar or well-practiced tasks, and that nicotine-enhancement will not induce performance improvements in unpracticed tasks. Minute by minute comparisons of the number of correct responses reveal that the participants in the present study were detecting fewer sequences per minute in both active and placebo conditions, when compared to the participants in the Warburton and Mancuso (1998) study. While this may suggest that task familiarity is an important component in nicotine-induced cognitive improvement, it is not sufficient to discount the suggestion that previously observed effects are attributable to the relief of withdrawal.

In summary, the present study did not find evidence for the theory that nicotine directly improves cognitive performance. While the present findings would seem to suggest that nicotine-induced improvements in cognitive performance are due to the relief of withdrawal and are as such consistent with Tiffany (1990), it is not possible to accept this explanation on the basis of non-significant differences, and the possibility of methodological problems. Future studies should further utilize the population of low-rate smokers in order to clarify this issue.
Table 7.2 RVIP data. Values are mean ± S.E.M.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Minute</th>
<th>Active Patch</th>
<th>Placebo Patch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Correct Responses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>4.45 (0.51)</td>
<td>4.45 (0.47)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3.80 (0.41)</td>
<td>3.70 (0.47)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3.80 (0.38)</td>
<td>3.45 (0.30)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3.40 (0.43)</td>
<td>3.10 (0.29)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>3.30 (0.32)</td>
<td>3.05 (0.27)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>4.15 (0.45)</td>
<td>3.30 (0.41)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>3.80 (0.60)</td>
<td>4.00 (0.56)</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>2.30 (0.38)</td>
<td>2.85 (0.29)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>3.50 (0.35)</td>
<td>3.05 (0.37)</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>3.00 (0.47)</td>
<td>2.95 (0.42)</td>
<td></td>
</tr>
<tr>
<td>Number of Incorrect Responses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.95 (0.47)</td>
<td>2.60 (0.45)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2.30 (0.57)</td>
<td>2.20 (0.47)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2.35 (0.69)</td>
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</tr>
<tr>
<td>4</td>
<td>3.95 (2.02)</td>
<td>2.20 (0.57)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1.85 (0.54)</td>
<td>1.75 (0.51)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1.90 (0.51)</td>
<td>2.05 (0.38)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1.90 (0.60)</td>
<td>1.85 (0.41)</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>1.60 (0.53)</td>
<td>1.30 (0.36)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>1.10 (0.39)</td>
<td>1.00 (0.27)</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>1.45 (0.53)</td>
<td>1.45 (0.36)</td>
<td></td>
</tr>
<tr>
<td>Reaction Time To Correct Responses (msec)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>488.05 (27.11)</td>
<td>461.75 (37.80)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>478.65 (32.95)</td>
<td>465.20 (32.50)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>619.95 (27.72)</td>
<td>573.60 (35.25)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>537.05 (37.49)</td>
<td>588.60 (35.50)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>545.25 (28.74)</td>
<td>564.95 (40.48)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>550.65 (43.23)</td>
<td>612.40 (29.46)</td>
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<td>533.90 (52.06)</td>
<td>573.25 (45.40)</td>
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<td>8</td>
<td>423.20 (59.77)</td>
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<td>9</td>
<td>487.05 (32.60)</td>
<td>559.20 (46.32)</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>448.80 (57.17)</td>
<td>455.75 (54.11)</td>
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</tbody>
</table>
Table 7.3 Mean (SEM) of Median Reaction Times

<table>
<thead>
<tr>
<th>Variable</th>
<th>Type of Choice</th>
<th>Active Patch</th>
<th>Placebo Patch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Decision Time (msec)</td>
<td>Simple</td>
<td>319.40 (10.41)</td>
<td>306.88 (10.54)</td>
</tr>
<tr>
<td></td>
<td>2 Choice</td>
<td>323.75 (10.19)</td>
<td>326.55 (11.38)</td>
</tr>
<tr>
<td></td>
<td>4 Choice</td>
<td>339.53 (10.62)</td>
<td>350.28 (9.72)</td>
</tr>
<tr>
<td></td>
<td>8 Choice</td>
<td>363.33 (11.50)</td>
<td>373.63 (10.13)</td>
</tr>
<tr>
<td>Median Movement Time (msec)</td>
<td>Simple</td>
<td>180.03 (11.73)</td>
<td>191.65 (16.20)</td>
</tr>
<tr>
<td></td>
<td>2 Choice</td>
<td>172.60 (10.31)</td>
<td>193.48 (17.51)</td>
</tr>
<tr>
<td></td>
<td>4 Choice</td>
<td>181.43 (10.29)</td>
<td>193.20 (14.22)</td>
</tr>
<tr>
<td></td>
<td>8 Choice</td>
<td>193.25 (9.67)</td>
<td>203.13 (15.51)</td>
</tr>
<tr>
<td></td>
<td>Intercept</td>
<td>314.40 (10.28)</td>
<td>305.74 (11.19)</td>
</tr>
<tr>
<td></td>
<td>Slope</td>
<td>14.74 (2.80)</td>
<td>22.40 (2.68)</td>
</tr>
</tbody>
</table>
8.1 Overview of findings

It is surprising that, despite the theoretical and practical significance of drug cravings, the concept has attracted little conceptual or empirical analysis, and in the past has, almost invariably, been evaluated using single item questionnaires of unknown reliability, or longer questionnaires with small validation samples, limited information on their psychometric properties, and founded on the assumption that urges reflect a unidimensional motivational state (e.g. Shiffman & Jarvik 1976; West et al. 1984). The primary aim of the present thesis was to further investigate the nature of craving and urges, by concentrating on cigarette smokers, and utilizing a multidimensional measure of cigarette cravings (The “QSU” – Tiffany & Drobes, 1991) that considers both the positive and the negative aspects of cigarette dependence. Tiffany (1991) proposed that a questionnaire of smoking urges needs to be developed that is psychometrically sound and has a broad enough content to capture various conceptualisations of the verbal aspects of urges to smoke. The findings of the present thesis suggest that the QSU is an easy to administer, psychometrically sound, instrument for the measurement of subjective cravings for cigarettes.

In chapter 2, the acute efficacy of nicotine gum was investigated. The results suggested that both nicotine and a placebo gum are equally effective at reducing acute levels of craving. However, the behavioural findings of chapter 2 did not substantiate the objective findings, and in the light of previous research, it was decided to further investigate the reliability and validity of the QSU in chapters 3 and 4, 5 and 6.
The results of chapter 3 suggested that the QSU is sensitive to brief periods of abstinence and to smoking-related cue exposure, but the behavioural measure provided only limited cross-validation of the subjective finding. Chapter 4 replicated Tiffany and Drobes' (1991) original factor analysis of the 32 items of the QSU and produced an almost identical 2-factor structure. In addition, the findings of chapter 4 provided additional evidence for the sensitivity of the QSU to both brief periods of abstinence, and exposure to cigarette-related cues.

In light of the consistency of results found with the QSU, and the failure to provide a suitable behavioural cross-validation of the subjective QSU, chapter 5 reported an attempt to develop an alternative behavioural method of evaluating craving, and validating the QSU. The findings of chapter 5 yet again found evidence for the sensitivity of the QSU to brief periods of abstinence, but again failed to provide a suitable behavioural cross-validation. It was concluded that the behavioural assessment of acute cigarette cravings is problematic, but that the consistency of the results found using the QSU were such as to confirm the reliability the questionnaire as a suitable measure of acute cigarette cravings.

