Cannabis Cue Exposure: A Pilot Study About Extinction Contexts

Ellise M. Barnier

Macquarie University

This thesis is submitted in partial fulfilment of the requirements for the Masters of Research degree, Macquarie University, 9th October 2015

Table of Contents

Acknowledgements....8

Declaration of Originality....9

Abstract....10

1. Introduction....11

1.1. Cue Reactivity....12

1.2. Conditioning Models of Addiction....13

1.3. Psychobiological Model of Addiction....15

1.4. Cue Reactivity and Relapse....17

1.5. Extinction and Renewal....18

1.6. Cue Exposure Therapy....20

1.7. Renewal in Drug Users Following Cue Exposure Therapy....22

1.8. Distress Tolerance....29

1.9. The Present Study....30

2. Methods....31

2.1. Participants....32

2.2. Design Summary....32

2.3. Materials and Apparatus....33

2.3.1. Demographic and Substance Use....33

2.3.2. Psychological Distress....34

2.3.3. Marijuana Consequences....34

2.3.4. Nicotine Dependence....34

2.3.5. Marijuana Motives....34

2.3.6. Cannabis Use Disorder....35

2.3.7. Cannabis Use....35

2.3.8. Cannabis Withdrawal....36
2.3.9. Cannabis Use Patterns....36
2.3.10. Quit Session....36
2.3.11. Physiological Recording....37
2.3.12. Subjective Units of Craving and Tolerance....37
2.3.13. Urinalysis....38
2.3.14. Audio Track and Cues....38
2.3.15. Subjective Report of Distress Tolerance....39
2.3.16. Behavioural Measure of Distress Tolerance....40
2.3.17. Marijuana Craving Questionnaire....40
2.3.18. Study Context....41
2.3.19. Lounge Room....41
2.3.20. Therapist Office....41
2.4. Procedure....42
2.4.1. Recruitment....42
2.4.2. Eligibility Interview (Session 0)....43
2.4.3. Pre-Exposure Assessment (Session 1) 44
2.4.4. Cue-Exposure Sessions (Sessions 2-3) 46
2.4.5. Post-Exposure Assessment (Session 4) 47
2.4.6. Intensive Participation....48
2.4.7. Payment for Participation....48
2.4.8. Confirmation of Abstinence....49
3. Results....49
3.1 Recruitment and Participant Flow....49
3.2. Demographic and Clinical Characteristics....51

3.3. Cue Reactivity, Cravings and Physiological Responses.....54

3.4. Intolerance for Distress.....59

3.5. Contexts and Cue Information.....65

4. Discussion.....67

4.1. Cue Exposure and Cravings.....67

4.1.1. Craving and Cue Reactivity in the Same Context.....67

4.1.2. Renewal of Craving and Cue Reactivity.....69

4.2. Physiological Responses.....70

4.2.1. Reactivity From Neutral to Cannabis Cues.....71

4.2.2. Physiological Responding Following Cue Exposure.....72

4.3. Intolerance.....73

4.3.1. Self-Reported Intolerance of Cravings.....73

4.3.2 Intolerance of Distress.....74

4.4. Strengths, Limitations, and Future Directions.....76

4.5. Conclusions.....78

5. References.....79

6. Appendix.....97

Appendix A – Eligibility Checklist.....97

Appendix B – Phone Screen.....98

Appendix C – Demographic Questions.....105

Appendix D – K-10.....107

Appendix E – The Brief Marijuana Consequences Questionnaire 108

Appendix F – The Fagerstrom Test for Nicotine Dependence.....110

Appendix G – Marijuana Motives Measure.....111

Appendix H – The Structured Clinical Interview for DSM Disorders 112

Appendix I – Timeline Followback Interview.....116

Appendix J – Subjective Units of Cannabis Withdrawal 117

Appendix K – Contextual Cue Assessment.....118

Appendix L – Quit Session.....122

Appendix M – Electrode Placement in Einthovens Triangle.....124

Appendix N – Skin Conductance Electrode Placement.....125

Appendix O – Subjective Units of Craving and Tolerance.....126

Appendix P – Subjective Units of Craving and Tolerance Progression Form.....127

Appendix Q – Audio Script.....128

Appendix R – Neutral Beach Cue.....130

Appendix S – Cannabis Cue.....131

Appendix T – Distress Tolerance Scale.....132

Appendix U – Mirror Tracing Persistence Task 133

Appendix V – Marijuana Craving Questionnaire.....134

Appendix W – Study Context Questionnaire.....136

Appendix X – Lounge Room.....138

Appendix Y – Therapy Room.....139

Appendix Z – Advertisements.....140

Appendix AA – Consultation Room.....147

Appendix AB – Information and Consent Form.....148

Appendix AC – Cue-Exposure Scene Description Script.....167

Appendix AD – Debriefing 168

List of Tables

Table 1 – Demographic Information and Clinical Characteristics within the AAA and ABA Conditions.....52

Table 2 – Overall Withdrawal Experienced During the Study.....54

Table 3 – Mean Cravings in the AAA and ABA Conditions.....55

Table 4 – Mean Intolerance in the AAA and ABA Conditions 60

Table 5 – Study Context Questionnaire.....66

List of Figures

Figure 1 – The progression of the cue-reactivity paradigm during Session 1 and Session 4...45

Figure 2 – CONSORT Flow chart. This figure illustrates the flow of participants through the study.....50

Figure 3 – How often participants encountered their personal paraphernalia in the last month when not smoking cannabis across all conditions.....53

Figure 4 – Average self-reported cravings across all sessions for each condition.....57

Figure 5 – Mean difference in self-reported cravings between neutral and cannabis cues from pre-exposure in Session 1 to post-exposure Session 4.....58

Figure 6 – Mean difference in the EDA between neutral and cannabis cues from pre-exposure in Session 1 to post-exposure Session 4. 58

Figure 7 – Mean difference in HR between neutral and cannabis cues from pre-exposure in Session 1 to post-exposure Session 4.....59

Figure 8 – Average self-reported intolerance to cravings across all sessions; lower scores indicate greater tolerance of cravings.....62

Figure 9 – Mean difference in self-reported intolerability between neutral and cannabis cues from pre-exposure in Session 1 to post-exposure Session 63

Figure 10 – Total average distress tolerance scores from the Distress Tolerance Scale in Session 1 and Session 4 for all conditions.....63

Figure 11 – Average latency to task termination on the MTPT-C at Session 1 and Session 4 for each condition.....64

Figure 12 – Average errors committed on the MTPT-C at Session 1 and Session 4 for each condition.....65

Acknowledgements

I would like to express deep thanks and gratitude to my mentor Dr Melissa Norberg. I sincerely appreciate her constructive guidance, scholarly advice and valuable input during the development of this research. I am thankful for the continued support and dedication she shows to her students.

I would like to express gratitude to associate investigators Dr Gabrielle Weidmann, Associate Professor Jennifer Cornish, Professor Ron Rapee, Professor and Carl Lejuez. I would also like to express gratitude to research assistant Kara Chakerian whose willingness to assist in data collection was greatly appreciated. Additionally, I would like to express thanks to Cathy Chen who assisted in the recruitment process. Finally, to my family and friends who provided me support throughout the entire process.

Declaration of Originality

The works found within this thesis have not been submitted for a higher degree to any other university or institution. All empirical research contained within this thesis was approved by the Human Research Ethics Committee at Macquarie University. Reference number: HREC 5201300865 (Protocol number: 8)

Signature:  Date: 9th October 2015

Abstract

Cue-exposure therapy can reduce cravings elicited by conditioned cues such as drug paraphernalia. However, relapse may still occur due to transient reductions in cravings. Cue-exposure therapy occurs in a therapeutic setting, while drug use occurs outside of this setting. Thus, cravings may return due to a change in context since extinction memories are best retrieved in the extinction context. In addition, increases in distress tolerance that may occur during cue-exposure may renew following a context change. The aim of this pilot study is to investigate renewal of cravings towards cannabis paraphernalia and distress intolerance. Participants (N=15) who smoke cannabis in their lounge room were randomly allocated to one of two conditions. In the AAA condition, participants underwent pre-exposure assessment, cue-exposure sessions, and post-exposure assessment in a lounge room. In the ABA condition, participants underwent the pre and post-exposure assessment in the lounge room, but cue exposure in a therapist office. Additionally, participants completed the study intensively or daily. Preliminary findings suggest that daily cue exposure in the same context is the most effective in reducing cravings and increasing tolerance. Furthermore, renewal of self-reported cravings may occur due to a context change following cue exposure. This pilot study provides methods for improving future research and treatment for cannabis use disorder.

Cannabis Cue Exposure: A Pilot Study About Extinction Contexts

Cannabis is the most commonly used illicit drug in Australia with approximately 35% of the population having tried it (Australian Institute of Health and Welfare, 2013). Approximately 6% of Australians will experience cannabis use disorder in their lifetime and 36% of these individuals will seek treatment (Teesson et al., 2012). Cognitive behavioural therapy has demonstrated limited efficacy in the treatment of cannabis use disorder as 85% of individuals relapse within 6 months (Magill & Ray, 2009; Marijuana Treatment Project Research Group, 2004). High relapse rates highlights that further investigation into factors driving relapse is required. The factors that contribute to relapse in cannabis users are not entirely known, but research has indicated that cravings could be one such factor (Fatseas et al., 2015; Ramo, Anderson, Tate, & Brown, 2005).

Cravings are believed to play a central role in substance use disorders (Tiffany & Wray, 2011). Cravings can be thought of as physiological and subjective reactions experienced in contexts where drug use occurs and when drug-related stimuli are encountered (phasic), as well as part of withdrawal (tonic; Drummond, 2000; Gray, LaRowe, Watson, & Carpenter, 2011). Craving is often a distressing experience for drug users and relapse may occur from a desire to escape an unpleasant experience (Tiffany & Wray, 2011). While drug craving does not always predict relapse, research linking the two phenomena together warrants research aimed at reducing cravings and/or increasing individuals ability to tolerate such cravings (Tiffany & Wray, 2011; Tiffany, Friedman, Greenfield, Hasin, & Jackson, 2011). Cannabis withdrawal might be effectively managed through pharmaceutical or psychological interventions (Budney, Moore, Vandrey, & Hughes, 2003; Drummond, 2000; O'Brien, 2005). Psychological interventions, however, may be most helpful for targeting the short-lived phasic cravings throughout a person’s lifetime (Drummond, 2000; Tiffany &

Wray, 2011). Since phasic cravings occur in response to contextual and drug related stimuli, psychological interventions may benefit from targeting this reactivity to stimuli.

1.1 Cue reactivity

Cue reactivity encompasses a multitude of reactions that occur in response to drug related cues and has been observed in many drug using populations (Carter & Tiffany, 1999; Drummond, 2000; Henry, Kaye, Bryan, Hutchison, & Ito, 2014; Martin, LaRowe, & Malcolm, 2010; Tiffany, 1999). Cue reactivity to a drug related cues can be symbolic-expressive (e.g. cravings, pleasure, and anxiety), Physiological, (e.g. drug-like or withdrawal-like symptoms), or behavioural (drug seeking or drug using; Drummond, 2000). Common symbolic expressive measures of cue reactivity consist of assessing self-reported urges or cravings (Carter & Tiffany, 1999; Martin et al., 2010). Physiological assessment often includes measures of heart rate (HR), skin conductance, and skin temperature as they are less subjected to bias from the individual as they are controlled by the automatic nervous system (Carter & Tiffany, 1999; Drobes & Tiffany, 1997; Tiffany, 1990).

Cue-reactivity paradigms typically expose individuals to cues associated with drug taking, and neutral cues unrelated to drug taking (Carter & Tiffany, 1999; Henry et al., 2014; Tiffany & Wray, 2011). Cannabis users have reported significantly greater cravings in response to cannabis cues than to neutral cues, and expectedly, cannabis cues elicit greater cravings in cannabis users when compared to healthy controls (Gray, LaRowe, & Upadhyaya, 2008; Haughey, Marshall, Schacht, Louis, & Hutchison, 2008; Henry et al., 2014). Cravings for cannabis have been observed to increase when cannabis users have been exposed to scripts that contain more cannabis related content as opposed to less cannabis related context, to the sight and smell of used cannabis paraphernalia, as well as to pictures of cannabis paraphernalia (Haughey et al., 2008; Singleton, Trotman, Zavahir, Taylor, & Heishman, 2002). Therefore symbolic-expressive reactivity has been clearly observed in cannabis using

individuals. However, physiological cue reactivity has also been observed in cannabis users (Gray et al., 2008; Gray et al., 2011; Lundahl & Johanson, 2011; Wölfling, Flor, & Grüsser, 2008).

Studies investigating physiological cue reactivity of skin conductance and HR in cannabis users have yielded mixed results. Past studies have seen increases in measures of skin conductance, but limited to no increase in HR, in response to cannabis related stimuli when compared to neutral cues (Gray et al., 2008; Gray et al., 2011; Lundahl & Johanson, 2011; Wölfling et al., 2008). Cannabis users have shown the most robust skin conductance reactivity to in vivo cues when compared to imagery and video cues (Gray et al., 2008; Gray et al., 2011; Wölfling et al., 2008). These findings suggest that skin conductance can be used to reliably measure cue reactivity. However, HR reactivity to cannabis stimuli is not clearly observed in cannabis using individuals. While cannabis use is typically followed by a substantial increase in heart rate that is dose dependent, tolerance to these cardiovascular effects develops rapidly when cannabis is used frequently (Fant, Heishman, Benowitz & Jones, 1975; Benowitz & Jones, 1981; Bunker, & Pickworth, 1998; Hart, van Gorp, Haney, Foltin, & Fischman, 2001; Heishman, Stitzer, & Yingling, 1989; Jones, 2002). Since no change in HR occurs with cannabis use, it may explain why no change in HR occurs when exposed to cannabis paraphernalia. Models of addiction may help explain the development and maintenance of addictive behaviour and the cue reactivity associated with it.

1.2 Conditioning Models of Addiction

Conditioning models of addiction can explain how cravings arise and perpetuate drug-taking behaviour. Conditioning models of addiction propose that environmental cues become associated with drug use and elicit physiological responses related to a drugs effect. Pavlov's (1927) theory of classical conditioning describes a process whereby a once neutral stimulus, such as a bong (drug cue), becomes a conditioned stimulus (CS) after repeated pairings with

an unconditioned stimulus (US), such as cannabis, which is followed by an unconditioned response (UR; a response elicited by the drug). Through this associative learning, the CS begins to predict the US, creating a CS-US association. This specific type of associative learning is a form of appetite conditioning, as the US (cannabis) is a pleasant stimulus that promotes approaching behaviour (drug taking; Tiffany, 1990; Todd, Winterbauer, & bouton, 2012). Three accounts of how the CS promotes drug-seeking behaviour are the conditioned withdrawal model, the conditioned compensatory model, and the incentive model (Siegel, 1983; Stewart, de Wit & Eikelboom, 1984; Wikler, 1948).