Having established the reliability of the QSU, an alternative approach to finding behavioural cross-validation was adopted in order to investigate the construct validity of the 2-factor structure of the QSU. Since by definition, non-dependent, occasional, cigarette smokers, or cigarette “chippers”, do not experience significant levels of withdrawal-based craving it was expected that the 2 factors of the QSU should be differentially sensitive to smoking-related cue exposure in chippers. In chapter 6, it was reported that this was indeed the case. Factor 1 items, which are
thought to reflect positive reinforcement, were elevated by the presence of smoking-related cues, whereas Factor 2 items, which are thought to reflect negative reinforcement aspects of craving, were insensitive to the influence of these cues in chippers. Thus, it was concluded that the two factors of the QSU measure qualitatively different components of acute cravings for cigarettes. In addition, since cigarette chippers do not experience significant levels of withdrawal-based craving it was decided that they provided the ideal opportunity to investigate whether reports of the cognitive enhancing effects of nicotine result from the direct nootropic pharmacological effects of nicotine on cognition, or from the alleviation of withdrawal. The study reported in chapter 7 did not find evidence for the cognitive-enhancing-effects of nicotine in a sample of cigarette chippers. This suggested that previous reports of nicotine-induced cognitive enhancement in regular smokers might be attributable to the alleviation of withdrawal.

The implications for these findings for theories of craving and dependence will now be considered.

### 8.2 Is the QSU really a subjective measure of “craving”?

As discussed in sections 1.1 and 1.2, there is much debate as to exactly what drug urges and cravings are, and as yet a universally acceptable definition of craving has not been found. Traditional assessment of craving has been based on unidimensional, single item questionnaires of unknown reliability and validity (Tiffany, 1992). The findings of the present thesis, suggest that craving is not a unitary concept. One implication of this is that although different craving questionnaires may each satisfactorily measure a component of craving, they may not
measure other equally important components. This may explain the lack of agreement amongst scientists and lay-people upon the definition of craving (Kozlowski & Wilkinson, 1987; Merikle, 1999).

In the factor analysis presented in chapter 4, the QSU items that referred specifically to urges or craving ("I crave a cigarette right now" and "I have an urge for a cigarette") loaded only on factor one. This would appear to contradict the notion of the multi-dimensional nature of "craving". It is inevitable that questions which use terms such as "craving" and "urges" should load on the same factor since the two words are often used interchangeably (see section 8.3). However, it should be noted that the term "craving" is being used as a term of convenience. Craving could be conceived of as a generic word encompassing a number of subjective experiences. Further support for the idea of craving as a multi-dimensional phenomenon may be found in "craving" questionnaires for other drugs of abuse. The alcohol craving questionnaire (ACQ: Singleton et al., 1994a), also considers craving to be multi-dimensional construct, and factor analysis of this questionnaire has revealed three factors reflecting positive and negative reinforcement, strong desires and intentions, and no desire to drink (Love et al., 1998). The desires for alcohol questionnaire (DAQ: Clark, 1994), similarly, has also been reported to have a 3-factor structure reflecting positive and negative reinforcement, strong desires and intentions, and mild desires and intentions (Love et al., 1998). Tiffany and colleagues (1993) have reported a 4-factor structure for a cocaine-craving questionnaire. Such evidence suggests that craving for a variety of different abused substances is multi-dimensional in nature and comprises at least two dimensions or factors. The next logical question is, "what exactly are these factors?" Tiffany and Drobes (1991) would not commit to precise
definitions of their 2-factors, preferring to refer to them simply as factor 1 and factor 2 since “labels may convey an overly simplistic understanding of the meaning of these manifestations of smoking urges”.

It is difficult to directly compare multi-dimensional craving questionnaires for different drugs, since they are necessarily different in construction. In the questionnaires mentioned above, the DAQ and ACQ had a single factor reflecting positive and negative reinforcement, whereas the QSU and CCQ had separate factors for positive and negative reinforcement. However, it should be remembered that nicotine and cocaine are stimulants whereas alcohol is classed as a sedative/hypnotic. In addition, alcohol exhibits a biphasic effect, such that it acts as a stimulant in low doses, and as a depressant in higher doses. It is therefore unsurprising that the factor structure of craving differs across different classes of abused substances.

The finding that the QSU exhibits two factors, one reflecting positive reinforcement and one reflecting negative reinforcement was replicated in the present thesis in chapter 4. It may be suggested that these two factors are important components in the subjective experience of craving, but may not necessarily be the only ones. Subtle intra-drug differences may exist. Thus, the subjective experience of craving for each class of drug may differ slightly. Nicotine shares many of the neuropharmacological properties of other abused psychostimulants (such as cocaine and amphetamine), which account for some of its addictive characteristics (Balfour et al, 2000). However, Balfour and colleagues (2000) have argued that aspects of the neuropharmacology of nicotine are also inconsistent with hypotheses that have been proposed to explain psychostimulant dependence. By implication, it would be
expected that differing classes of drugs should have different types of subjective craving associated with them, reflected by the differing factor structures of psychometric urge questionnaires. For example, while amphetamine, cocaine and nicotine all act on the mesocorticolimbic dopamine system to enhance dopaminergic activity in the nucleus accumbens, nicotine acts at the level of the ventral tegmental area (VTA), while amphetamine and cocaine have an indirect agonist effects at the level of the nucleus accumbens. However, it has been demonstrated that repeated nicotine exposure (as would be expected to occur in a regular smoker) causes inactivation or desensitisation of the dopamine secreting cells of the VTA in rats (Pidoplichko et al., 1997). An explanation for why smokers continue with their habit despite the nicotine ceasing to stimulate the nucleus accumbens, which is thought to mediate reward, could be that the negative withdrawal aspects of the craving are more important than the positive reinforcement aspects in nicotine addiction, compared to other stimulant drugs. This remains a question to be answered by future research, but it is clear that multi-dimensional measures of craving have a role to play in any such investigations in humans. This issue is also further complicated by the effects of cigarette smoke on Monoamine Oxidase, and will be considered further in section 8.4.

It is clear, however, that while drugs of abuse may have similar effects on the mesocorticolimbic dopamine system (e.g. Fibiger and Phillips, 1988), in other respects they have different pharmacological properties, and as such may not result in identical forms of addiction.

8.3 What is the difference between “urges” and “craving”?

Kozlowski and colleagues (1989) reported that there was a clear lack of agreement among problem drug users as to the meaning of a “craving”. These authors
reported that 49.5% of participants indicated that a craving is a strong urge or desire to take a drug, and that 35.5% stated that a craving is any urge or desire to take a drug, even a weak urge. Kozlowski and Wilkinson (1987), however, suggest that urges and cravings represent qualitatively and quantitatively different constructs. They suggested that the term “urge” refers to the whole continuum of desires to use drugs, whereas “craving” refers to states of intense and urgent desire. It seems apparent from Kozlowski and Wilkinson’s suggestion that the definition of a craving is dependent upon where the boundaries are set. Examination of table 4.2 in chapter 4 reveals that items on the QSU that referred to “Urge” (item 23) and “crave” (item 20) loaded on the same factor (factor 1), suggesting that they are perceived as at least similar constructs. Tiffany and Drobes (1991) chose to refer to urges in the title of their questionnaire, but state that they were reporting “the development and initial validation of a questionnaire of smoking urges and cravings”. From this quote it is clear that they viewed both terms as interchangeable, and did not distinguish between them. Tiffany later suggested that research, as yet, had not produced any empirical or psychometric justification for a substantive distinction between the term urge and the term craving (Tiffany et al, 1993). Similar to the findings reported in chapter 4, Tiffany and colleagues (1993) reported that items related specifically to “urge” and “craving” loaded on the same factor of their CCQ-Now cocaine-craving questionnaire. Furthermore, these authors reported that participants who identified craving as only a strong desire (as opposed to any urge or desire, even a weak one), did not rate the specific “urge” and “craving” items on the Cocaine Craving Questionnaire any differently from those who did not make this distinction (Tiffany et al., 1993). In other words, respondents to these authors questionnaire did not consider there to be a distinction between the term “craving” and the term “urge”.
8.4 The Relationship between Craving and Relapse