According to the withdrawal model, individuals consume drugs to escape aversive states that arise in response to drug related cues and contexts (Wikler, 1948). This theory is therefore driven by negative reinforcement, and proposes that stimuli, such as drug cues or a context, paired repeatedly with withdrawal, become a CS that elicits cravings (conditioned responses; CR) as part of a withdrawal syndrome (Drummond, Troy, & Glautier, 1990; Wikler, 1948). This theory can explain why drug-using individuals, even after a long period of abstinence, experience cravings and return to drug use when exposed to an environment where drug use has occurred. However, this theory cannot explain what occurs when individuals encounter cues associated with drug use only, and not withdrawal.

Similarly, the compensatory response model posits that negative reinforcement is a mechanism that perpetuates drug taking (Siegel, 1983; Siegel, Baptisia, Kim, McDonald, & Weise-Kelly, 2000). However, this model also posits that the environmental stimuli that precede drug taking, as opposed to follow drug withdrawal, evoke compensatory CRs that counteract the primary effects of the drug and lead to drug tolerance (Siegel, 1983; Siegel, 2005; Siegel et al., 2000). This is because drug administration evokes an agonist effect and a compensatory response occurs which becomes associated with a CS (Siegel, 1983; Siegel et al., 2000). This compensatory response is opposite to the effect of the drug and occurs in an

attempt for the body to maintain homeostasis (Siegel, 1983; Siegel et al., 2000; Skinner & Aubin, 2010). As such, when use is ceased and individuals are presented with a CS, cravings occur to promote drug use in order to escape the discomfort brought on by the compensatory response (Siegel, 2005; Siegel et al., 2000). The difference between compensatory response model and the withdrawal model is in the temporal relationship between the cues and unconditioned effects of the drug. In the conditioned compensatory model the CS is paired with drug use, while in the withdrawal model, the CS is only paired with withdrawal.

Stewart, de Wit & Eikelboom (1984) proposed the incentive model of drug addiction that focuses on the motivational salience of drug-paired cues. This differs from the conditioned compensatory model as it places focus on the appetitive features of the drug that promote drug use. The appetitive features of the drug often include its action on dopamine in the brain, which provides pleasure and positively reinforces the use of the drug (Cheer, Wassum, Heien, Phillips, & Wightman, 2004; Tanda & Goldberg, 2003). This model places emphasis on the CSs effect on voluntary behaviour. In this sense, cravings reflect a strong motivational state, to experience the agreeable effects of the drug, rather than a desire to experience relief from withdrawal. Psychobiological models of addiction may explain the motivational salience of the CS and draw together conditioning models of addiction (Robinson & Berridge, 1993).

1.3 Psychobiological Model of Addiction

The incentive sensitisation theory can explain why those abstaining from drugs still exhibit a motivation to use substances (Robinson & Berridge, 1993). It is believed that this motivation to use drugs can occur independently of the desire for the pleasurable effects of the drug (liking; Robinson & Berridge, 1993). Wanting drugs also occurs despite the negative effects of substance use, such as loss of job, friends and family (Skinner & Aubin, 2010). Robinson and Berridge (1993) propose that long-term use of substances repeatedly activates

the dopaminergic system leading to a sensitisation of this system. Incentive salience (wanting) is the psychological process whereby the perception of neutral stimuli becomes salient due to the repeated exposure to the rewarding effects of drugs (Robinson & Berridge, 1993). This has been supported by Filbey, Schacht, Myers, Chavez and Hutchison (2009) who used functional Magnetic Resonance Imaging (fMRI) and presented cannabis related objects and neutral objects to cannabis users who abstained for 72 hours. Structures involved in the reward pathway such as the ventral tegmental area, demonstrated greater activation to the cannabis cue compared to the neutral cue. The ventral tegmental area releases dopamine during motivationally relevant events such as drug taking which is rewarding and positively reinforces drug use (McClure, Daw, & Read Montague, 2003). The repeat activation of these neural systems is believed to be responsible for the attribution of incentive salience to stimuli (Filbey, Schacht, Myers, Chavez, & Hutchison, 2009; Kalivas & Volkow, 2005; McClure et al., 2003).

Furthermore, repeated activation of the dopamine system during drug use is believed to lead to neuroadaptations in the brain that are responsible for cravings (Filbey et al., 2009; Robinson & Berridge, 1993; 2008). These adaptations are thought to occur because the brain attempts to maintain homeostasis during the altered state in the presence of the drug, and are responsible for cravings (Robinson & Berridge, 1993; 2008). Cravings play a different role during early abstinence and long-term abstinence (Robinson & Berridge, 1993; Skinner & Aubin, 2010). In the early stages of abstinence, cravings occur to promote drug-seeking behaviour to reacquire the homeostasis that was maintained in the presence of the addictive substance (Robinson & Berridge, 1993; Siegel et al., 2000). However, cravings still occur even after the imbalance in the brain returns to normal after long periods of abstinence (Robinson & Berridge, 2008). Cravings occur because the dopamine system has become hyper-sensitive to drug related stimuli and associated memories return about the rewarding

properties of drug use, and of when drug use alleviated negative feelings (Henry et al., 2014; Robinson & Berridge, 1993; 2008). This can explain why relapse occurs when individuals are presented with drug related stimuli during abstinence (Robinson & Berridge, 1993). Therefore, incentive sensitisation theory can explain why substance-using individuals continue to crave drugs even after long periods of abstinence.

1.4 Cue Reactivity and Relapse

Cue reactivity to drug related cues has been associated with relapse in individuals with substance use disorders (Abrams, Monti, Carey, Pinto, & Jacobus, 1988; Drummond, 2000; Drummond & Glautier, 1994; Paliwal, Hyman, & Sinha, 2008; Papachristou, Nederkoorn, Giesen, & Jansen, 2014; Sinha & Li, 2007). A recent study by Papachristou, Nederkoorn, Giesen and Anita (2014) on individuals with alcohol use disorder revealed that higher cue elicited craving was associated with a greater probability of relapse following treatment. Similarly, high skin conductance levels have been seen to predict latency to heavy drinking in an alcohol dependent population (Drummond & Glautier, 1994). However, there is some disparity in the literature as evidence suggests that cravings are not always associated with greater likelihood of drug use (Weiss et al., 2003). Weiss et al. (2003) demonstrated that craving in cocaine users did not predict relapse following individual and group therapy (Weiss et al., 2003). However, this study did not employ a cue-reactivity paradigm and therefore did not examine cue-elicited cravings. These findings indicate that perhaps it is cue reactivity rather than self-reported cravings after treatment that can predict relapse. Therefore, cue reactivity should be targeted during treatment for substance use.

Reducing cue reactivity is not a primary outcome of treatment for substance use disorders (Abrams et al., 1988; Donovan et al., 2011; Drummond, 2000; Drummond & Glautier, 1994; Paliwal et al., 2008; Papachristou et al., 2014; Sinha & Li, 2007). Rather, treatments for substance use disorders often aim to reduce or completely eliminate drug use

(Donovan et al., 2011). However, if cue reactivity can be effectively reduced during treatment, perhaps the incidence of relapse following treatment would decrease. Thus, the primary outcomes of treatment should shift to focus on reducing cue reactivity to drug related cues.

1.5 Extinction and Renewal

Treatment options may be improved by understanding how to reduce reactivity to drug cues. Cue reactivity may be reduced through extinction. Extinction occurs when the CS is repeatedly presented without the US. After many presentations of the CS without the expected outcome, reactivity to such cues should decrease because the CS no longer predicts the US (CS-noUS). Extinction is therefore believed to work through violating the CS-US expectancy (Bouton, 2004). In animal models, extinction has been used to successfully reduce drug self-administration in response to the CS (Crombag & Shaham, 2002; Myers & Carlezon, 2010). In the context of cannabis use, repeated exposure to a bong (CS) without using cannabis (US) should result in diminished cravings in response to the bong.

Initially, extinction training was believed to lead to the destruction of the CS-US association (Rescorla & Wagner, 1972). However, extinction of the CS-US association has been seen to renew when the CS is encountered in a context that differs in their tactile, olfactory, and visual respects from the extinction context (Bouton, 2004; Bouton & Bolles, 1979). Further, a study by Bouton and Bolles (1979) trained rats to press a lever for food. They then conditioned a tone stimulus to signal the administration of an electric shock to the rats. When the CS (tone) signalled electric shock, rats would suppress lever-pressing behaviour. Rats then underwent extinction of this CS-US pairing in a context that differed from the acquisition context. During extinction the CS (tone) was presented repeatedly without the US (electric shock). When rats returned to the acquisition context and were exposed to the CS (tone), suppression of lever pressing behaviour was renewed to the same

level as rats that did not undergo extinction. According to Bouton's (1993, 1994) associative learning theory the likelihood of recovery of an extinguished association increases when a context greatly differs from the extinction context. Renewal also has been demonstrated for drug cues following extinction, in a study by Crombag and Shaham (2002). Rats learned that a CS predicted drug use in one context, and then were extinguished in another context. Even though extinction training led to a decrease in drug seeking behaviour in the extinction context, when rats returned to the site where the original CS-US pairing occurred, responding to the CS renewed. This did not occur in rats that were conditioned and extinguished in the same context. Renewal studies suggest that the original learning about the CS-US association is retained following extinction training.

The inhibitory learning theory posits that extinction training creates secondary learning about the CS-US pairing that inhibits the original response (Bouton, 1993). After extinction the CS has two possible associations with the US, one inhibitory and one excitatory, and the context determines which meaning will be retrieved (Bouton, 2004). Therefore, inhibitory learning explains that renewal occurs from a switch in the context because the excitatory memory is retrieved.

Additionally context may be quite specific and the CS-US association may contain information about the temporal delay between the CS and the US (Prenoveau, Craske, Liao, & Ornitz, 2013). The For example, during fear acquisition participants have been seen to develop a temporal expectation about when the US will occur following the feared stimulus (Prenoveau et al., 2013). Extinction that lasts longer than this temporal expectation may allow the CS-US association to be more effectively violated (Bouton, Westbrook, Corcoran, & Maren, 2006). For example, if a person uses a bong to smoke cannabis, but upon seeing the bong does not smoke for 10 minutes, then exposure needs to last longer than 10 minutes in order to violate the CS-US expectancy. If the extinction lasts 3 minutes, then the CS-US

expectancy will not be violated. Therefore, extinction must last long enough to violate the CS-US expectancy.

Furthermore, the kinds of cues that are extinguished may attenuate recovery of responding following extinction. Subjects' show substantially more responding if individual extinguished stimuli are presented in compound, when that compound has not been extinguished. Resclora (2006) used animal models to demonstrate that if a compound of stimuli is extinguished the extinction is deepened and is less susceptible to recovery, while also slowing reacquisition of the CS-US association. In a fear-conditioning paradigm rats were trained to fear multiple CS. Each CS was extinguished individually, and responding recovered when the stimulus were presented in compound. This did not occur when stimuli were also extinguished in compound. Therefore the nonreinforcement of the compound of CS will deepen the extinction (Rescorla, 2006). Overall, there are many factors that can contribute to the return of conditioned responding following extinction.

1.6 Cue-Exposure Therapy

Exposure therapy was initially developed from extinction to extinguish fears in humans (Wolpe, 1958). Wolpe (1958) was among the first to investigate exposure therapy by gradually presenting anxiety-provoking stimuli to anxious individuals using a hierarchy of feared stimuli. During exposure, relaxation techniques are practiced to lower the level of anxiety at each level of the hierarchy. This process was known as systematic desensitisation. However, recent research suggests that relaxation techniques are unnecessary and slow graded exposure to stimuli may not contribute to successful therapeutic outcomes (Arch & Craske, 2011; Craske & Barlow, 2008). Exposure therapy has had some great success in treating anxiety disorders, however, the benefits have not been as clear treating substance use disorders (referred to as cue-exposure therapy; Conklin & Tiffany, 2002; Norton & Price, 2007).

Drug using individuals relapse more frequently when exposed to environments that are associated with drug use (Carter & Tiffany, 1999; Chaudhri, Sahuque, & Janak, 2008). This may be explained by associative learning as described by Bouton (1993, 1994). Since a person's context determines whether the CS-US association or the CS-noUS association will be retrieved, renewal may contribute to relapse in individuals with substance use disorder. Consider a cannabis using individual who gets high in their lounge room at home (context A), then receives cue-exposure therapy in a therapists office (context B), and following therapy the person returns home (context A). Relapse should occur because of renewed cravings and urges to use cannabis in the excitatory context. Since memories are context dependent, the recall of the CS-US associations is better in the context that was present during encoding (Egstrom, Wedlman, Baddeley, Cuccari, & Wills, 1972). Similarly, memories of a CS-noUS association are better recalled in the exposure context. Therefore, cue-exposure therapy may be more beneficial in drug-associated contexts where the CS-US association was learned, as this may prevent renewal from occurring (Perry, Zbukvic, Kim, & Lawrence, 2014).

Exposure therapy to drug cues in populations with substance use disorder has been efficacious in reducing cue reactivity, but not in achieving abstinence (Conklin & Tiffany, 2002). Many cue-exposure treatment studies have been limited in similar ways, which may explain why treatment has been unsuccessful. First, individuals are not required to remain abstinent during treatment (Kavanagh et al., 2006; McLellan, Childress, Ehrman, O'Brien, & Pashko, 1986; Sitharthan, Sitharthan, Hough, & Kavanagh, 1997). This differs from rat studies that do not administer drugs to rats between extinction trials, as this negates the extinction and restores drug seeking behaviour (Davis & Smith, 1978; De Vries, Schoffelmeer, Binnekade, Mulder, & Vanderschuren, 1998). Similarly, if drugs are used between cue-exposure sessions the CS-US association will be further strengthened, negating

the CS-US violation that occurs during cue-exposure treatment (Bouton, 1993; 2004; Bouton et al., 2006). Those who require abstinence during cue-exposure therapy have had slightly more success in preventing relapse following treatment (Loeber, Croissant, Heinz, Mann, & Flor, 2010). Nonetheless, relapse still occurs (Dawe et al., 1993). Additionally, cue-exposure therapy is often conducted in contexts that differ from the acquisition context. For example, cue-exposure therapy is often conducted within hospital and therapist settings, whereas drug use occurs outside of these settings. Thus, cravings may return due to a change in context since extinction memories are best retrieved when individuals are in the extinction context (Bouton, 1993; 1994)**.** Finally, extinguishing responses to stimuli that are conceptually related to the original CS do not generalise beyond that extinguished stimulus (Vervoort, Vervliet, Bennett, & Baeyens, 2014). When the CS-US association is violated using the original CS, the extinguished CRs generalise to conceptually related stimuli (Vervoort et al., 2014). Therefore, personal paraphernalia should be used during cue-exposure. Together these limitations highlight that cue-exposure treatment may have been unsuccessful in the past, as important factors about the CS and context have been neglected.