The clinical importance of precisely defining craving lies in the potential role of craving in relapse amongst abstinent drug users. Many investigators argue that craving is a powerful predictor of relapse amongst dependent drug users (e.g. Swan et al., 1996). If craving is not a significant predictor of relapse, there seems to be little clinical purpose in precisely defining and measuring it. However, Tiffany’s (1990) cognitive processing model of drug urges and drug use appears, on the surface, to cast doubt on the importance of conscious craving for relapse. Tiffany argues that the mechanisms linking drug-related stimuli to drug-use behaviour operate independently of the processes that control craving. Hence, according to this model, drug use-behaviour is an automatic, non-conscious behaviour much akin to other automated skills such as driving a car. However, further explanation of this model has revealed that, under certain conditions, craving, and physiological and behavioural responses to cues, could be predictive of relapse (Tiffany, 1995). Most cue-reactivity research is based upon the assumption that physiological reactions to drug stimuli are mediated primarily through the process of classical conditioning. Tiffany’s model, however, rejects this assumption and suggests instead that many of the physiological responses associated with urge reports represent reactions to the cognitive demands of craving, and are not classically conditioned withdrawal or appetitive effects (Tiffany, 1995). In addition, Tiffany’s model suggests that somatovisceral responses invoked by cue manipulations, may have multiple determinants, possibly reflecting elements of physiological reactions encoded within the action schema that has been impeded (Tiffany, 1995). An implication of this theory is that the relationship between craving and relapse may not be a straightforward one.
Empirical evidence for a relationship between craving and relapse is not as clear cut as would be intuitively expected, and may be even more complex than Tiffany’s (1990) model implies. Studies have demonstrated dissociations between drug craving and drug use. Gawin and colleagues (1989), for example, reported that desipramine (an antidepressant drug that blocks noradrenaline reuptake) decreased cocaine usage after two weeks of medication, but that it was several weeks until craving was reduced. Nemeth-Coslett and Henningfield (1986) reported that nicotine gum decreased actual smoking, but not self-reports of desire to smoke. Foltin and Fishman (1994) reported a similar result with cocaine users given Buprenorphine (mixed opioid agonist-antagonist). Other studies have reported the opposite effect of reductions of craving without any effect on drug self-administration, for example, in a sample of cocaine users given desipramine (Fishman et al., 1990) and the SSRI fluoxetine (Grabowski et al., 1995). A similar finding has been reported in smokers given the opioid receptor antagonist naltrexone (Sutherland et al., 1995; Houtsmuller et al., 1996). More recently, Houtsmuller and Sitzer (1999) have reported that the rapid smoking technique (Tiffany et al., 1986), a procedure designed to promote cigarette-related nausea, suppressed craving scores, but that craving scores were not predictive of actual smoking behaviour.

The findings presented in chapters 3 and 6 of the present thesis may shed some light on the nature of the relationship between craving and relapse. The findings of chapter 3 demonstrated that although cigarette-related cues elevated factor 1 and factor 2 scores on the QSU, this effect was maximal in non-abstinent smokers. A similar result was reported in chapter 4. The findings of chapter 6 demonstrated that in non-dependent smokers, cue’s significantly raised appetitive but not withdrawal
based craving. These findings are consistent with the view that craving and associated responses to cues may be predictive of relapse under certain conditions. In addition, these findings suggest that reactivity to smoking-related cues (possibly as a result of physiological responses encoded within blocked action schema) may be a better predictor of relapse than the ability to remain abstinent. However, it should be kept in mind that the present studies were designed to assess the reliability and validity of the Questionnaire of Smoking Urges, and not to specifically examine the relationship between craving and relapse. Future studies should embrace a broader cognitive physiological approach to the assessment of the relationship between craving and relapse, and look beyond the simplistic and problematic classical conditioning based assumptions.

8.5 Neuropharmacological basis of Tiffany’s theory

The findings presented in chapter 6 suggest that the QSU measures qualitatively different components of acute cravings for cigarettes. One implication of the hypothesis that craving has more than one component is the possibility that craving is modulated by more than one neurochemical system. Reports often suggest that the success rates of nicotine substitution therapies are low, with typically less than 20% of participating smokers still abstinent after 1 year (Balfour & Fagerstöm, 1996). Balfour and colleagues (2000) have suggested that one reason for this poor success rate may be that the neurobiology underpinning tobacco dependence is more complex than currently appreciated, and that “a more complete understanding of the neural mechanisms involved will facilitate the introduction of improved therapeutic approaches”.

125
There is a plethora of evidence that implicates dopamine systems in the positive reinforcing and rewarding effects of drugs (Wise 1988, Robinson and Berridge, 1993). Di Chiara and Imperato (1988) demonstrated that drugs abused by humans increase dopamine neurotransmission in rats. It has been demonstrated that animals will work for injections of drugs directly into appropriate parts of the mesotelencephalic dopamine system (Wise & Hoffman, 1992). Since Wise concluded that dopamine mediates positive reinforcement (Wise 1988) it is likely that dopamine is the main mediator of the urge to smoke reflected by Tiffany and Drobes (1991) QSU factor 1. However, when considering nicotine addiction, what we are really considering is addiction to smoking. As a result, substances other than nicotine may be implicated in the habit of cigarette smoking. For example, smoking is known to inhibit monoamine oxidase (MAO) A and B. MAO is an enzyme that breaks down catecholamine neurotransmitters. As a result MAO inhibition increases dopamine levels in the brain. Indeed, it is this elevation in dopamine levels resulting from MAO inhibition that is utilised by antidepressants such as phenelzine. It was suggested in section 8.1 that repeated nicotine administration might lead to sensitisation of the dopamine secreting cells of the VTA. However, this does not take account of the influence of MAO inhibition, and the resultant increase in dopaminergic activity. One reason why smoking is such an addictive habit could be due to heightened sensitivity to its positive reinforcing effects as a result of MAO inhibition in addition to the neuropharmacological effects of nicotine. West and colleagues (2000) report that the abuse liability of nicotine replacement treatments (NRTs) is low. In addition, participants in their study did not rate these products as satisfying. These findings could well reflect the fact that NRTs do not inhibit MAO.
Rasmussen, Kallman and Helton (1997) have presented evidence from animal studies implicating 5-HT-1A receptors in the neurophysiology of nicotine withdrawal. Indeed, Baumann and Rothman (1988) have proposed that withdrawal from cocaine, may serve as a useful animal model of depression. Balfour and Ridley (2000) have suggested that chronic nicotine exposure elicits changes in hippocampal 5-HT formation and release, which are depressogenic. It is therefore possible that 5-HT is the main modulator of the urges that are reflected by Tiffany and Drobes (1991) factor 2.

This speculation over the relative roles of dopamine and 5-HT in smoking addiction should be further investigated in the future regardless of the debates over whether a dopamine-based or 5-HT based model of depression is most appropriate. In humans, it has been demonstrated that smoking is more prevalent in people who suffer from depression (Breslau et al, 1993; Covey et al, 1998). Future research should consider investigating responding to multi-dimensional craving measures after administration of dopamine and 5-HT antagonists. Do 5-HT antagonists (such as Selective Serotonin Re-uptake Inhibitors) influence factor 2, but not factor 1 scores? Does the inverse apply to dopaminergic antagonists? Such investigations using multi-dimensional craving measures may help to substantially advance our understanding of the neuropharmacology of addiction.