1.7 Renewal in Drug Users Following Cue-Exposure Therapy

While the concept of renewal seems applicable to humans with substance use disorder, there is disparity in the literature. To date, there have only been four cue-exposure studies that tested for renewal in substance using populations (Collins & Brandon, 2002; MacKillop & Lisman, 2008; Stasiewicz, Brandon, & Bradizza, 2007; Thewissen, Snijders, Havermans, van den Hout, & Jansen, 2006). Renewal was observed in two studies examining social drinkers and tobacco smokers (Collins & Brandon, 2002; Thewissen et al., 2006). However, renewal has not been observed in the remaining studies which studied alcohol using individuals (MacKillop & Lisman, 2008; Stasiewicz et al., 2007). There are a number of possible methodological reasons for this disparity.

The first to examine renewal in human drug users was Collins and Brandon (2002), who assessed low risk drinkers in a one-day study. Participants were required to be abstinent for 24 hours prior to the study and participated in the afternoon to early evening. Participants underwent a baseline assessment pre exposure and were assessed for cue reactivity during a baseline period wherein they were asked to focus on the environment, and then assessed for cue reactivity during exposure to beer. Participants showed a significant increase in urges and salivation to beer compared to baseline. Cue exposure to the same beer cue consisted of a minimum of seven trials and participants' completed this session in a context that differed from baseline. Trials lasted 3 minutes each with 2-minute rest periods. Up to an additional three trials could be added if participants did not return to baseline urge. Participants urge to drink decreased during exposure trials by 35%. Following exposure, participants had a 25-minute distracting break in a waiting room where they completed a crossword puzzle. Participants' completed the final assessment in a context that was either similar to, or different from the exposure context. Both rooms had a one-way mirror, but differed in dimension, decor, odour, ambient temperature, lighting, furniture, experimental equipment and location. They were also located on different levels of a building. During exposure and assessment the experimenter spoke to participants through an intercom, but participants were exposed to the experimenter between sessions. Urges and salivation when exposed to beer from the end of cue exposure were compared to urges and salivation post-exposure assessment. Results indicated that cue exposure was more effective for individuals who were tested in the same context as cue exposure. Those assessed in a different context demonstrated renewal of urges and salivation during the final assessment. On average, participants renewed by 0.80 points on a 7-point Likert scale of urges, while those who received exposure in the same context decreased by 0.03 points. While renewal was observed, evidence suggests that novel stimuli may increase drug seeking behaviour, and

using cravings at a baseline period may not be accurate in reflecting changes in cue reactivity (Bastle et al., 2012). Therefore, neutral cues should be used in comparison to drug cues to assess cue reactivity (Bastle et al., 2012).

Stasiewicz, Brandon and Bradizza (2007) attempted to replicate Collins and Brandons' (2002) findings in a clinical sample of alcohol dependent outpatients. The study took place over three days and participants were required to achieve a blood alcohol level of >.00 to begin each session, but did not need to remain abstinent throughout the study. Participants were interviewed and assessed for alcohol dependence on the first day in either context A or B. On the second day participants underwent a baseline assessment pre exposure and were assessed for their cravings and salivation in response to a water cue, and an alcohol cue which was their most frequently consumed alcoholic beverage (context A). During cue exposure participants were encouraged to smell their preferred alcoholic beverage for five seconds, this occurred six times in each 3-minute trial. Cravings were recorded at the end of each trial and the maximum time participants could spend doing exposure was 60 minutes. Following cue exposure, participants were assessed for their cravings and salivation in response to drinking water and drinking alcohol. On the third day, a renewal test was conducted in the same context as the first day (context A or B). No renewal was observed, and all groups demonstrated a significant reduction in cravings, although, it is not reported by how much. Renewal may not have been observed because participants were not required to remain abstinent during the study, which may have reduced the cravings that would typically be experienced. This is a serious problem because, if participants drank after extinction training, it would have strengthened the US-CS pairing (Conklin & Tiffany, 2002; Wölfling et al., 2008). The cue exposure rooms were both university rooms and differed in dimension, decor, lighting, furniture, and location, but not odor or temperature. There is no mention of participants being told to focus on the characteristics of the room. Furthermore, the

experimenter did not appear to differ between conditions and may have acted as a reminder cue of the extinction context. Extinction cues are stimuli that are paired with the extinction context and become associated with the inhibitory CS-US association that is learned during extinction (Collins & Brandon, 2002). Therefore, extinction cues may assist in retrieval of the extinction memory in other contexts, and can explain why no renewal was observed.

In the third study, Thewissen, Snijders, Havermans, Hout and Jansen (2006) conducted a one-day cue-exposure study with tobacco smokers. Smokers were required to be abstinent two hours prior to the experiment. Initially, participants were told the meaning of two coloured trays that either signalled smoking availability or unavailability. This occurred in a waiting room. Following this, the participants were moved to an 'office' (context A) or a 'therapy room' (context B) for a pre-acquisition phase. The two rooms differed on their physical characteristics such as style, colour, odour and location, the respiratory tubes used to blow smoke were of different material and colour, but could be considered the same stimuli. Participants were told to concentrate on the room and urge to smoke was recorded, this was completed in both contexts. Following a 5-minute reading break in the waiting room, participants were escorted to the room where the second pre-acquisition phase took place. The trays signalling either smoking availability or unavailability were presented to the participants for 25 seconds, and the participants were asked to report on their urge to smoke. Following this, the participant's favourite cigarettes, a lighter and ashtray were placed on the tray. Participants were told to engage with the paraphernalia without smoking, reporting on their urges after 25 seconds. Participants were allowed to puff the cigarette and blow the smoke out through a respiratory tube in the room when the coloured serving tray indicated that smoking was allowed. A 3-minute reading break was given between six trials and this session lasted approximately 30 minutes. This process allowed experimenters to control the acquisition context of the CS. Cue exposure followed the same procedure, as before, yet

participants were not allowed to smoke when any tray was present. Following cue exposure, half of the participants read for 5 minutes in the waiting room while the others were escorted to the other context. During the post-exposure assessment phase, participants were presented with one of the two trays and asked for their urge to smoke, this was repeated for their smoking cues. Following a 3-minute reading break the next tray was presented and the same steps were repeated. This process was then completed in the alternative context. During exposure urges to smoke reduced by 30%. Renewal occurred when the post-exposure assessment occurred in a different context than where extinction occurred. While this study did not include any physiological measures of cue reactivity, it appears that one-day studies observe renewal of self-reported urges and cravings.

Finally, MacKillop and Lisman (2008) examined renewal in a four-day study using a sample of heavy alcohol users. Participants underwent three sessions of extinction (one each day) and one renewal session (on the fourth day). Sessions were completed at the same time in the evening each day. Participants were not required to remain abstinent throughout the study which may allow the US-CS pairing to be strengthened between cue exposure sessions (Conklin & Tiffany, 2002; Wölfling et al., 2008). Initially participants completed baseline measures of cravings and salivation in a neutral laboratory room. Following baseline assessment, participants were exposed to visual, auditory, olfactory, tactile, and proprioceptive alcohol cues in a room that contained drinking paraphernalia, and were left for 90 seconds to observe all the cues. The research assistant then returned and poured the participant's favourite beer in front of them. Participants smelled the beer and listened to an audio track that described beer drinking and a situation related to one of seven reasons for drinking (happiness, tension, boredom, negative affect, anger, habit, and gustatory enjoyment) that had been assessed during screening. The neutral cue exposure was identical but related to drinking water, lasting approximately 10 minutes. Cue exposure followed and

lasted 40 minutes, with urges to drink and salivation assessed every 10 minutes. Participants were either allocated to a control condition that received neutral cues throughout cue-exposure and alcohol cues on Day 4; a single context condition that received exposure in the same context every day and a different context on Day 4; or a multiple context condition where participants received exposure in a different context each day. Five different experimental rooms (four alcohol cue exposure, one water cue exposure) were used throughout the study. The contexts were developed to map on to existing conditioning contexts and contained different alcohol paraphernalia across contexts. Different narrators described imaginable scenes in each room and research assistants were different each day for all participants. Therefore, research assistants did not act as a retrieval cue for the extinction context. Additionally, each room was located in a different area and each room was allocated a colour theme. The door had coloured paper and there was respective coloured lights, lamps and tablemats inside the rooms. During cue exposure participants who were exposed to alcohol cues showed a significant decrease in self-reported cravings. However, when participants were tested for renewal in a novel context, there was no evidence of renewal in any group following a context shift, and there was no evidence of significantly greater extinction due to extinction in multiple contexts. If all the rooms looked like university rooms it may account for why no renewal was observed. This is because of the generalisation gradient (Bouton, Nelson, & Rosas, 1999). Responding to stimuli decreases as the test stimulus deviates from the original US (Bouton et al., 1999). During cue exposure, the context becomes associated with the inhibitory CS-US association. If the post-exposure context is similar to the extinction context, it may retrieve the extinction memory and inhibitory responding to the CS may occur. This would not allow renewal to be observed. Therefore, future studies should focus on clearly differentiating the cue exposure context from the renewal assessment context.

Inconsistencies in the literature make it difficult to generate conclusions about renewal in drug using populations. Unreliable results may be due to vast differences in procedure, ranging from the number of exposure sessions, length of the study, difference in populations, abstinence requirements, and differentiation (or lack thereof) between exposure and assessment contexts. Additionally, physiological information is not consistently used throughout the studies and should be used to objectively measure changes in cue reactivity. Overall, it appears that temporally massed exposure may be more susceptible to renewal than temporally spaced exposure. It is also possible that researchers may act as retrieval cues. It is therefore clear that renewal needs to be more carefully examined in future studies with more stringent procedures.

1.8 Distress Tolerance

Even if renewal may sometimes occur, strengthening tolerance of craving might help to reduce relapse. Distress tolerance is the ability to withstand negative psychological states and is related to poor emotion regulation (Bonn-Miller, Vujanovic, & Zvolensky, 2008; Brandon et al., 2003; Daughters, Lejuez, Bornovalova, Kahler, Strong, & Brown, 2005a; Daughters, Lejuez, Kahler, Strong, & Brown, 2005b; Simons & Gaher, 2005). Greater levels of substance use and substance-related problems are associated with distress intolerance and these individuals are at an increased risk of relapse following treatment (Brandon et al., 2003; Daughters et al., 2005a; Daughters et al., 2005b; Simons & Gaher, 2005). Evidence suggests that those who use drugs may do so to regulate their emotions and avoid negative psychological states (Brandon et al., 2003; Daughters et al., 2005a; Daughters et al., 2005b; Simons & Gaher, 2005). When substance using individuals attempt to abstain from drugs, their withdrawal and cravings become a negative state (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Bonn-Miller et al., 2008). Those intolerant of distress may relapse to avoid these

negative states, while those tolerant of distress may be able to tolerate such feelings and continue with abstinence (Baker et al., 2004).

Attempts to down regulate negative emotions by suppression, avoidance or escape can be critical to the maintenance of the CS-US association (Arch & Craske, 2011; Salkovskis, 2008). Anxiety research has demonstrated that people avoid situations where feared stimuli may be encountered (Arch & Craske, 2011; Craske et al., 2008; Quirk & Mueller, 2007). Craske et al. (2008) suggested that avoidance perpetuates fear by preserving the CS-US association. By avoiding the CS in contexts outside therapy, the CS-US expectancy is not violated and new learning cannot occur, maintaining and preserving the excitatory CS-US association. In the context of drug use, when the CS is unexpectedly encountered, compensatory behaviours (i.e. drug taking) may occur to alleviate cravings, and the rewarding properties of the drug serve to strengthen the CS-US association. Since exposure to paraphernalia increases cravings, people may be encouraged to use unless their tolerance for aversive feelings are high. Tiffany and Wray (2011) suggest that interventions should target cravings during treatment, proposing that treatment should focus on the amelioration of cravings. Further, they suggest that cravings should be a target of treatment whether they impact drug use or not, because it may teach tolerance of aversive or distressing feelings. Therefore, emphasis should be placed on tolerance of emotions during exposure.

Extinction and inhibitory learning are believed to be a form of emotion regulation (Quirk & Beer, 2006; Quirk & Mueller, 2007). Extinction occurs in three separate phases: acquisition, consolidation, and retrieval. Inhibitory learning involves a network of regions such as the amygdala, the prefrontal cortex, and the hippocampus (Milad & Quirk, 2002; Quirk & Mueller, 2007). Activity in the medial prefrontal cortex (mPFC) has been seen to predict the strength of extinction learning (Milad & Quirk, 2002). The mPFC is important for the consolidation and retrieval of extinction memories and damage to the prefrontal cortex in

animals has been associated with failure to inhibit responses to a CS following extinction (Kolb, 1984). Activity in the amygdala has been associated with negative emotional stimuli and negative emotional responses, (Phan et al., 2005; Urry et al., 2006). Additionally, extinction memories may depend on contextual factors that may be controlled by the hippocampus (Sotres-Bayon, Cain, & LeDoux, 2006).

Such findings have been linked to emotion regulation in humans. During emotion regulation, the mPFC becomes activated exhibits inhibitory control over the amygdala (Quirk & Beer, 2006). Increased activity in the amygdala has been observed when participants increase their negative emotional responses, thus, reduced activity in the amygdala would suggest control over these emotional responses (Urry et al., 2006). This suggests that emotion regulation and inhibitory learning share the same neurological processes. Therefore, extinction may improve emotion regulation since inhibitory learning occurs as part of emotion regulation.

Within exposure sessions, people learn to cope with aversive feelings through inhibitory learning (Craske et al., 2008). Therefore, exposure to drug stimuli (CS) in the absence of drug taking (US) directly teaches individuals that they can cope with cravings without using drugs. Additionally, by receiving exposure in a familiar environment rather than an arbitrary environment such as a therapist office, individuals may develop greater coping skills and tolerance for cravings in that specific environment (Craske et al., 2008). These improvements in distress tolerance may also be subject to renewal since they also involve secondary inhibitory learning during the violation of the CS-US association.

1.9 The Present Study

Conditioning and psychobiological models of addiction explain how addictive behaviours are acquired and maintained (Robinson & Berridge, 1993; Siegel, 1983; Stewart et al., 1984; Wikler, 1948). The associations between drug paraphernalia and administration

of the drug can perpetuate drug use (Tiffany, 1990; Todd et al., 2012). In addition, incentive salience describes how the brain becomes sensitive to drug cues generating excessive cravings and compelling drug seeking behaviour (Henry et al., 2014; Robinson & Berridge, 1993; 2008). Extinguishing the learned associations through exposure therapy provides a good basis for treating addictive behaviours because it can reduce cue reactivity which has been seen to predict relapse (Bouton & Bolles, 1979; Conklin & Tiffany, 2002; Myers & Carlezon, 2010; Quirk, 2002). However, cue-exposure therapy has had limited success in populations with substance use disorder, as it has not improved abstinence rates (Conklin & Tiffany, 2002). Renewal of cravings may explain why cue-exposure therapy has not reduced the incidence of relapse. However, this has not been reliably observed in substance using populations, or in a cannabis using population. Furthermore, inhibition learning is believed to be part of emotion regulation and involves the same neural mechanisms. Therefore, cue exposure in the absence of drug use directly teaches people that they can cope with cravings without using drugs. Cue exposure may therefore improve people's ability to tolerate distress.

Therefore, the current study aims to examine the feasibility of an approach to examine the role of context in cue-exposure therapy. The current study seeks to address a gap in the literature, which has not examined whether extinguished cue elicited cravings renew after a change in context in a cannabis using population. Additionally, this study seeks to understand whether distress tolerance increases following of cue-exposure therapy and whether these changes are also subject to renewal. Therefore, this pilot study seeks to examine the feasibility of administering cue-exposure therapy and examining the potential for renewal with cannabis using individuals. Furthermore, to refine study procedures based on the methodological weaknesses of previous studies and provide methods for improving future studies and treatment for cannabis use disorder.

Method

2.1 Participants

Three hundred cannabis users expressed interest in the study from the community. Age ranged from 18 to 63 years (*M* = 27.14, 95% CI = [26.02, 28.26]) and 77% (n= 231) were male. Participants were eligible if they were between the age of 18 and 65 years of age, used cannabis at least 5 days a week, reported a somewhat intense craving or urge for cannabis, mulled tobacco with cannabis or smoked a tobacco cigarette within 15 minutes of smoking cannabis, primarily used cones and bongs to smoke cannabis, and if they reported smoking cannabis in a lounge room or lounge-like environment. Participants were excluded from the study if they were currently receiving treatment for substance use, or had received treatment in the past three months, had a history of substantial adverse events during abstinence, were in a state of acute psychiatric distress (Kessler Psychological Distress Scale score of 30 or more), drank alcohol on 10 of the past 30 days and had more than 50 standard drinks in the past 30 days, used any illicit drug on more than 4 of the past 30 days, had a history of high blood pressure, heart disease, and mitral valve prolapse or any cardiovascular problems (see Appendix A; B).

Sample size was based on the pragmatics of recruitment. While 15.33% (*n*=46) of the people who expressed interest were eligible, we were only able to recruit 8% (*n*=24) in to the study. Age ranged from 18 to 49 years (*M* = 23.29, 95% CI = [20.73, 25.85]) of which 66.67% (n=16) were male. Once enrolled participants were excluded if they showed no increase in response to laboratory's cannabis cues in Session 1 in comparison to neutral cues (less than 10-pt self-reported increase; see Appendix A).

2.2 Design Summary

The study contained five sessions, an eligibility interview (Session 0) a pre-exposure assessment phase (Session 1), two cue-exposure therapy sessions (Session 2 and Session 3) and a post-exposure assessment phase (Session 4). Participants were randomly allocated to an

AAA or an ABA condition. In the AAA condition, participants will receive their pre-exposure assessment, cue-exposure sessions, and post-exposure assessment in a lounge room. In the ABA condition, participants will undergo the pre-exposure assessment and post-exposure assessment in the lounge room, but will receive cue exposure sessions in a therapist's office. The laboratory's paraphernalia was encountered in Sessions 1 and Session 4, while participants experienced cue-exposure therapy with their personal paraphernalia during Sessions 2 and 3. Additionally, participants could choose to participate daily over 5 days, or intensively 4 days after the eligibility interview (Session 0).

Variables of interest were subjective report of cravings, physiological measures of electrodermal activity (EDA) and heart rate (HR), self-report measures of distress tolerance, and a behavioural measure of distress tolerance. Self-reported cravings and intolerability of cravings were obtained from two items on the Subjective Units of Craving and Tolerance Form in Session 1 and Session 4. These items were used to measure cravings and intolerability since they were consistently used throughout the study, including during Session 2 and Session 3 making them comparable across sessions. Cue reactivity to cannabis paraphernalia was calculated by subtracting self-reported craving, EDA, and HR during the neutral cue assessment phase from the respective scores during the cannabis cue assessment phase, in Session 1 and Session 4.

This pilot study was a small-scale preliminary study conducted in order to evaluate feasibility, time, and cost, before conducting a full-scale experiment. Since it is not possible to learn about the efficacy of cue-exposure therapy and renewal by conducting inferential statistics with a small sample, no analyses will be proposed (Leon, Davis, & Kraemer, 2011).

2.3 Materials and Apparatus

2.3.1 Demographics and Substance Use. Demographic items queried age, gender, marital status, ethnicity, employment status and highest completed education (see Appendix

C). Information about substance use, such as frequency and smoking habits were also collected to determine eligibility (see Appendix B).

2.3.2 Psychological Distress. Participants' level of psychological distress over the past four weeks was measured using The Kessler Psychological Distress Scale (K.10; see Appendix D; Kessler & Mroczek, 1994). The scale consisted of 10 items which were rated on a 5-point Likert scale ranging from *1=None of the time* to *5=All of the time*. Scores above 30 on the scale indicate a very high level of psychological distress (Andrews & Slade, 2001). Prior Cronbach's alpha indicates good internal consistency at $\alpha = 0.93$ (Fassaert et al., 2009).

2.3.3 Marijuana Consequences. The Brief Marijuana Consequences Questionnaire (see Appendix E) was used to assess cannabis related problems experienced in the past month (Simons, Dvorak, Merrill, & Read, 2012). The scale consisted of 21 items that were rated on a binary scale, 0 = *No* and 1 = *Yes*. High scores indicated more cannabis related problems. Prior Cronbach's alpha indicated good internal consistency at $\alpha = 0.95$ (Simons et al., 2012).

2.3.4 Nicotine Dependence. The Fagerstrom Test for Nicotine Dependence (see Appendix F) queried tobacco use (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991). The scale consisted of six items and the rating scale differed among items. A total score of one to two indicated low dependence on nicotine, three to four indicated low to moderate dependence, five to seven indicates moderate dependence and a score of eight or above indicated high dependence on nicotine. Prior Cronbach's alpha coefficient indicate poor to moderate internal consistency ranging from $\alpha = 0.55$ to 0.74 (Meneses-Gaya, Zuardi, Loureiro, & Crippa, 2009).

2.3.5 Marijuana Motives. The Marijuana Motives Measure (see Appendix G) was used to assess why individuals used cannabis in the past month (Simons, Correia, Carey, & Borsari, 1998). The scale consisted of 24 items measuring five different motives, social,

coping, expansion, conformity and enhancement. Items were rated on a 5-point Likert scale ranging from 1 = *Almost never or never using for that reason,* and 5 = *Always or almost always using for that reason*. Items within each subscale contained a different number of items and were averaged. The highest scoring factor indicted the individual's greatest motivation for using cannabis. Prior Cronbach's alphas indicated substantial internal consistency among the five factors as social motives $\alpha = 0.86$, coping motives $\alpha = 0.89$, expansion motives $\alpha = 0.93$, conformity motives $\alpha = 0.86$, and enhancement motives $\alpha = 0.92$ (Simons et al., 1998).

2.3.6 Cannabis Use Disorder. The Structured Clinical Interview for DSM Disorders (SCID-RV) modified for the DSM-5 (see Appendix H) was used to assess lifetime cannabis use and cannabis use disorder (First, Williams, Spitzer, & Gibbon, 2007; Panlilio, Goldberg, & Justinova, 2015). The DSM-5 substance use disorder criteria are the DSM-IV substance abuse and dependence criteria combined into a single list with some exceptions. The SCID-RV was modified such that the recurrent legal problems criterion was removed, and craving or a strong desire or urge to use a substance was included as a criterion (American Psychiatric Association, 2013). The presence of two to three symptoms indicates mild severity of cannabis use disorder, the presence of four to five symptoms indicated a moderate disorder and a presence of six or more symptoms indicates a severe level of cannabis use disorder.

2.3.7 Cannabis Use. The Timeline Followback (TLFB; see Appendix I) method was used throughout to assess how many joints or cones the participant had on each of the 30 days prior to Session 0 (Sobell & Sobell, 1996). This method was also used to track other drug use throughout the study. The TLFB has good reliability, with test-retest reliability ranging from $r = 0.79$ to $r = 0.96$, up to 360 days prior to the interview (Norberg, Mackenzie, & Copeland, 2012; Robinson, Sobell, Sobell, & Leo, 2014).

2.3.8 Cannabis Withdrawal. The Subjective Units of Cannabis Withdrawal (SUCW; see Appendix J) was developed for this study to be a brief interview, by querying the most common and disrupting cannabis withdrawal symptoms (Allsop et al., 2012). The interview consisted of seven items, these were *"In the past 24 hours how intensely did you think about smoking cannabis?, How intense was your anger and/or irritability?, How much trouble did you have sleeping last night?, How intense or strange were your dreams or nightmares?, How tense or anxious did you feel? How much did life feel like an uphill struggle?"* and *"Did your appetite change?".* Items were rated on a scale ranging from 0 = *Not at all* to 100 = *Extremely*.

2.3.9 Cannabis Use Patterns. A Contextual Cue Assessment (see Appendix K) was used to understand the participant's current cannabis smoking habits, such as how much cannabis smoking involved other people, where they smoke, and their rituals involved in smoking, among others. This interview was developed for the current study based on Marlatts and Gordons' (1985) Contextual Cue Assessment to examine event characteristics associated with drug use including items such as such as when, with whom, where, how, why, and how much. The assessment also asked participants to rank their personal cannabis paraphernalia on a scale of 0 to 100 indicating the level of craving they expected to experience when seeing these objects during abstinence, 0 = *No cravings or urge to use cannabis* and 100 = *Immense cravings or urge to use cannabis, under no circumstances could this get any higher.*

2.3.10 Quit Session. A Quit Session (see Appendix L) was used to assist participants in remaining abstinent from cannabis and all other drugs throughout the study. This interview was developed for the study based on cognitive-behavioural therapy techniques to assist with self-efficacy (Larimer, Palmer, & Marlatt, 1999). During this session the participant was asked to answer 10 questions about how confident they are in resisting the urge to use cannabis in different situations. For example, if a participant was "*angry or frustrated*" over

the next week, how confident was he/she to resist using. Participants responded with a number from 0 to 100; 0 = *0% confident could resist using any drugs* and 100 = *100% confident could resist using any drugs*. Lower confidence scores indicated the kinds of situations that participants should avoid during the course of the study.

2.3.11 Psychophysiological Recording. Electrocardiographic signals (ECG; heart rate; HR) and were measured using a Biopac MP150 system (Biopac Systems Inc., Goleta, CA). Pre-gelled, general purpose, Ag/AgCl biopotential electrodes with a circular contact were configured in Einthoven's triangle (see Appendix M) to record the ECG signal. Signals were filtered with a low pass filter of 35Hz and the acquisition sample rate for the ECG was set at 1000Hz.

Electrodermal activity (EDA; skin conductance) was measured using a Biopac MP150 system. Two pre-gelled, general purpose, high conductivity, Ag/AgCl biopotential electrodes with a circular contact were placed on the palm of the hand to record EDA (see Appendix N). These electrodes were placed on clean skin, wiped with an alcohol swab. The Biopac MP150 system constantly delivered 0.5 volts and the sampling rate for EDA was set at 250Hz. All psychophysiological data was stored using Acq*Knowledge* 4 software (Biopac Systems Inc., Goleta, CA). Biopac MP150 system was connected to a HP laptop, which ran the Acq*Knowledge* 4 software.

2.3.12 Subjective Units of Craving and Tolerance. A Subjective Unit of Craving and Tolerance form was used to query cravings for cannabis (see Appendix O). This scale was developed for the current study using the framework of the subjective units of distress scale used in clinically anxious populations (Vijanovic & Zvolesky, 2009; Wolpe, 1969). The scale consisted of five items, these were, *"Right now, how intense is your current craving and urge to use cannabis?, Right now, how pleasant would it be to use cannabis?, Right now, how unacceptable is this current level of craving and urge to use cannabis? How unbearable*

or intolerable is this level of craving and urge to use cannabis?" and *"If you were at home and not in this study, how likely would it be that you would use cannabis when experiencing this level of craving and urge to use cannabis?".* Items were rated on a scale from 0 to 100, 0 = *No urge or craving* and 100 = *Very intense urge or craving.*

A short Subjective Unit of Craving and Tolerance Progression Form (see Appendix P) was developed for the study to monitor cravings during extinction. This is a short version of the Subjective Unit of Craving and Tolerance form. Participants were asked to report on their cravings and ability to tolerate the craving. Two items queried cravings and tolerance of the craving, these were "*Right now, how intense is your current craving and urge to use cannabis?"* and *"How unbearable or intolerable is this level of craving and urge to use cannabis?".* Items were rated on a scale from 0 = *Completely tolerable* to 100 = *Completely intolerable*. Higher scores on the craving question indicated greater cravings, while higher scores on the tolerance question indicated greater intolerance of the cravings.

2.3.13 Urinalysis. The inactive urinary metabolite of cannabis, 11-nor-Δ^9-tetrahydrocannabinol-9-carboxylic acid (THC-COOH) was quantified by gas chromatography-mass spectrometry and normalized by urinary creatinine concentration (THC-COOH) to validate self-reported abstinence. Urine was tested for THC-COOH, creatinine, cocaine, benzodiazepines, amphetamines and opiates, by immunoassay. The levels for THC-COOH were reported in ug/L, and THC-COOH:Creatinine ratio was reported in ng/mg. Following seven days of abstinence THC-COOH levels have been observed to fall by 64–80% (Karschner et al., 2009; Lewis, Molnar, Allsop, Copeland, & Fu, 2015).

2.3.14 Audio Track and Cues. Baseline and imagery scripts (see Appendix Q) were recorded using *Eprime* software (Psychology Software Tools, Pittsburgh, PA). This recording contained three 5-minute baseline periods, two 2-minute scripts describing different scenes, and the Subjective Units of Craving and Tolerance questions. The scripts described situations

that depicted a person at the beach and had no mention of smoking marijuana (no-urge script), another described a person experiencing a strong desire to smoke cannabis (high-urge script; Singleton et al., 2002). Scripts were modified to fit an Australian sample from scripts used previously (Singleton et al., 2002). The cannabis script was modified to take place in a lounge room and pertain to smoking cones. All scripts contained positive affect descriptors. Visual cues were also presented during the respective scene descriptions.