8.6 Evaluation and extension of Tiffany’s (1990) cognitive automatic theory

Tiffany’s (1990) cognitive model of drug urges rejects the assumption that craving represents the central motivational process responsible for drug use behaviour, and instead suggests that drug-use behaviour is an automatic, cognitively
effortless behaviour. However, one limitation of Tiffany's theory is that it merely provides a snapshot of drug-use behaviour in the dependent user. While this model suggests that drug-use behaviour becomes automatised as a result of repeated usage, it is vague as to precisely how a drug user becomes dependent. Tiffany's model seems to suggest that regular drug use will inevitably lead to dependence as drug use becomes automatic, yet "chippers" demonstrate that this is not necessarily the case. A fully comprehensive theory needs to account for the factors that determine who becomes a dependent user, and why such users become dependent whereas other users do not.

A major obstacle to this is that it would be extremely difficult to collect data from people who are at varying points between casual user and addicted user without employing a longitudinal study with an extremely large sample size. In addicted smokers, all aspects of drug-use behaviour become automatic in some users as envisaged by Tiffany, and barriers to the successful execution of such behaviours results in craving. The findings of chapter 6 suggests that in chippers, cigarette-related cues influence aspects of smoking related to desires and intentions to smoke, and the anticipation of pleasure from smoking. Aspects related to relief of withdrawal are unaffected by cues. What cannot be concluded from the present findings is why this should be the case. This remains a theoretical question for future research.

Tiffany's cognitive automatic theory has implications for the investigations of the cognitive effects of nicotine. If, as Tiffany's model suggests, craving is cognitively effortful, then it is likely that the reported cognitive enhancing effects of smoking (e.g. Warburton, 1992) may be due to the alleviation of withdrawal, rather
than the nootropic effects of nicotine *per se*. The findings reported in chapter 7, did not provide any evidence for the cognitive-enhancing effects of nicotine in a group of non-dependent smokers, which suggested that such effects may be due to alleviation of withdrawal. Parrott and Kaye (1999) reported that nicotine-deprived smokers reported significantly reduced pleasure, and elevated arousal, stress, hassles and uplifts, and cognitive failures compared to groups of non-smokers and non-deprived smokers. Such findings may be indirectly interpreted as evidence for Tiffany’s assertion that craving is cognitively effortful, since smoking appears to return participants back to normal cognitive levels, rather than actually improving performance.

8.7 Methodological considerations

While the methodological considerations relevant to each of the experimental chapters have been individually discussed in the respective chapters’ discussion sections, one issue relevant to all the chapters is the notion of dependence. The most widely used tests for nicotine dependence are the Fagerstöm Tolerance Questionnaire (FTQ – Fagerstöm & Schneider, 1989), and the shorter Fagerstöm Test for Nicotine Dependence (FTND – Heatherton et al, 1991). Despite studies indicating the reliability of these measures (Heatherton et al, 1991; Kozlowski et al, 1994; Pomerleau et al, 1994), other investigators have voiced concerns over the internal consistency and content validity of these questionnaires (Payne et al, 1994; Pomerleau et al, 1989; Pomerleau et al, 1990). A recent study by Etter and colleagues (1999), assessed the validity of the FTND and concluded that in populations of relatively light (approximately 12 per day) smokers, the FTND was no better a predictor of dependence than the raw number of cigarettes smoked per day. As a consequence of
such concerns over the FTND, for the purposes of this thesis it was decided to not make assumptions about participants' levels of dependence.

Given that the present thesis was concerned with testing the reliability and validity of a psychometric test of craving, and the concerns surrounding the psychometric validity of the FTND (e.g. Etter et al, 1999), it was decided not to directly refer to smokers as “dependent smokers”, in the absence of a psychometrically sound dependency measure. Instead, smokers were referred to as “regular” or (in the case of “chippers”) “non-regular smokers”. While it is accepted that this was not ideal, it can be accepted on the basis of Etter and colleagues findings, that a degree of dependency could be assumed by the fact that regular smokers smoked at least 10 cigarettes a day in the study reported in chapter 4, and at least 15 cigarettes a day in the studies reported in chapters 2, 3 and 5.

8.8 Future research directions

While the findings of the present thesis suggest that the QSU is a psychometrically valid measure of cravings for cigarettes, and that the multi-dimensional approach to the assessment of cravings and urges in all drugs of abuse should be adopted, the present thesis does not provide any direct evidence for the validity of Tiffany’s (1990) theory. Further research in this area is required. As discussed in section 1.2.4, research by Sayette and by Tiffany has provided evidence for the idea that craving is associated with the activation of non-automatic cognitive processes. Since craving is cognitively effortful, drug-related cue exposure is detrimental to performance on a cognitive task (Sayette et al., 1994; Sayette &
Hufford, 1994; Cepeda-Benito & Tiffany, 1996). What is unclear is whether or not the reverse is true; does performance on a cognitive task decrease craving? If so, such a finding would have implications for the treatment of dependent drug-users. This could be investigated by employing a cognitively demanding task such as the vigilance task used in chapter’s 5 and 7 and probe questions. However, it should be noted that presentation of a full multi-dimensional craving questionnaire would be impractical in such a study. Instead it may be more practical to present one question from each of the factors. Papadimitriou (2000) employed single item “probe” questions that corresponded to the two factors of the QSU in a pilot study that was recently undertaken at the University of Wales Swansea to investigate the effect of high or low cognitive demand versions of the RVIPT on cravings for cigarettes. The results indicated that participants in a low-cognitive demand group exhibited lower craving on a probe item corresponding to QSU factor 1 scores towards the end of the task than participants in a high-cognitive demand condition. There were methodological shortcomings with this study, however, that included small sample sizes, an abstinence period of only two hours, and participants were only required to perform the RVIPT for 10 minutes. Nevertheless, the results provide preliminary support for Tiffany’s theory that cravings for cigarettes are cognitively demanding, conscious, processes. The latter study should be replicated with larger sample sizes and longer periods of abstinence and RVIPT performance.

Further validation of Tiffany’s (1990) model may be obtained by examining the somatovisceral responses (problem solving and support physiology), which Tiffany suggested are activated when automatic drug-use behaviour is impeded (see
Are such physiological changes measurable, and can they be correlated to overt behaviours and verbal reports? Future research should consider these questions.

In their recent meta-analysis of cue-reactivity studies, Carter and Tiffany (1999) concluded that, compared to neutral cues, exposure to drug-related cues elevated subjective reports of craving for a variety of other substances of abuse including alcohol, heroin and cocaine, in dependent users. However, none of these investigations used multi-dimensional measures of craving. Indeed, the findings presented in chapters 3 and 4, are amongst the first to demonstrate that exposure to cues elevates craving in regular smokers. Tiffany and colleagues (2000) recently used the QSU to investigate the effects of transdermal nicotine patches on abstinence and cue-induced cigarette cravings. Although these authors reported that abstinence and cue-exposure increased craving, and that nicotine patches attenuated abstinence-induced, but not cue-induced craving, these authors utilised a brief version of the QSU and did not report factor 1 and factor 2 scores. Thus, further research is required to determine if exposure to drug-related cues has more influence than brief periods of abstinence on multi-factorial measures of negative reinforcement-induced craving in dependent users of cigarettes, and other substances of abuse.