The neutral cue was a beach cue, designed to be un-related to cannabis use (see Appendix R). The beach cues were presented on a tray to participants and consisted of a black thermos bottle, sunscreen, a rolled up blue towel, a pair of black sunglasses and a green tube of zinc. The cannabis cues (see Appendix S) were presented on a tray to participants and were set up in a similar way to the beach cues. The cannabis cues consisted of a black bong, marijuana 'look alike' in a glass jar, a blue incense holder with an incense stick, an open black chopper, and a green lighter.

2.3.15 Subjective Report of Distress Tolerance. The Distress Tolerance Scale (DTS; see Appendix T) was used to measure emotional distress tolerance (Simons & Gaher, 2005). This scale can be separated in to 4 subscales, tolerability (e.g. the aversiveness of the emotional state), appraisal (e.g. the acceptability of the emotional state), absorption (e.g. the tendency of the emotional state to absorb attention and disrupt functioning, and regulation (e.g. the ability to either avoid or attenuate negative emotional experiences). The scale consisted of 15 items and answers were rated on a 5-point Likert scale ranging from 1 = *Strongly agree* to 5 = *Strongly disagree*. One item, *"I can tolerate being distressed or upset as well as most people"* was reverse scored. Higher average scores indicated better tolerance of emotional distress. Good internal consistency in a cannabis using population has previously been reported at $\alpha = 0.86$ (Bujarski, Norberg, & Copeland, 2012).

2.3.16 Behavioural Measure of Distress Tolerance. The Computerised Mirror Tracing Persistence Task (MTPT-C; see Appendix U) was used as a behavioural measure of distress tolerance (Strong et al., 2003). Participants were instructed to trace four stars using a mouse (three practice stars and one test star) on a laptop. The cursor moved in the opposite direction of physical movement, simulating tracing a mirrored image. Errors, such as moving the cursor outside of the shape or hesitation to move was accompanied by a loud buzzer sound and resulted in the participant returning to the beginning of the shape. The task adapted to the participant's ability based on performance during the three practice stars. When presented with the test star participants were informed that they could discontinue the task by pressing any key on the keyboard. The task provides an incentive for people to continue with the task (up to $3.50) to mimic real life events that include distressing and rewarding properties. Tolerance for distress is measured by the amount of time taken to give up on the task. Those who terminate sooner have lower distress tolerance. For the MTPT-C, construct validity has been demonstrated through a significant positive correlation with the paced auditory serial addition task (PASAT-C), another widely used measure of distress tolerance (Bornovalova, Gratz, Daughters, Hunt, & Lejuez, 2012; Lejuez, Kahler, & Brown, 2003).

2.3.17 Marijuana Craving Questionnaire. The Marijuana Craving Questionnaire (MCQ; see Appendix V) assessed the current level of craving on four subscales, either compulsivity (e.g. inability to control cannabis use), emotionality (e.g. anticipating relief by smoking cannabis), expectancy (e.g. anticipating positive outcomes from smoking cannabis), and purposefulness (e.g. planning to use cannabis for positive outcomes; Heishman et al., 2009). Twelve statements were rated on a 7-point Likert scale ranging from 1 = *strongly disagree* to 7= *strongly agree*. Higher total scores on any subscale indicate a high level of craving. Previous Cronbach's alphas have indicated good internal consistency for the compulsivity subscale (α=0.82), emotionality subscale (α=0.78), and moderate internal

consistency for the expectancy (α=0.55) and purposefulness (α=0.68) subscales (Heishman et al., 2009).

2.3.18 Study Context. A Study Context Questionnaire (see Appendix W) was developed and used to ask participants about the rooms they encountered. These items included open-ended questions asking participants to describe the rooms encountered during the study. Items also queried about the rooms similarity to where they regularly use cannabis, and their preference for the laboratory's or their own personal paraphernalia. Items were rated on a scale from 0 = *Not at all Similar* to 100 = *Completely Similar*.

2.3.19 Lounge room. The lounge room had a cool colour scheme (see Appendix X). The lounge room contained dark wooden coffee tables, a small dark wooden study desk with a wooden chair, a dark wooden TV unit with a flat screen TV and X-Box, and a brown-grey sofa and two brown recliners. The walls were pale grey-blue, with two blue and grey paintings, a clock, and a window to allow for natural light. The carpet was grey-blue and plush, there was a ceiling fan with a light, and both were on during the session. The room was set at 21°C and had a vanilla ambipur scented wall plug. Assorted items were scattered throughout the room, such as candles, magazines, plants, 'home sweet home' cushions, and a blue patchwork blanket. When entering the room a welcome sign hung on the door and there was a 'home sweet home' doormat. There were also 2 laptops and a portable IPod speaker on the coffee table that were connected to the Biopac MP150 system, which was hidden under the coffee table. The attached electrodes were hidden behind the cushions on the couch. A black clipboard was used to record answers in this room.

2.3.20 Therapist Office. The therapist's office had a warm colour scheme (see Appendix Y). The therapist's office consisted of an orange birch wood large custom-built desk and shelving unit, with matching cupboards, a black filing cabinet, large office chair, and a black round meeting table, with two black armchairs. The carpet was black and white

with an intricate pattern. The walls were painted bright orange with white sponging, four diplomas and an inspirational picture of a lion hung on the wall. There were no windows, fluorescent lights, and the room was set at 23.5°C. Items in the room included textbooks, a desktop computer, files, in trays, and office supplies. A green clipboard was used in this room to record responses.

2.4 Procedure

2.4.1 Recruitment. Participants expressed interest in the study that they found through advertisements placed on noticeboards and social media (see Appendix Z). Advertisements ran over 9 months and a total of 38 ads were included in newspapers and magazines. Participants were incentivised and compensated with up to $282 for participation in the study. Participants contacted the Behavioural Science Lab at Macquarie University via email or telephone if they were interested in the study, and were given more information and the opportunity to complete an eligibility interview. Participants completed the 25-minute eligibility interview over the phone and were allocated an identification number. Following the phone interview participants were notified of their eligibility and eligible participants booked appointments to participate. Participants who scored above 30 on the K.10 were informed of mental health care plans and prompted to seek treatment if they were not already in treatment.

Appointments were scheduled around the time of day when the participant would typically be smoking cannabis to ensure that the temporal context of cannabis smoking was consistent with their natural behaviour. There were two options for participation. Participants who chose the daily option came in every day for five days. Appointments last between 75 minutes and two hours. Alternatively, those who chose the intensive option would come in twice in five days; once for two hours to complete the eligibility session, and again four days later to complete the rest of the sessions. If participants smoked tobacco on average more

than five cigarettes every day, they were encouraged to complete the daily option to avoid significant withdrawal symptoms during intensive participation. Otherwise participants were free to choose which option they preferred. These options were included to maximise convenience and increase participation.

Participants were given a call the day before their appointment to remind them of the appointment times and abstinence requirements of the study. Participants were also asked what cannabis paraphernalia they were planning to bring and reminded not to bring any cannabis with them.

2.4.2 Eligibility Interview (Session 0). On arrival, participants were greeted and entered the consultation room (see Appendix AA). Participants provided informed consent (see Appendix AB). The purpose of the session was to gather information about the participants cannabis use. Participants then completed a TLFB Interview. If participants had used cannabis or other drugs in the last 12 hours they were asked to reschedule for the next week, if they had not used in the last 12 hours, they were able to continue with the session. The researcher had the last 30 days calculated on the calendar and discussed how many cones were smoked on each day in the past 30 days. Participants were also asked when they had their last cigarette or caffeinated beverage. The following questionnaires and assessments were then administered; SCID-RV, demographic questions, Brief Marijuana Consequences Questionnaire, Fagerstrom Test for Nicotine Dependence, Marijuana Motives Measure, Subjective Units of Cannabis Withdrawal, Contextual Cue Assessment and the Quit Session.

During this session urine was collected in a sterile screw top 70ml container, the samples were at least 20mls full. Urine was checked for warmth before it was stored for urinalysis. If eligible for further participation, mailing information was collected, participants' cannabis paraphernalia was collected, they were reminded of their appointments, to remain abstinent, and not to consume any tobacco or caffeine 2 hours prior

to their remaining appointments. Participants who smoked tobacco cigarettes were also asked to continue smoking the same number of cigarettes throughout the study and not increase their use. Ineligible participants were thanked for their time and their payment details were collected.

2.4.3 Pre-Exposure Assessment (Session 1). Participants waited in a waiting room for the researcher. Once greeted, participants were escorted to the lounge room and personal belongings were taken and placed out of sight to avoid distractions. Participants were explained the purpose of the session and asked whether they had maintained abstinence. The research assistant used the TLFB to record use of cigarettes and caffeine since the Session 0 appointment. Participants were also asked if they had any alcohol, sedatives, stimulants, opioids, cocaine, hallucinogens, or any other drugs. Participants then completed the Subjective Units of Cannabis Withdrawal interview.

Participants were connected to the Biopac MP150 system with electrodes. ECG electrodes were placed on the top right and left shoulder and the top left of the pelvis, and the two electrodes measuring EDA were placed on the palm of the right hand. Once connected, they were instructed to listen to the audio track and follow the instructions. The 26.5-minute audio track instructed participants to imagine and visualize different scenarios and report on their cravings. They were told there would be a gap in the audio of about 10 seconds for them to answer the questions asked by the audio track; they were instructed to give only one response that best reflected what they were feeling. They would not be able to return to a question once it had been asked. Participants were also informed of the sensitivity of the equipment and were asked to get comfortable and stay as still as possible. The participants then listened to the audio track. The Acq*Knowledge* 4 software was used to record physiological responses and track each new phase in the audio track. The baseline period encouraged participants to focus on the characteristics of the room. Following the baseline

period, the neutral script described a scene at the beach lying on a towel, with friends, in the sun, it described sensations in the environment and included beach sounds such as waves. Following a second baseline period, the craving script described feeling relaxed in a comfortable chair, watching friends pass a bong around, thinking about how enjoyable it would be to smoke a cone. The script included sounds associated with smoking such as the bubbling of a bong, burning of the cone, and the sound of smoke being exhaled. The baseline, neutral and cannabis phases were followed by the Subjective Units of Craving and Tolerance questions. During the baseline phase participants were asked to focus on the characteristics of the room. The process can be seen in Figure 1.

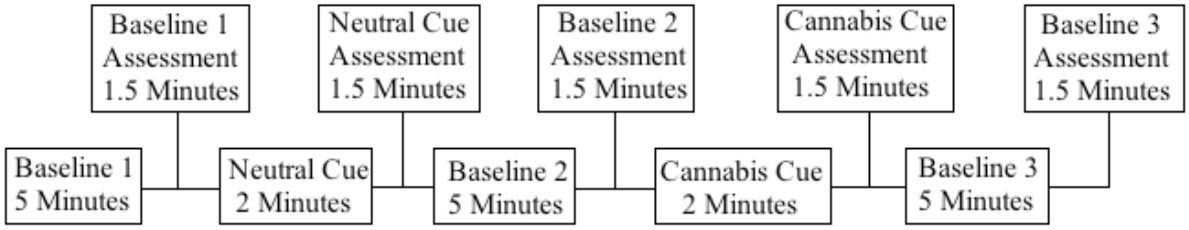


Figure 1. The progression of the cue-reactivity paradigm during Session 1 and Session 4.

Following this, the electrodes were removed and participants were given the DTS to complete. They then were asked to complete the MTPT-C on a laptop as the study desk. Before finishing the session participants were asked to complete the MCQ. Those who scored above 14 on any subscale were asked to stay until their cravings reduced. Participants were given the option to watch television on the television in the waiting room until their cravings reached an acceptable level. If participants insisted on leaving, they were called after the appointment to ensure their cravings were manageable, and if cravings were intolerable they were encouraged to distract themselves. Participants who scored under 14 on any of the subscales were thanked for their time and allowed to leave. At the end of each session participants were thanked for their time and reminded of their abstinence requirements. Participants were eligible if their cravings increased by 10 points from the neutral cue to the

cannabis cue. Eligible participants were reminded of the time and place of their following appointments. Those ineligible were excluded from participation.

2.4.4 Cue-Exposure Sessions (Sessions 2-3). A different experimenter to the one encountered in Session 1 and 4 conducted Session 2 and Session 3. Participants were blind to their random allocation to an ABA or an AAA condition before the start of the cue-exposure session. Those who were randomly allocated to the AAA condition received cue-exposure therapy in the lounge room (context A). Those randomly allocated to the ABA condition received cue-exposure therapy in the therapist office (context B).

Participants completed the same TLFB protocol as in Session 1. Participants then completed the Subjective Units of Cannabis Withdrawal interview. The cue-exposure session then began with the experimenter explaining that the aim of the session is to discover what happens to cravings for cannabis when presented with objects that remind them of their use. Participants were going to be interacting with their own five cannabis related objects over the next two cue-exposure sessions. Each object was presented individually, and then together, with each exposure lasting 15 minutes. Ranking of paraphernalia was taken from the Contextual Cue Assessment wherein the least provoking paraphernalia was presented first. A scene description (see Appendix AC) was used during cue exposure to help participants imagine their smoking environment. The scene described a lounge room with friends smoking nearby, the scene was made realistic to the participant by using information obtained from the Contextual Cue Assessment. Additionally, participants were encouraged to make the scene realistic to them. Two of five descriptive paragraphs were also integrated in the story based on the top two scoring motives in the Marijuana Motives Measure based on social motivations, smoking for enhancement, coping, expansion or conformity to enhance the scene (Simons et al., 1998). Additionally, the Subjective Units of Craving and Tolerance

Progression Form tracked their level of craving and tolerance at the beginning, middle and end of each exposure session.

Before the first item was given to participant, they were asked to look around the room and describe what they saw. When the first item was given to the participant and they were asked to engage with the object using their senses such as sight, touch, sound, and smell, and report on their level of craving and tolerance. The participant was asked to engage with the object, and describe each sensation. The participant was also encouraged to describe or show the rituals and motions associated with the object. The participant was asked to imagine a scene based on the Marijuana Motives Measure that reminded them of their use and encouraged to make the scene realistic to them. The participant was informed to stay in the moment and let their cravings arise and fall naturally. They continued focusing on their cravings, scenes and sensations, engaging with the object until the end of the 15 minutes. This process was repeated for each item, separately, and then all items together to deepen the extinction (Rescorla, 2006). Two-minute breaks were given in between cue exposure to each item and the participant was encouraged to talk or think about things to distract themselves. Participants completed the MCQ and the same protocol for ending the session was followed as in Session 1.

2.4.5 Post-Exposure Assessment (Session 4). The structure of the final session followed the same structure as the first session. The TLFB was conducted followed by the Subjective Units of Cannabis Withdrawal interview. Participants then underwent the exposure assessment listening to the audio and observing cues while connected to Biopac MP150 system and then completed the DTS and the MTPT-C. In addition, the Study Context Questionnaire was administered. As in Session 0, urine was collected in a sterile screw top 70ml container; the sample was checked for warmth before it was stored. Upon completion of

the study participants were debriefed about the study and informed of its purpose (see Appendix AD).

2.4.6 Intensive Participation. Those who decided to participate intensively had slight differences in the procedure form those who participated daily. First, participants were given breaks between each session in the waiting room. Participants had a 10-minute break between the first and second session. Between Session 2 and 3 participants had a 22-minute break where they could watch TV. Between Session 3 and Session 4 there was a 45-minute break where participants could eat, watch TV or surf the Internet. The waiting room contained two TVs on the wall, a kitchenette, and a large long table with numerous yellow dining chairs.

Second, some measures were not administered in each session since it would have been redundant. The Subjective Units of Cannabis Withdrawal interview and the TLFB was only administered at the start of Session 1. Additionally, the Marijuana Craving Questionnaire was only administered at the end of Session 4.

2.4.7 Payment for Participation. Participants received up to $282 for participating in this study. Participants received $50 for completing Session 0, $25 for completing Session 1, $50 for completing Session 2, $50 for completing Session 3, and $50 for completing Session 4. Participants could also earn up to $7 for their performance on the MTPT-C during Sessions 1 and 4. Reimbursement occurred through bulk deposits into participants' bank accounts within one month of completing the study. In addition, participants whose ongoing abstinence was verified by the urine drug screens received an additional payment of $50.

As an additional incentive, participants earned $30 for each friend that they referred into the study. The friend must have completed Session 0 and nominate the referee. This method of recruitment is referred to as snowball sampling (Biernacki & Waldorf, 1981). This can yield a sample through the referrals made by people who know others that share the same characteristics (Biernacki & Waldorf, 1981).

2.4.8 Confirmation of Abstinence. Abstinence from cannabis and all drugs was confirmed using the TLFB and urinalysis. Following completion of the study participants' urine was taken to the Drug Toxicology Unit at the NSW Forensic & Analytical Science Service. Creatinine normalized urine THC-COOH levels were compared between the first appointment and the final appointment. Any participant with a stable or an increase in urine THC-COOH levels was excluded from analysis and did not receive their abstinence payment. Those who had cocaine, benzodiazepines, amphetamines and opiates in their system were not discarded from the study, but did not receive their abstinence payment.

Results

3.1 Recruitment and Participant Flow

Over a total of nine months 38 ads were used to generate interest in the study. Three hundred participants were interviewed for the study. Of the entire sample, 15.33% (n=46) were eligible. Of those who were eligible, we encountered a 47.83% drop out rate. Only 5.33% (n=16) of the entire sample could be included in the final sample. The flow of participants through each stage of the study can be observed in Figure 2. This highlights the number of exclusions at each stage and the reasons for exclusion.

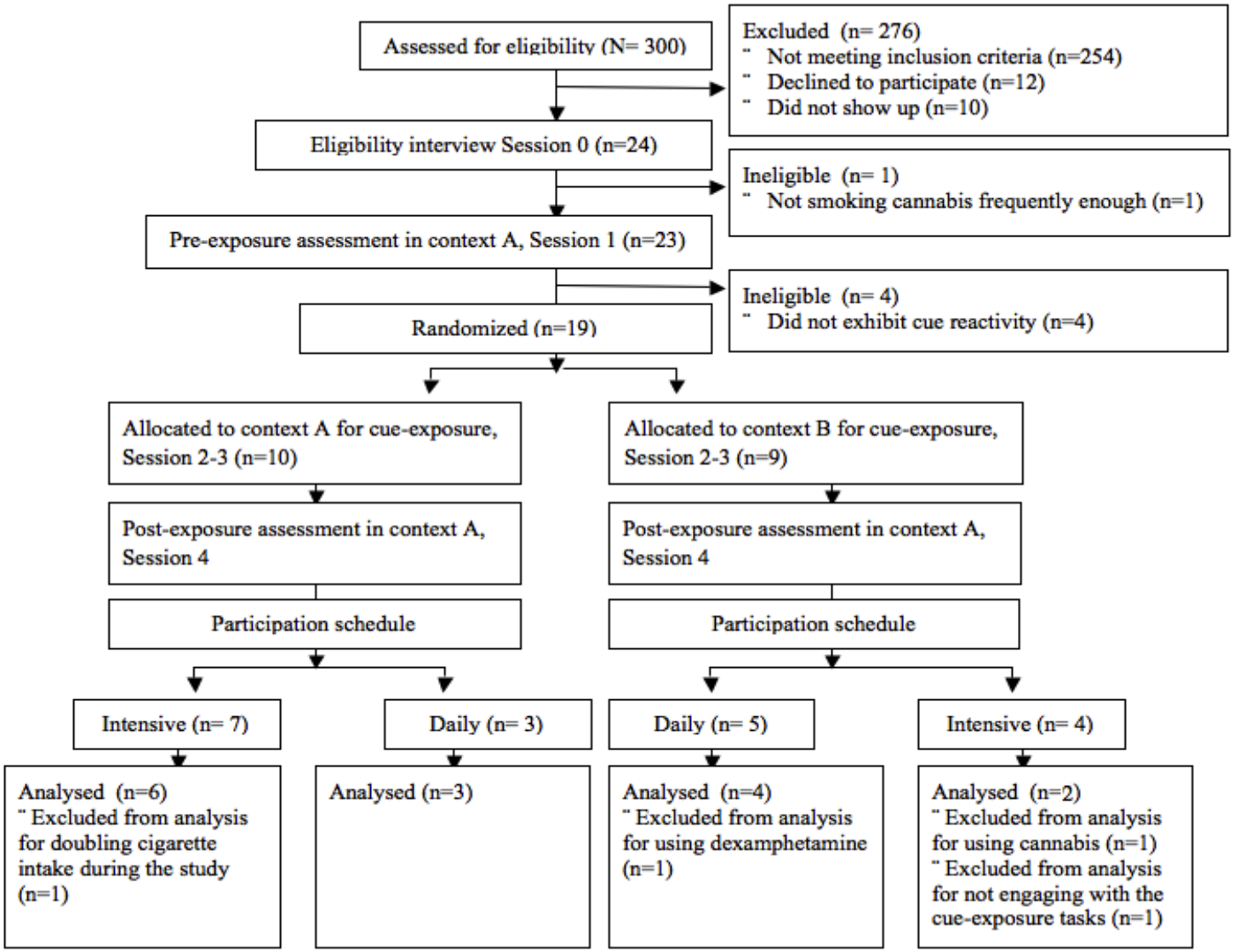


Figure 2. CONSORT Flow chart. This figure illustrates the flow of participants through the study.

3.2 Demographic Information and Clinical Characteristics

The final sample consisted of 15 participants, age ranged from 18 to 26 (*M* = 21.80, 95% CI = [20.38, 23.22]) and 53.3% (n=8) were male. Participants smoked cannabis on *M* = 25.80 (95% CI = [23.76, 27.84]) of the last 30 days smoking approximately *M* = 7.60 (95% CI = [4.12, 11.07]) cones per day. Participants also smoked tobacco cigarettes on *M* = 22.80 95% (CI = [18.34, 27.26]) of the last 30 days. The means and confidence intervals of the demographic and clinical characteristics can be seen in Table 1.

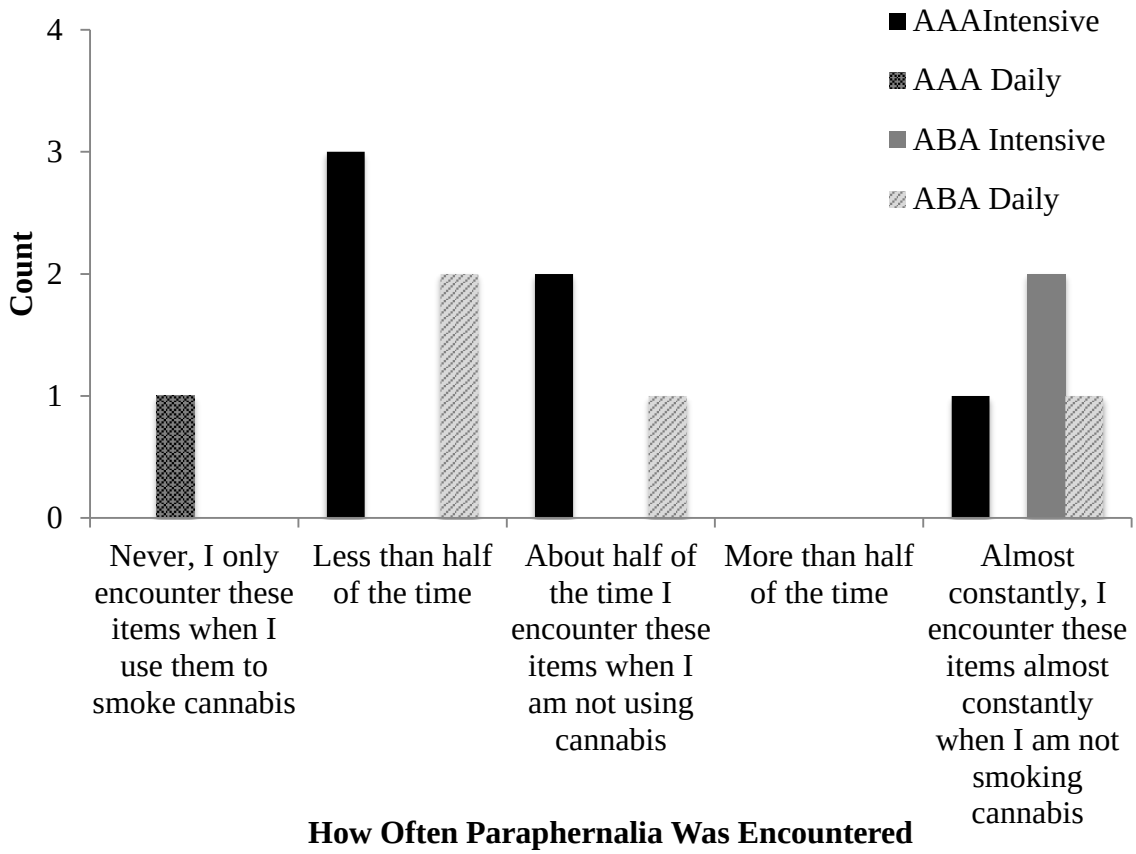
Table 1

Demographic Information and Clinical Characteristics within the AAA and ABA Conditions

Condition	AAA N=9	AAA Intensive N=6	AAA Daily N=3	ABA N=6	ABA Intensive N=2	ABA Daily N=4
Gender proportion male	55.56	66.67	33.33%	50.00%	100%	75.00
[95% CI]	[22.22, 88.89]	[33.33, 100.00]	[0.00, 100.00]	[16.67, 83.33]		[25.00, 100.00]
Age	20.67	21.00	20.00	23.50	26	22.25
M [95% CI]	[18.86, 22.47]	[18.52, 23.48]	[12.43, 26.57}	[21.43, 25.57]		[21.45, 23.05]
Days smoked cigarettes out of	19.11	15.83	25.67	28.33	30	27.50
30 days	[12.93, 25.29]	[8.11, 23.56]	[12.92, 38.41]	[24.05, 32.62]		[19.54, 35.46]
M [95% CI]						
Cigarettes daily	4.33	3.83	5.33	8.67	3.00	11.50
M [95% CI]	[2.06, 6.61]	[1.48, 6.17]	[-5.87, 16.53]	[-0.30, 17.64]	[-22.41, 28.41	[=3.34, 26.34]
Days smoked cannabis out of	25.78	25.67	26.00	25.83	23.00	27.25
last 30 days	[23.72, 27.84]	[22.37, 28.96]	[21.03, 30.97]	[20.42, 31.24]	[-15.12, 61.12]	[18.50. 36.00]
M [95% CI]						
Cones daily	5.88	5.07	7.50	10.17	2.47	14.02
M [95% CI]	[4.19, 7.57]	[3.29, 6.85]	[1.29, 13.71]	[0.24, 20.10]	[0.77, 4.16]	[-1.05, 29.10]
SCID proportion with severe	88.88%	100%	[a]66.67%	100%	100%	100%
CUD [95% CI]	[66.67, 100.00]		[0.00, 100.0]			

Note. SCID = Structured Clinical Interview for DSM Disorders, CUD = Cannabis Use disorder. [a]= 33.33% met criteria for mild cannabis use disorder.

Habits regarding cannabis use were collected from the Contextual Cue Assessment. All participants smoked cannabis most frequently in a lounge room or a lounge like environment. How often participants encountered their cannabis paraphernalia when not using cannabis in the month prior to participation can be seen in Figure 3. It appears that in the AAA group, and the ABA Daily group items are most often encountered half of the time or less, when not using cannabis. While those in the ABA Intensive group encounter the items almost constantly when not smoking cannabis.



Note: 2 cases missing from the AAA Daily condition
Figure 3. How often participants encountered their personal paraphernalia in the last month when not smoking cannabis across all conditions.

The scores on the Subjective Units of Cannabis Withdrawal Scale were averaged to create a total withdrawal score, see Table 2. High scores indicated greater severity of total withdrawal. Participants overall withdrawal on Day 0 (*M*=23.97, 95% CI = [16.56, 31.38])

was lower than on Day 4 (*M*=44.37, 95% CI = [36.30, 52.43]). Overall, it appears as though withdrawal was more severe on the fifth day of abstinence. The ABA intensive group scored higher severity of withdrawal symptoms overall.

Table 2

Overall Withdrawal Experienced During the Study

	Withdrawal Day 0 M [95% CI]	Withdrawal Day 1 M [95% CI]	Withdrawal Day 4 M [95% CI]
AAA	24.57 [13.03, 36.11]	-	44.68 [34.44, 54.92]
AAA Intensive	22.76 [6.90, 38.62]	-	44.31 [28.54, 60.08]
AAA Daily	28.19 [-14.95, 71.33]	44.62 [22.81, 66.43]	42.43 [0.30, 84.56]
ABA	23.07 [10.69, 35.45]	-	43.69 [26.06, 61.32]
ABA Intensive	37.50 [14.81, 60.19]	-	55.00 [9.62, 100.38]
ABA Daily	15.86 [8.44, 23.27]	37.32 [25.07, 49.58]	38.04 [8.96, 67.11]

3.3 Cue Reactivity, Cravings and Physiological Responses

Self-reported cravings and physiological responses of GSR and HR were collected to examine cue reactivity and cravings throughout the sessions. Average reported cravings and physiological reactivity can be seen in Table 3. The table indicates that all groups show an increase in self-reported cravings from the neutral to the cannabis cue during Session 1 (*M*= 33.53, [95% CI = 23.99, 43.08]), indicating reactivity to the cannabis paraphernalia. Similarly, all groups show an increase in EDA from the neutral cue to the cannabis cue during Session 1(*M* = 1.58, 95% CI = [0.61, 2.54]). Indicating more skin conductance during the presentation of the cannabis cue. HR increases overall, across conditions (*M* = 2.06, 95% CI = [1.09, 5.20]). Yet, the AAA groups demonstrate almost no change in HR from the neutral cue to the cannabis cue. While the ABA groups show an increase in HR to the cannabis cue.