Since there is evidence suggesting that nicotine acts on the neural pathways implicated in depression (Balfour & Ridley, 2000), by implication, it is possible that anti-depressant drugs may be useful in the treatment of the symptoms associated with cigarette withdrawal. Further to the suggestions made in section 8.4, therefore, another potentially significant line of research would be to investigate the effects of chronic administration of antidepressants on responding to multi-dimensional craving.
measures. Selective Serotonin Re-uptake Inhibitors (SSRIs) have been demonstrated to reduce smoking rates in depressed patients, but to have little effect on normal smokers (Aubin et al, 1996; Cornelius et al, 1997). Balfour and Ridley (2000) have suggested that these observations support the hypothesis that depressive disorders increase tobacco dependence, and that treatment of depression diminishes the desire to smoke. Further, Aubin and colleagues (1996) suggest that drugs that increase the availability of 5-HT in the brain may be more efficacious in the treatment of tobacco dependence in normal smokers, if treatment begins several weeks prior to smoking cessation. Buproprion (Zyban™) is a new aid to smoking cessation approved for use in the USA by the FDA in May 1997. Buproprion was originally marketed as an anti-depressant. Clinical trials have suggested a significantly improved abstinence rate in smokers wishing to give up, who used Buproprion compared to traditional nicotine replacement therapies, and even greater abstinence rates when the 2 therapies were combined (Glaxo Wellcome, 1997). Although the pharmacology of Buproprion is not well understood, it is believed to be a weak blocker of 5-HT, noradrenaline and dopamine (Litten & Allen, 1999). However, since it is not a nicotine replacement, it is almost certainly working by reducing cravings or diminishing the reinforcing effects of nicotine. Future studies could utilise the QSU to assess the effects of Zyban, and other anti-depressant compounds on subjective craving, and to investigate whether or not it has differential effects on factor 1 and factor 2.

A further implication of the speculative suggestion made in section 8.4 is that the key to difference between “chippers” and dependent smokers may lie in the neurobiology of the serotonergic system. Future studies should assess the differences
between "chippers" and dependent smokers to traits known to be reflective of serotonergic functioning such as impulsivity and depression.

Finally, future studies should concentrate on assessing how drug use behaviour becomes automated and the various pathways to dependence. Tiffany’s (1990) merely provides a snapshot, and as suggested in section 8.5, longitudinal studies with large sample sizes, are needed to investigate the different pathways that can result in dependence or otherwise. Such an understanding may help to explain relationships between craving and relapse. Future studies could assess which components of craving are most influenced by internal and external cues at different stages of the pathways from first time user to dependent user or chipper.


References


References


References


References


142


References


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References


References


References


References


151


References


QUESTIONNAIRE OF CIGARETTE SMOKING

First, we need to get some information about you and your experiences with cigarette smoking.

Subject number:............................
Time:..............................................

1) How many cigarettes a day do you smoke? _____________________________

2) What brand do you smoke? __________________________________________

3) Have you ever used nicotine gum Yes □ No □ or patches? Yes □ No □

4) Do you inhale? (Please tick one) Always □ Sometimes □ Never □

5) Do you smoke more during the morning than the rest of the day? Yes □ No □

6) How soon after you wake up do you smoke your first cigarette?__________

7) Of all the cigarettes you smoke in a day, which would you most hate to give up?__________________________________________________________

8) Do you find it difficult to refrain from smoking in places where it is forbidden, e.g. in church, at the library, cinema etc.? Yes □ No □

9) Do you smoke if you are so ill that you are in bed most of the day? Yes □ No □

10) How long ago did you smoke your last cigarette (Not including the cigarette you are smoking now)? _______ Hours _______ Mins.

11) What time did you get up today? _______________________________________

12) How old were you when you smoked your first cigarette? __________ Years

13) For how long have you regularly smoked cigarettes?_________________

PTO
14) Have you ever tried to give up smoking? Yes □ No □
   If your answer to question 14 was “No”, please go to question 18. If your answer was “Yes”, please also answer 15, 16 and 17.

15) How many times have you tried giving up smoking? _____________________

16) What is the longest period of time you have been able to give up for?
   _____ Years _____ Months

17) Have you attempted to give up smoking within the last 6 months?
   Yes □ No □

18) Which of the following two sentences best describes what you mean by “craving for a cigarette”? (Please tick one)
   □ A craving for a cigarette is only a strong urge or desire to smoke a cigarette.
   or □ A craving for a cigarette is any urge or desire to smoke a cigarette, even a weak one.

19) On a scale from 0 to 10 where 0 is “not at all”, and 10 is “the most imaginable”, how much do you crave for a cigarette after you have gone at least four hours without one? __________

20) If you tried to give up smoking now, how confident are you that you could go for more than a month without smoking? (Please tick one)
   Not confident □
   A little confident □
   Moderately confident □
   Very confident □
   Extremely confident □
SUBJECT INSTRUCTIONS

• Finish your last cigarette 4 hours before your arranged testing time, and then do not smoke until after the testing session. A breath Carbon Monoxide reading will be taken just before testing to ensure that no cigarettes have been smoked within the previous 4 hours.

• Now complete the 2 questionnaires.

• Half an hour after you finish your last cigarette chew the first piece of gum in the following way:

The gum you have been given is not regular gum and is not chewed in the regular way.

1) Chew the gum several times very slowly.
2) Stop chewing when you notice a peppery taste, or a slight tingling in your mouth.
3) “Park” the gum between your cheek and gum, and leave it there.
4) When the peppery taste or tingle is almost gone, start to chew a few times slowly again. When the peppery taste or tingle returns, stop again.
5) Park the gum again (in a different place in your mouth).
6) Repeat steps 1 to 5 until half an hour has elapsed since you began chewing that piece.
7) Carefully discard the gum.

<table>
<thead>
<tr>
<th>Chew each of the four pieces in this way at half hourly intervals:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finish cig</td>
</tr>
<tr>
<td>Gum1</td>
</tr>
<tr>
<td>0---------30------60-------90-----120-----150-----180------210--240 (Minutes)</td>
</tr>
</tbody>
</table>

i.e. You don’t chew for 1/2 hour, then chew for 1/2 hour, then don’t chew for half hour etc until your test time.

Do not continue chewing the gum if you feel nauseas, sick, develop a headache, or feel unwilling to continue in any way.

You may carry on with your normal day to day activities whilst you chew, but please only drink during the half hour periods when you are not chewing. Please do not eat during your 4 hours abstinence.
MOOD FORM

Please circle the number below each mood listed that best describes how much you are experiencing that mood right now.

<table>
<thead>
<tr>
<th>Mood</th>
<th>Not at all</th>
<th>Very slightly</th>
<th>Somewhat</th>
<th>Moderate amount</th>
<th>Much</th>
<th>Very much</th>
<th>Extremely much</th>
</tr>
</thead>
<tbody>
<tr>
<td>Happy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Depressed/blue</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Joyful</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Unhappy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Pleased</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Enjoyment/fun</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Frustrated</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Worried/anxious</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Angry/hostile</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>
QSU INSTRUCTIONS
(Computer Version)

"Indicate the extent to which you agree or disagree with each of the following statements by moving the cursor, across, along each line between STRONGLY DISAGREE and STRONGLY AGREE, by pressing the LEFT and RIGHT cursor keys. Press RETURN when the cursor is in the desired place. The closer you place the cursor to one end or the other indicates the strength of your agreement or disagreement. We are interested in how you are thinking or feeling RIGHT NOW as you are completing the questions. There are no right or wrong answers. If you feel that you have made a mistake, press the DELETE button and go back to the previous questions. Press return to continue."
Indicate the extent to which you agree or disagree with each of the following statements by placing a single tick along each line between STRONGLY DISAGREE and STRONGLY AGREE. The closer you place your tick to one and or the other indicates the strength of your agreement or disagreement. We are interested in how you are thinking or feeling **right now** as you are filling out the questionnaire.

<table>
<thead>
<tr>
<th>Statement</th>
<th>Tick Placement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Smoking would make me feel very good right now.</td>
<td>![Strongly Agree]</td>
</tr>
<tr>
<td>2. I would be less irritable now if I could smoke.</td>
<td>![Strongly Agree]</td>
</tr>
<tr>
<td>3. Nothing would be better than smoking a cigarette right now.</td>
<td>![Strongly Agree]</td>
</tr>
<tr>
<td>4. I am not missing smoking right now.</td>
<td>![Strongly Agree]</td>
</tr>
<tr>
<td>5. I will smoke as soon as I get the chance.</td>
<td>![Strongly Agree]</td>
</tr>
<tr>
<td>6. I don't want to smoke now.</td>
<td>![Strongly Agree]</td>
</tr>
<tr>
<td>7. Smoking would make me less depressed.</td>
<td>![Strongly Agree]</td>
</tr>
<tr>
<td>8. Smoking would not help me calm down.</td>
<td>![Strongly Agree]</td>
</tr>
</tbody>
</table>
9. If I were offered a cigarette, I would smoke it immediately.  
STRONGLY DISAGREE  ___________  _______  _______  _______  _______  STRONGLY AGREE

10. Starting now, I could go without smoking for a long time.  
STRONGLY DISAGREE  ___________  _______  _______  _______  _______  STRONGLY AGREE

11. Smoking a cigarette would not be pleasant.  
STRONGLY DISAGREE  ___________  _______  _______  _______  _______  STRONGLY AGREE

12. If I were smoking this minute, I would feel less bored.  
STRONGLY DISAGREE  ___________  _______  _______  _______  _______  STRONGLY AGREE

13. All I want right now is a cigarette.  
STRONGLY DISAGREE  ___________  _______  _______  _______  _______  STRONGLY AGREE

14. Smoking right now would make me feel less tired.  
STRONGLY DISAGREE  ___________  _______  _______  _______  _______  STRONGLY AGREE

15. Smoking would make me happier now.  
STRONGLY DISAGREE  ___________  _______  _______  _______  _______  STRONGLY AGREE

16. Even if it were possible, I probably wouldn’t smoke now.  
STRONGLY DISAGREE  ___________  _______  _______  _______  _______  STRONGLY AGREE

17. I have no desire for a cigarette right now.  
STRONGLY DISAGREE  ___________  _______  _______  _______  _______  STRONGLY AGREE
18. My desire to smoke seems overpowering.
STRONGLY DISAGREE [ ] [ ] [ ] [ ] [ ] STRONGLY AGREE

19. Smoking now would make things seem just perfect.
STRONGLY DISAGREE [ ] [ ] [ ] [ ] [ ] STRONGLY AGREE

20. I crave a cigarette right now.
STRONGLY DISAGREE [ ] [ ] [ ] [ ] [ ] STRONGLY AGREE

21. I would not enjoy a cigarette right now.
STRONGLY DISAGREE [ ] [ ] [ ] [ ] [ ] STRONGLY AGREE

22. A cigarette would not taste good right now.
STRONGLY DISAGREE [ ] [ ] [ ] [ ] [ ] STRONGLY AGREE

23. I have an urge for a cigarette.
STRONGLY DISAGREE [ ] [ ] [ ] [ ] [ ] STRONGLY AGREE

24. I could control things better right now if I could smoke.
STRONGLY DISAGREE [ ] [ ] [ ] [ ] [ ] STRONGLY AGREE

25. I am going to smoke as soon as possible.
STRONGLY DISAGREE [ ] [ ] [ ] [ ] [ ] STRONGLY AGREE

26. I would not feel better physically if I were smoking.
STRONGLY DISAGREE [ ] [ ] [ ] [ ] [ ] STRONGLY AGREE

27. A cigarette would not be very satisfying now.
STRONGLY DISAGREE [ ] [ ] [ ] [ ] [ ] STRONGLY AGREE
28. If I had a lit cigarette in my hand I probably wouldn't smoke it.

STRONGLY DISAGREE  ☐  ☐  ☐  ☐  ☐  STRONGLY AGREE

29. If I were smoking now I could think more clearly.

STRONGLY DISAGREE  ☐  ☐  ☐  ☐  ☐  STRONGLY AGREE

30. I would do almost anything for a cigarette.

STRONGLY DISAGREE  ☐  ☐  ☐  ☐  ☐  STRONGLY AGREE

31. I need to smoke now.

STRONGLY DISAGREE  ☐  ☐  ☐  ☐  ☐  STRONGLY AGREE

32. Right now, I am not making plans to smoke.

STRONGLY DISAGREE  ☐  ☐  ☐  ☐  ☐  STRONGLY AGREE

3.7

4.1
SELF-EVALUATION QUESTIONNAIRE

Developed by Charles D. Spielberger
in collaboration with
R. L. Gorsuch, R. Lushene, P. R. Vagg, and G. A. Jacobs

STAI Form Y-1

Date __________ S ______

____ Sex: M _____ F _____

ONS: A number of statements which people have used to
themselves are given below. Read each statement and then
t the appropriate circle to the right of the statement to indi-
you feel right now, that is, at this moment. There are no right
answers. Do not spend too much time on any one statement
answer which seems to describe your present feelings best.

1. calm ................................................................................................................................. 1
2. insecure ............................................................................................................................ 3
3. tense .................................................................................................................................. 2
4. strained ............................................................................................................................. 1
5. at ease ............................................................................................................................... 0
6. upset .................................................................................................................................. 0
7. presently worrying over possible misfortunes ............................................................. 3
8. satisfied ............................................................................................................................... 3
9. frightened .......................................................................................................................... 4
10. comfortable .................................................................................................................... 1
11. self-confident .................................................................................................................. 1
12. nervous ............................................................................................................................ 4
13. jittery .................................................................................................................................. 4
14. indecisive ........................................................................................................................... 4
15. relaxed ................................................................................................................................ 4
16. content ................................................................................................................................ 4
17. worried ............................................................................................................................. 4
18. confused ............................................................................................................................ 4
19. steady .................................................................................................................................. 4
20. pleasant ............................................................................................................................. 4

Consulting Psychologists Press, Inc.
3803 E. Bayshore Road • Palo Alto, CA 94303
# SELF-EVALUATION QUESTIONNAIRE

**STAI Form Y-2**

**Name** ___________________________  **Date** ___________________________

**DIRECTIONS**: A number of statements which people have used to describe themselves are given below. Read each statement and then blacken in the appropriate circle to the right of the statement to indicate how you generally feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you generally feel.

<table>
<thead>
<tr>
<th>Statement</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>21. I feel pleasant</td>
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<tr>
<td>22. I feel nervous and restless</td>
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<tr>
<td>23. I feel satisfied with myself</td>
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<tr>
<td>24. I wish I could be as happy as others seem to be</td>
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<tr>
<td>25. I feel like a failure</td>
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<tr>
<td>26. I feel rested</td>
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<td></td>
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<tr>
<td>27. I am “calm, cool, and collected”</td>
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<tr>
<td>28. I feel that difficulties are piling up so that I cannot overcome them</td>
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<tr>
<td>29. I worry too much over something that really doesn’t matter</td>
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<tr>
<td>30. I am happy</td>
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<tr>
<td>31. I have disturbing thoughts</td>
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<td>32. I lack self-confidence</td>
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<tr>
<td>33. I feel secure</td>
<td></td>
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<tr>
<td>34. I make decisions easily</td>
<td></td>
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<td>35. I feel inadequate</td>
<td></td>
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<tr>
<td>36. I am content</td>
<td></td>
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<tr>
<td>37. Some unimportant thought runs through my mind and bothers me</td>
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<tr>
<td>38. I take disappointments so keenly that I can’t put them out of my mind</td>
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<tr>
<td>39. I am a steady person</td>
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<tr>
<td>40. I get in a state of tension or turmoil as I think over my recent concerns and interests</td>
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</tr>
</tbody>
</table>

*Copyright 1968, 1977 by Charles D. Spielberger. Reproduction of this test or any portion thereof in any process without written permission of the Publisher is prohibited.*
In a few minutes time, you will have the opportunity to smoke a cigarette if you wish. You must earn the puffs on the cigarette.