Table 3

Mean Cravings in the AAA and ABA Conditions

Measure	AAA M [95% CI] N=9	AAA Intensive M [95% CI] N=6	AAA Daily M [95% CI] N=3	ABA M [95% CI] N=6	ABA Intensive M [95% CI] N=2	ABA Daily M [95% CI] N=4
Cravings During N Cue Assessment, Pre-Exposure	37.22 [17.99, 56.45]	38.33 [10.04. 66.62]	35.00 [-29.54, 99.54]	29.17 [2.12, 56.21]	12.50 [-19.27, 44.27]	37.50 [-8.20, 83.20]
Cravings During C Cue Assessment, Pre-Exposure	68.67 [51.08, 86.25]	65.50 [40.86, 90.14]	75.00 [12.90, 137.10]	65.83 [45.53, 86.83]	72.50 [40.73, 104.27]	62.50 [24.34, 100.66]
Craving Difference from N to C Cue During Assessment, Pre-Exposure	31.44 [19.50, 43.38]	27.17 [10.57, 43.77]	40.00 [7.14, 72.86]	36.67 [14.99, 58.34]	60.00 [-3.53, 123.53]	25.00 [5.51, 44.49]
Peak HR During N Cue Assessment, Pre-Exposure	110.69 [93.59, 129.79]	115.14 [87.56, 142.72]	101.79 [80.42, 123.17]	86.15 [75.62, 96.67]	89.10 [-57.99, 236.18]	84.67 [71.40, 97.95]
Peak HR During C Cue Assessment, Pre-Exposure	110.41 [93.01, 127.81]	115.27 [86.98, 143.57]	100.69 [89.89, 111.48]	91.71 [83.28, 100.13]	96.60 [29.61, 163.58]	89.26 [76.42, 102.09]
Difference in Peak HR to N and C Cue During Assessment, Pre-Exposure	-0.28 [-3.14, 2.58]	0.14 [-3.75, 4.02]	-1.11 [-12.10, 9.89]	5.56 [-1.39, 12.50]	7.50 [-72.60, 87.60]	4.59 [-5.81, 14.99]
Peak EDA During the N Cue Assessment, Pre-Exposure	5.60 [0.43, 10.77]	3.67 [1.45, 5.89]	9.46 [-19.55, 38.47]	10.26 [1.53, 18.99]	7.20 [-13.59, 28.00]	11.79 [-4.46, 28.04]
Peak EDA During the C Cue Assessment, Pre-Exposure	7.02 [1.17, 12.87]	4.93 [1.87, 7.99]	11.21 [-21.28, 43.70]	12.07 [4.28, 19.86]	11.13 [-22.18, 44.44]	12.54 [-2.25, 27.32]
Difference in EDA Response to N and C Cue During Assessment, Pre-Exposure	1.42 [0.27, 2.57]	1.26 [-0.15, 2.67]	1.75 [-3.36, 6.85]	1.81 [-0.49, 4.10]]	3.92 [-8.59, 16.44]	0.75 [-1.93, 3.42]
End of Session Cravings to All Personal Paraphernalia, Session 2	61.67 [44.37, 78.96]	55.83 [33.72, 77.95]	73.33 [12.06, 134.60]	46.67 [13.84, 79.49]	50.00 [-77.06, 177.06]	45.00 [-17.70, 107.70]
End of Session Cravings to All Personal Paraphernalia, Session 3	49.56 [29.37, 69.74]	49.17 [24.91, 73.42]	50.33 [-43.29, 143.95]	40.83 [5.49, 76.18]	75.00 [-115.59, 265.59]	23.75 [-14.34, 61.84]
Cravings During N Cue Assessment,	24.78	24.17	26.00	23.33	40.00	15.00

Post-Exposure	[4.04, 45.52]	[-2.05, 50.39]	[-65.21, 117.21]	[2.70, 43.97]	[-87.06, 167.06]	[-12.56, 42.56]
Cravings During C Cue Assessment, Post-Exposure	40.22 [17.87, 62.57]	43.67 [15.38, 71.96]	33.33 [-61.53, 128.20]	50.83 [14.57, 87.10]	87.50 [-71.33, 246.33]	32.50 [-4.53, 69.53]
Craving Difference from N to C Cue During Assessment, Post-Exposure	15.44 [3.24, 27.65]	19.50 [0.68, 38.32]	7.33 [-11.31, 25.98]	27.50 [3.86, 51.14]	47.50 [-238.39, 333.39]	17.50 [0.94, 34.06]
Peak HR During the N Cue Assessment, Post-Exposure	101.21 [89.61, 112.81]	100.58 [80.80, 120.37]	102.46 [91.68, 113.23]	88.73 [77.29, 100.17]	87.59 [82.72, 92.47]	89.29 [66.98, 111.61]
Peak HR During the C Cue Assessment, Post-Exposure	105.72 [84.31, 127.13]	108.06 [71.46, 144.66]	101.03 [92.25, 109.82]	92.69 [88.75, 86.64]	91.47 [80.84, 102.10]	93.31 [85.92, 100.69]
Difference in Peak HR to N and C Cue During Assessment, Post-Exposure	4.51 [-7.34, 16.36]	7.48 [-12.03, 26.99]	-1.42 [-8.34, 5.50]	3.97 [-4.51, 12.45]	3.88 [-11.53, 19.38]	4.01 [-12.50, 20.53]
Peak EDA During the N Cue Assessment, Post-Exposure	4.26 [2.51, 6.01]	4.70 [2.40, 7.01]	3.36 [-3.12, 9.85]	11.07 [2.65, 19.49]	2.92 [-26.97, 32.80]	15.15 [5.45, 24.85]
Peak EDA During the C Cue Assessment, Post-Exposure	4.79 [2.72, 6.87]	5.56 [2.63, 8.47]	3.25 [-1.97, 8.49]	13.49 [2.56, 24.42]	3.94 [-39.46, 47.34]	18.26 [3.86, 32.66]
Difference in Peak EDA to N and C Cue During Assessment, Post-Exposure	0.53 [-0.50, 1.56]	0.85 [-0.67, 2.38]	-0.11 [-2.59, 2.38]	2.42 [-1.27, 6.11]	1.02 [-12.49, 14.54]	3.12 [-3.61, 9.84]

Note. N= neutral, C= cannabis, HR= heart rate, EDA= Electrodermal Activity

Self-reported cravings across all sessions can be observed in Figure 4. The figure indicates the most evident decline in self-reported cravings across all sessions in the AAA Daily condition, which appears stable from Session 1 to Session 2, but then declines from Session 2 to Session 4. Self-reported cravings consistently decline across all sessions in the AAA Intensive condition. Further, a decrease in self-reported cravings is observed in the ABA Intensive condition from Session 1 to Session 2, followed by an increase from Session 2 to Session 4. Finally in the ABA Daily condition self-reported cravings increase from Session 1 to Session 2, decrease from Session 2 to Session 3, and Increase from Session 3 to Session 4.

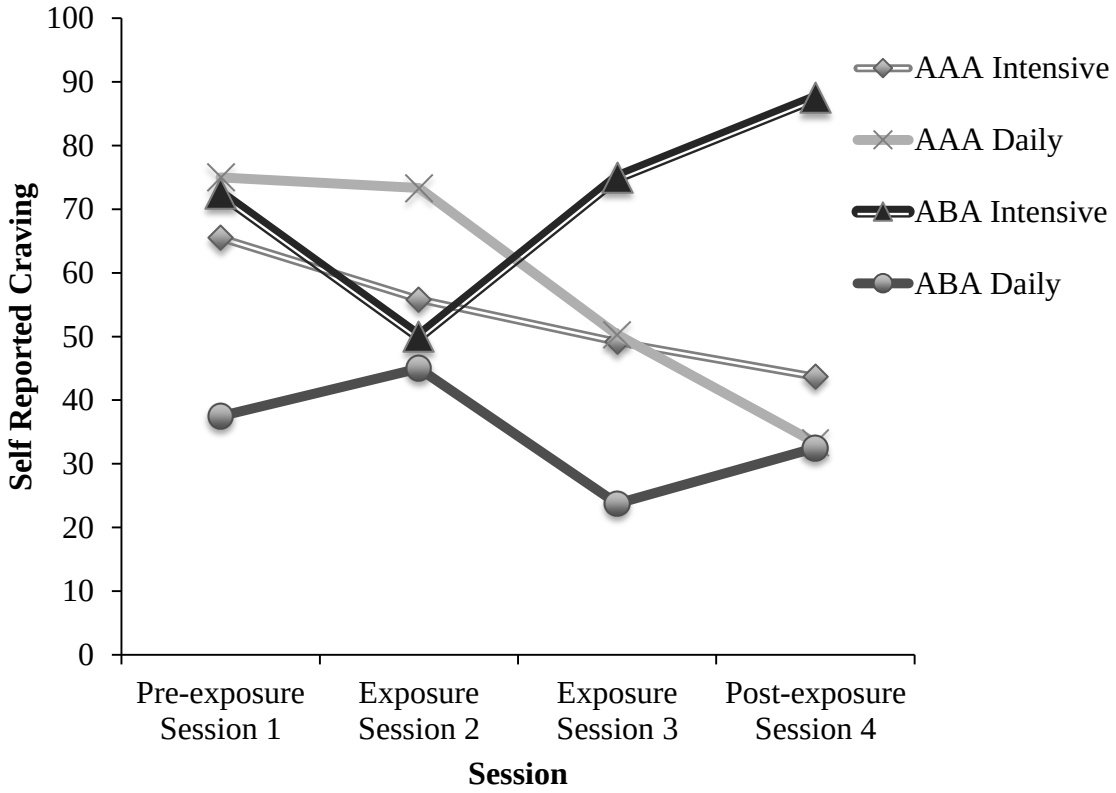


Figure 4. Average self-reported cravings across all sessions for each condition.

Self-reported cue reactivity was examined pre and post-exposure. Self-reported cue reactivity pre-exposure in Session 1 and post-exposure Session 4 can be seen in Figure 5. The graph indicates a decline in means from Session 1 to Session 4, which appears to be most evident in the AAA Daily condition.

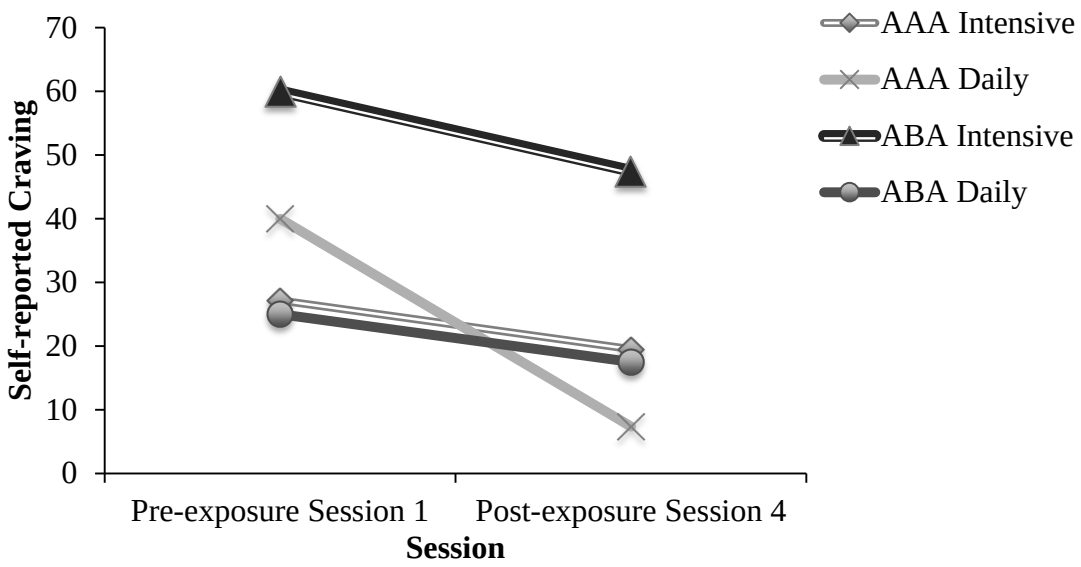


Figure 5. Mean difference in self-reported cravings between neutral and cannabis cues from pre-exposure in Session 1 to post-exposure Session 4.

Physiological cue reactivity during pre-exposure in Session 1 and post-exposure Session 4 was examined for each condition. Changes in EDA (see Figure 6) indicate a decline in means from Session 1 to Session 4, which appears to be most evident in the AAA daily and ABA Intensive condition. Second, the ABA daily condition shows an increase in responding from Session 1 to Session 4.

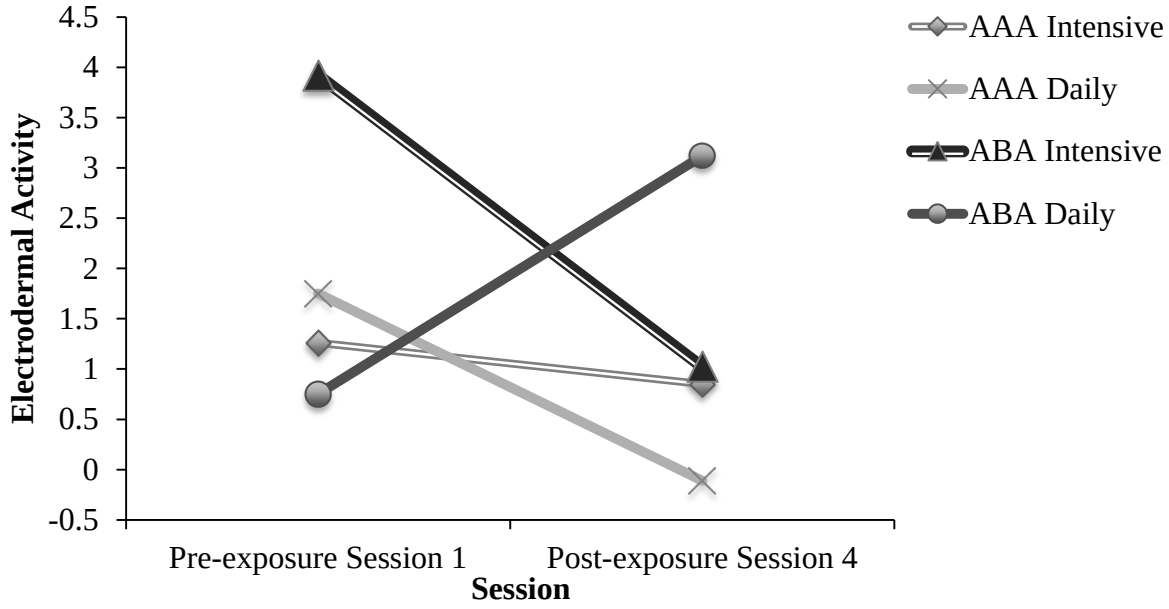


Figure 6. Mean difference in the EDA between neutral and cannabis cues from pre-exposure in Session 1 to post-exposure Session 4.