By pressing the spacebar you can earn puffs on a cigarette. When you hear this sound {BEEP1}, it means that you have to press the spacebar again to obtain a puff. When you hear this sound {BEEP2}, it means that you have gained one puff. I will give you a lit cigarette to smoke with a 4mm puff marked on it. You may then smoke the cigarette to that point. After your first puff you will have to work harder at gaining subsequent puffs. You may stop responding whenever you wish, and a delay in responding of 60 seconds will end the task.

Remember, you will be required to smoke the puffs that you earn. If you do not want to smoke, do not earn any puffs. Do not earn more puffs than you are prepared to smoke. You may, however, earn as many puffs as you like.

Remember, do not hit the spacebar if you do not wish to smoke. If you do wish to smoke, earn as many puffs as you are willing to smoke. This task is designed to test how much you want to smoke a cigarette. It is important that you are honest in your responses.
PR INSTRUCTIONS
(Points)

In a few minutes time, you will have the opportunity to smoke a cigarette if you wish. You must earn the puffs on the cigarette.

By pressing the spacebar you can earn points, which will represent puffs on a cigarette. When you hear this sound {BEEP1}, it means that you have to press the spacebar again to obtain a puff. When you hear this sound {BEEP2}, it means that you have gained one point. I will give you a paper clip representing one puff on a cigarette you have earned so that you can see for yourself how many you have. After your first point you will have to work harder at gaining subsequent points. You may stop responding whenever you wish, and a delay in responding of 60 seconds will end the task.

Remember, you will be required to smoke the number of puffs that you earn. If you do not want to smoke, do not earn any puffs. Do not earn more puffs than you are prepared to smoke. You may, however, earn as many puffs as you like.

Remember, do not hit the spacebar if you do not wish to smoke. If you do wish to smoke, earn as many puffs as you are willing to smoke. This task is designed to test how much you want to smoke a cigarette. It is important that you are honest in your responses.
QUESTIONNAIRE OF CIGARETTE SMOKING

First, we need some information about you and your experiences with cigarette smoking.

Subject number: ........................................
Time: .....................................................

1) How often do you smoke cigarettes? (i.e. Every Day, Every week etc.)

2) What brand do you smoke?

3) Approximately how many cigarettes do you smoke on a day when you are smoking?

4) Do you inhale? (Please tick one) Always □ Sometimes □ Never □

5) Please list in order below five situations in which you smoke. (i.e. at a pub, after a meal). Place the situation within which you most often smoke first. If you cannot think of five, complete as many as possible.

1) ____________________________________________________
2) ____________________________________________________
3) ____________________________________________________
4) ____________________________________________________
5) ____________________________________________________

6) Have you ever been a regular smoker (i.e. more than 10 a day)? Yes □ No □

If “Yes”, how many a day did you used to smoke? ____________________________
If “Yes”, how long ago did you stop smoking regularly? ______________________

7) How old were you when you smoked your first cigarette? __________________

8) Have you ever experienced a “craving” for a cigarette? Yes □ No □

9) How long ago did you smoke your last cigarette? __________________________

10) If you were told to give up smoking now, how confident are you that you could go for more than a month without smoking? (Please tick one)

   Not confident □
   A little confident □
   Moderately confident □
   Very confident □
   Extremely confident □
11) What is the longest period of time that you have gone for without a cigarette?

12) How soon after you wake up do you smoke your first cigarette on days when you are smoking?

13) What time did you get up today?

14) Of all the cigarettes you smoke in a day, which would you most hate to give up?

15) For how long have you been an occasional smoker?
SAS Factor Analysis

0001 x 'cd c:sas\';
0002 libname out '.';
0003 data QSU;
0004 infile 'comp.dat'; (or 'paper.dat')
0005 input q01 q02 q03 q04 q05 q06 q07 q08 q09 q10 q11 q12 q13 q14 q15 q16
0006 q17 q18 q19 q20 q21 q22 q23 q24 q25 q26 q27 q28 q29 q30 q31 q32;
0007 run;
0008 proc factor priors=smc mineigen=1 scree rotate=promax msa re;
0009 run;

Place ASCII data files to be analysed into the SAS directory.
You will now perform a task which will enable you to earn cigarettes. The number of cigarettes you earn will depend upon how long you are willing to do the task for. You will earn one cigarette after having performed the task for a set amount of time. The time needed to earn subsequent cigarettes will get progressively longer. THE TASK WILL END WHEN YOU TELL THE EXPERIMENTER THAT YOU NO LONGER WISH TO CONTINUE. A series of digits will appear in the middle of the screen. When either three odd, or three even numbers appear one after another, press the space bar. When you are ready to begin the task, press the return key. You should look in the middle of the screen and await the appearance of the first digit. A practice session of half a minute will occur initially.
MIQ

For each number, please indicate whether you would prefer the reward or the money. In a few minutes time you will randomly draw a number between 1 and 25. The reward you get will depend on whether you have indicated that you would prefer the money, or a cigarette, for the number that you draw.

<table>
<thead>
<tr>
<th>Number</th>
<th>Reward</th>
<th>Money</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 Cigarette □</td>
<td>£0.10 □</td>
</tr>
<tr>
<td>2</td>
<td>1 Cigarette □</td>
<td>£0.11 □</td>
</tr>
<tr>
<td>3</td>
<td>1 Cigarette □</td>
<td>£0.12 □</td>
</tr>
<tr>
<td>4</td>
<td>1 Cigarette □</td>
<td>£0.13 □</td>
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<tr>
<td>5</td>
<td>1 Cigarette □</td>
<td>£0.14 □</td>
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<tr>
<td>6</td>
<td>1 Cigarette □</td>
<td>£0.16 □</td>
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<td>7</td>
<td>1 Cigarette □</td>
<td>£0.18 □</td>
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<td>8</td>
<td>1 Cigarette □</td>
<td>£0.19 □</td>
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<tr>
<td>9</td>
<td>1 Cigarette □</td>
<td>£0.21 □</td>
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<tr>
<td>10</td>
<td>1 Cigarette □</td>
<td>£0.24 □</td>
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<td>11</td>
<td>1 Cigarette □</td>
<td>£0.26 □</td>
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<td>21</td>
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<td>22</td>
<td>1 Cigarette □</td>
<td>£0.75 □</td>
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<td>23</td>
<td>1 Cigarette □</td>
<td>£0.83 □</td>
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<td>24</td>
<td>1 Cigarette □</td>
<td>£0.91 □</td>
</tr>
<tr>
<td>25</td>
<td>1 Cigarette □</td>
<td>£1.00 □</td>
</tr>
</tbody>
</table>

Participant Number ______________________

Number Drawn ______________________
Immediate Word Recall
Subject Number ______

Delayed Word Recall

DO NOT SMOK

DO NOT CONDUCT PHYSICAL EXERCISE.

You should remove your patch once:

YOU BEGIN TO FEEL IRRITATION OR YOU NOTICE THE AREA OF THE PASTE IS REDDISH.

If you do remove your patch, the researcher will examine the area of skin.

Please return for a brief period today. TODAY at 4:30 pm in ROOM 908.

You should also follow the "Patch Study" instruction on the 9th floor.
INSTRUCTIONS

Whilst wearing your patch:

**DO NOT SMOKE**
**DO NOT DRINK CAFFEINE OR ALCOHOL**
**DO NOT ENGAGE IN PHYSICAL EXERCISE**

You should remove your patch only if:

**YOU BEGIN TO FEEL UNWELL**
**YOU BEGIN TO EXPERIENCE SKIN IRRITATION (N.B. a mild sensation on the arm is not unusual).**

If you do remove your patch, you should contact the experimenter ASAP.

Please return for a brief period of testing TODAY at 3pm in ROOM 931 9th floor science tower. Follow signs for “Patch study” from the 9th floor lifts.
DECLARATION OF INFORMED CONSENT

1) I have been informed that to participate in this study I must be a non-regular smoker of at least 1 years standing. I confirm that I do not smoke daily as a matter of habit.

2) I have been informed that participation in this study will involve me wearing a patch for 6 hours. I have been informed that the patch may be an active nicotine patch or a placebo patch and that I will not be informed which I am wearing.

3) I have been informed that there are no known long-term risks involved in my participation in this study.

4) I understand that there are no disguised procedures and that everything can be taken at face value.

5) I understand that I should only take part in the experiment if I am presently healthy and have no long-term medical problems. If I was in any doubt I discussed this matter with the experimenter. I have completed and signed the “health risk assessment form” and understand that I must not participate in the study if I have answered “YES” to any of the questions (with the exception of the question “Do you smoke?”).

6) I have been informed that the experimenter will answer my questions regarding its purpose when the study has finished.

7) I have been informed of the potential side effects. If any occur, or I suspect that they may be incurring, I understand that I should immediately discontinue from the study and inform the experimenter.

8) I understand that I may discontinue from the study at any point and for any reason.

9) I know of no reason why I should not take part in this study.

10) I understand that I will receive payment of £10 upon completion of my participation in the experiment.

11) I understand that whilst wearing the “nicotine patch”, I MUST NOT engage in vigorous exercise, smoke or consume alcohol or caffeine containing drinks.

SIGNATURE ______________________ DATE / / ADDRESS
______________________________
______________________________
______________________________
HEALTH RISK ASSESSMENT FORM

1) Do you suffer or have you suffered from any of the following? YES □ NO □

Angina
Myocardial infarction (heart attack)
Cardiac arrhythmias (irregular heart beat)
Systemic hypotension
Peripheral vascular disease
Diabetes
Hyperthyroidism
Phaeochromocytoma
Diseases of the skin (i.e. psoriasis, eczema)

2) Are you currently taking prescription medication (EXCLUDING the female oral contraceptive pill)? YES □ NO □

3) Do you suffer from dizzy spells, frequent headaches and nausea? YES □ NO □

4) (Females only) Are you currently pregnant? YES □ NO □

5) Do you know of any medical reason why you should not take part in this study? YES □ NO □
   If “YES”, please state........................................................................................................

6) Do you smoke cigarettes? YES □ NO □
   If “YES”, how many_________ per ____________ (day, week, month)?

7) Do you smoke every day? YES □ NO □

Signed ___________________________   Date ___________________________

Sub No. _______
DECLARATION OF INFORMED CONSENT

1) I have been informed that to participate in this study I must be a non-regular smoker of at least 1 year standing. I confirm that I do not smoke daily as a matter of habit.

2) I have been informed that participation in this study may involve me smoking a cigarette.

3) I have been informed that there are no known risks involved in my participation in this study.

4) I understand that there are no disguised procedures and that everything can be taken at face value.

5) I understand that I should only take part in the experiment if I am presently healthy and have no long-term medical problems. If I was in any doubt I discussed this matter with the experimenter. I have completed and signed the “health risk assessment form” and understand that I must not participate in the study if I have answered “YES” to any of the questions (with the exception of the question “Do you smoke?”).

6) I have been informed that the experimenter will answer my questions regarding its purpose when the study has finished.

7) Although I understand that there is no reason to expect side effects, if any occur, or I suspect that they may be incurring, that I should immediately discontinue from the study and inform the experimenter.

8) I understand that I may discontinue from the study at any point and for any reason.

9) I know of no reason why I should not take part in this study.

10) I understand that I will receive payment of 30 minutes credit upon completion of my participation in the experiment, or £2 if a non-psychology student.

SIGNATURE________________________ DATE__/__/____
ADDRESS__________________________
______________________________
HEALTH RISK ASSESSMENT FORM
The information on this form will be held in the strictest confidence.

Do you suffer from asthma? YES □ NO □

Do you suffer from emphysema? YES □ NO □

Do you suffer from bronchitis? YES □ NO □

Do you suffer from angina? YES □ NO □

Do you suffer from high blood pressure? YES □ NO □

Do you suffer from low blood pressure? YES □ NO □

Do you suffer from dizzy spells? YES □ NO □

Do you frequently faint or pass out? YES □ NO □

Do you suffer from any heart conditions? YES □ NO □

Are you currently taking any prescription drugs? YES □ NO □ (excluding oral contraceptive pill)

Are you diabetic? YES □ NO □

Are you currently pregnant? YES □ NO □

Do you suffer from epilepsy? YES □ NO □

Do you suffer from anxiety or panic attacks? YES □ NO □

Have you ever had pneumonia or any other disease of lungs or lower respiratory tract? YES □ NO □

Have you ever had viral encephalitis? YES □ NO □

Have you ever had meningitis? YES □ NO □

Do you smoke? YES □ NO □

If "YES", Which Brand? ________________

How many _________ per _________ (day / week / month)?

Signed ___________________________ Date _____ / _____ / _____

Subject # _____
RVIPT On-screen instructions

A series of digits will appear in the middle of the screen. When either three odd, or three even numbers appear one after another, press the space bar. When you are ready to begin the task, press the return key. A warning sound will be heard after a few seconds and you should look in the middle of the screen and await the appearance of the first digit. A practise session of half a minute will occur initially, remember you should press the SPACE BAR when three odd or even numbers appear in a row.
SIMPLE REACTION TIME

1. The procedure will be the same as the practice session except only one lamp will light up.

2. Only lamp 4 will light up for the next 20 trials so you need only look at this one lamp.

3. To proceed, press the Return key, the computer screen will go blank. The test will begin when you press the home key.
TWO LAMP REACTION TIME

1. In the next stage, one of two lamps will light up.

2. Either lamp 4 or 5 will light up for the next 20 trials.
   You need only look at these two lamps.

3. To start, press the Return key, the computer screen will go blank.
   The test will begin when you press the home key.
FOUR LAMP REACTION TIME

1. In the next sequence, one of four lamps will light up.

2. One of lamps 3, 4, 5 or 6 will light up for the next 20 trials. You need only look at these four lamps.

3. To start, press the Return key. The test will begin when you press the home key.
EIGHT LAMP REACTION TIME

1. In this sequence, one of eight lamps will light up.

2. You need to examine all the lamps on the console, of which one will light up at each trial.

3. To start, press the Return key. The test will begin when you place your finger on the home key.
REACTION TIME MEASUREMENT

PRACTICE SESSION

There will be 20 practice trials, each taking the following sequence:

1. Place the forefinger of your preferred hand on the home key (in the middle of the bottom of the black console).

2. A warning sound will be heard.

3. One of the eight lamps will light up.

4. When you see a lamp is lit, move your finger from the home key to the button underneath that lamp AS QUICKLY AS POSSIBLE.

5. When you are ready for the next trial, place your finger on the home key and the sequence will be repeated.

6. When you understand these instructions press the Return key and the computer screen will go blank. The test will begin when you press the home key.

7. At the end of the practice session you will hear five beeps - look then at the computer screen for new instructions.