Changes in HR (see Figure 7) indicate a decline in the difference in HR in the ABA Intensive condition between neutral and cannabis cues from Session 1 to Session 4. While the AAA Intensive group had a greater difference in heart rate at Session 4 than Session 1. Finally, the AAA Daily and ABA Daily group had no trend of an increase or decrease following treatment.

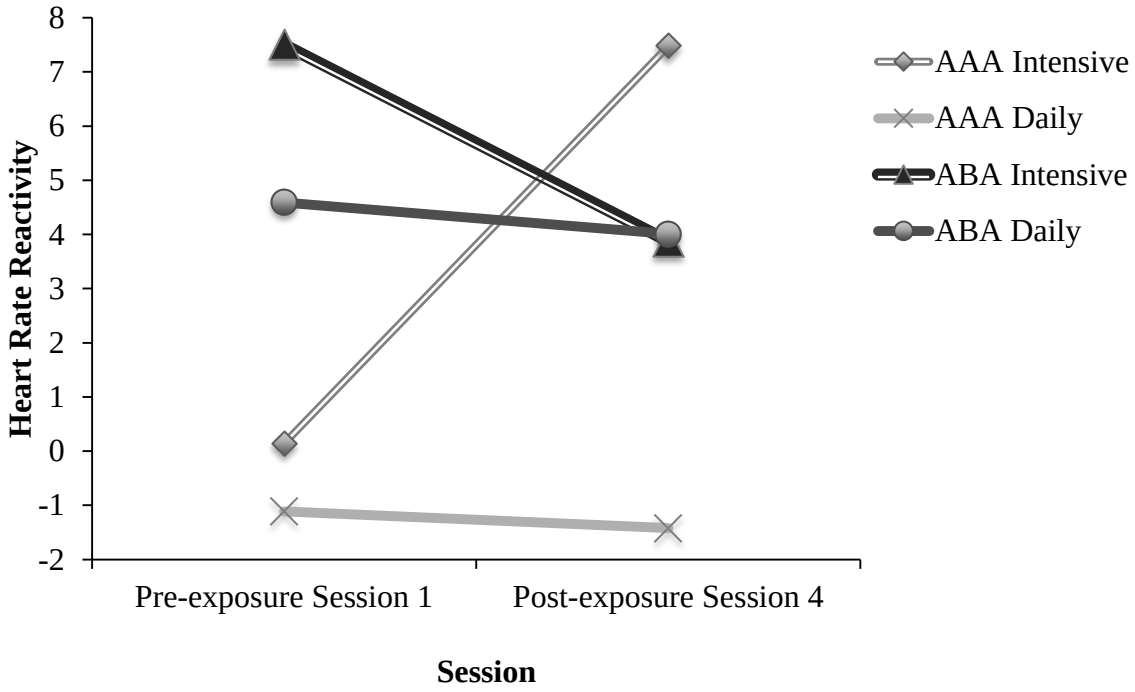


Figure 7. Mean difference in HR between neutral and cannabis cues from pre-exposure in Session 1 to post-exposure Session 4.

3.4 Intolerance for Distress

Average reported Intolerance for cravings can be seen in Table 4. Across all conditions, greater average intolerance of cravings is observed towards the cannabis cues than the neutral cues in Session 1 (*M*= 27.60, 95% CI = [15.37, 39.83]). The AAA Daily and ABA Intensive conditions revealed the greatest change in intolerability of cravings from the neutral cue to the cannabis cue in Session 1.

Table 4

Mean Intolerance in the AAA and ABA Conditions

Measure	AAA M [95% CI] N=9	AAA Intensive M [95% CI] N=6	AAA Daily M [95% CI] N=3	ABA M [95% CI] N=6	ABA Intensive M [95% CI] N=2	ABA Daily M [95% CI] N=4
Intolerance During N Cue Assessment, Pre-Exposure	23.67 [2.19, 45.15]	27.17 [-7.83, 62.16]	26.67 [-21.28, 54.61]	15.83 [-2.47, 34.14]	7.50 [-87.80, 102.80]	20.00 [-11.82, 51.82]
Intolerance During C Cue Assessment, Pre-Exposure	49.11 [24.40, 73.82]	40.00 [2.90, 77.10]	67.33 [27.18, 107.49]	46.67 [15.95, 77.38]	62.50 [30.73, 94.27]	38.75 [-15.75, 93.25]
Intolerance Difference from N to C Cue During Assessment, Pre-Exposure	25.44 [7.61, 43.28]	12.83 [0.95, 24.71]	50.67 [0.90, 100.43]	30.83 [7.74, 53.92]	55.00 [-8.53, 118.53]	18.75 [-4.10, 41.60]
DTS Pre-Exposure	[a]2.94 [2.19, 3.69]	3.08 [2.31, 3.85]	2.71 [a][-0.74, 6.16]	2.80 [1.66, 3.94]	2.13 [0.44, 3.83]	3.13 [1.17, 5.10]]
MTPT-C Seconds Latency to Termination Pre-Exposure	162.78 [63.36, 262.19]	168.08 [0.97, 335.18]	152.18 [10.06, 294.30]	242.71 [94.97, 390.44]	292.78 [-1324.11, 1909.68]	217.67 [-5.81, 441.15]
MTPT-C Errors Pre-Exposure	66.33 [5.29, 127.37]	74.17 [-28.22, 176.56]	50.67 [-22.79, 124.12]	84.67 [4.77, 164.56]	39.00 [-62.65, 140.65]	107 [-30.59, 245.59]
End of Session Intolerance to All Personal Paraphernalia, Session 2	26.67 [6.98, 46.36]	20.83 [-6.62, 48.28]	38.33 [-22.94, 99.60]	26.67 [-9.02, 62.36]	27.50 [-131.33, 186.33]	26.25 [-41.69, 94.19]
End of Session Intolerance to All Personal Paraphernalia, Session 3	20.78 [4.78, 36.77]	22.50 [-1.60, 46.60]	17.33 [-31.49, 66.16]	19.17 [-2.39, 40.72]	40.00 [-87.06, 167.06]	8.75 [-13.88, 31.38]
Intolerance During N Cue Assessment, Post-Exposure	15.67 [-5.81, 37.14]	12.83 [-16.70, 42.37]	21.33 [-59.94, 102.60]	7.50 [-4.81, 19.81]	15.00 [-175.59, 205.59]	3.75 [-3.87, 11.37]
Intolerance During C Cue Assessment, Post-Exposure	19.00 [-2.39, 40.39]	18.83 [-11.96, 47.62]	21.33 [-59.94, 102.60]	25.83 [-5.02, 56.68]	.00 [-262.66, 372.66]	11.25 [-9.67, 32.17]
Intolerance Difference from N to C Cue During Assessment, Post-Exposure	3.33 [-0.39, 7.06]	5.00 [-0.51, 10.51]	0	18.33 [-1.76, 38.43]	40.00 [-87.06, 167.06]	7.50 [-6.28, 21.28]
DTS Post-Exposure	3.07	3.27	2.73	2.96	2.33	3.27

	[2.26, 3.88]	[2.46, 4.08]	[-0.92, 6.39]	[1.77, 4.14]	[0.64, 4.03]	[1.17, 5.36]
MTPT-C Seconds Latency to Termination Post-Exposure	133.42 [2.93, 263.90]	108.01 [-59.51, 275.54]	184.22 [-347.08, 715.51]	205.38 [22.61, 388.14]	216.18 [-2373.99, 2806.36]	199.97 [-39.24, 439.87]
MTPT-C Errors Post-Exposure	63.89 [-9.90, 137.68]	66.33 [-55.80, 188.47]	59.00 [-75.76, 193.76]	76.83 [15.66, 138.00]	75.50 [-6.70, 161.70]	77.50 [-6.70, 161.70]

Note. N= neutral, C= cannabis [a] = 1 missing case, DTS = Distress Tolerance Scale, MTPT-C = Mirror Tracing Persistence Task – Computerised.

To examine intolerability in a cannabis using population, self-reported intolerance for cravings across all sessions can be seen in Figure 8. The figure indicates a decline in intolerability of cravings in the AAA Daily condition and ABA Daily condition from Session 1 to Session 3, and appears stable from Session 3 to Session 4. In the AAA Intensive and ABA Intensive condition there was a decrease in the intolerability of cravings from Session 1 to Session 2. The intolerability of cravings appear stable from Session 2 to Session 4 in the AAA Intensive condition, but intolerability increases from Session 2 to Session 4 in the ABA Intensive condition.

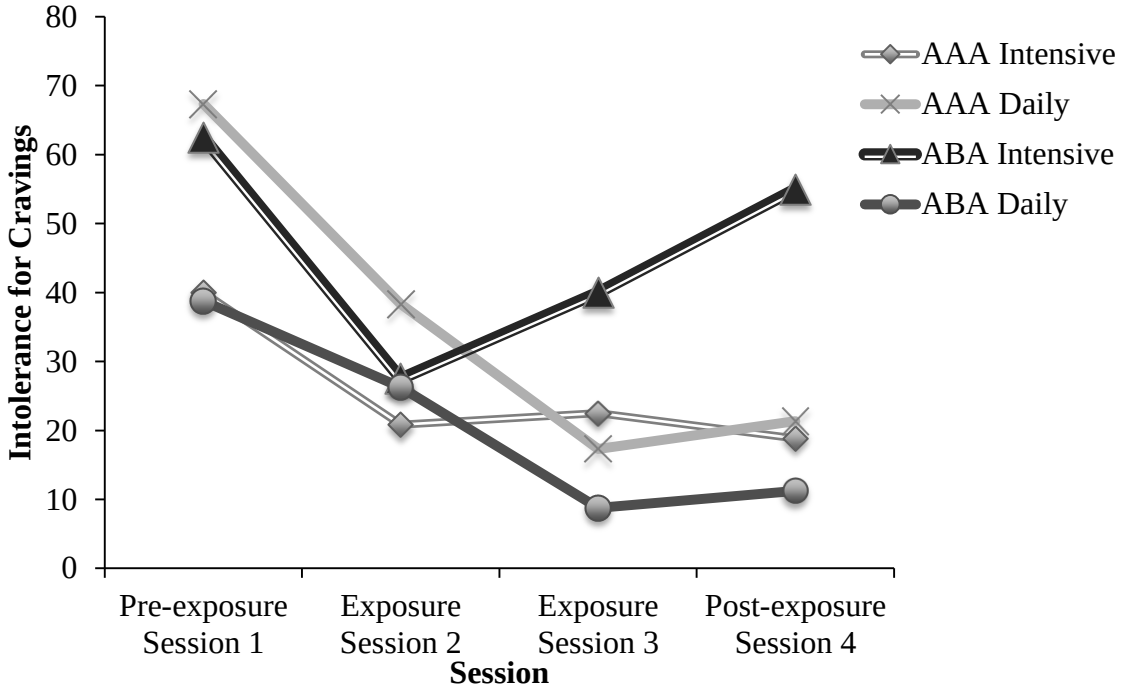


Figure 8. Average self-reported intolerance to cravings across all sessions; lower scores indicate greater tolerance of cravings.

To further examine intolerance in cannabis using population, intolerance of cravings was examined in Session 1 and Session 4 pre and post-exposure. The difference in self-reported intolerance of cravings between the neutral cue and the cannabis cue from Session 1 to Session 4 for each condition is seen in Figure 9. The graph indicates a decline in intolerability from pre to post exposure, which appears to be most evident in the AAA Daily condition.

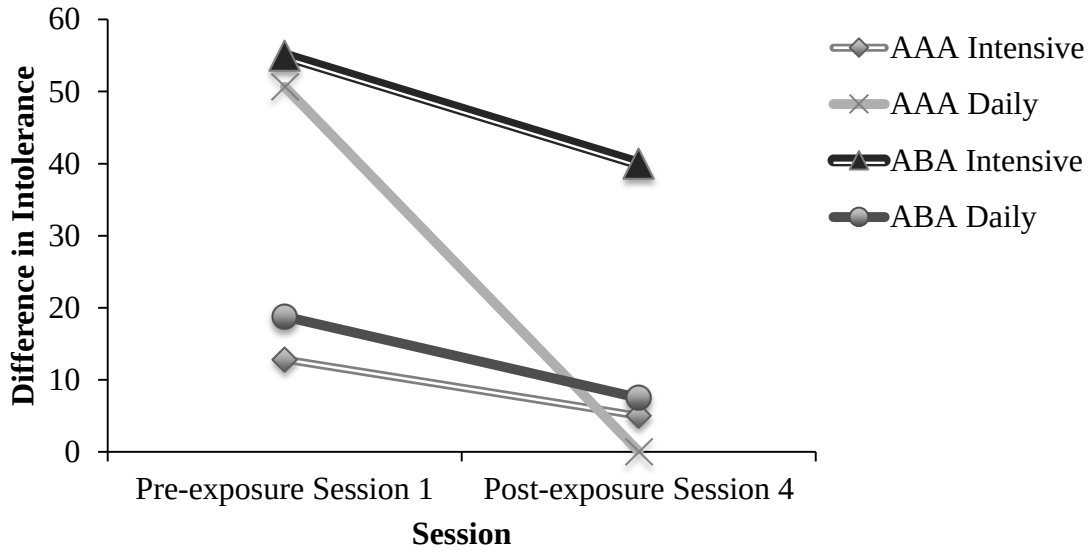


Figure 9. Mean difference in self-reported intolerability between neutral and cannabis cues from pre-exposure in Session 1 to post-exposure Session 4.

Furthermore, to examine overall distress tolerance, a self-report measure was used in Session 1 and Session 4. Average scores on the DTS at Session 1 and Session 4 can be seen in Figure 10. This Figure indicates almost no change in self-reported distress tolerance from Session 1 to Session 4 in all groups.

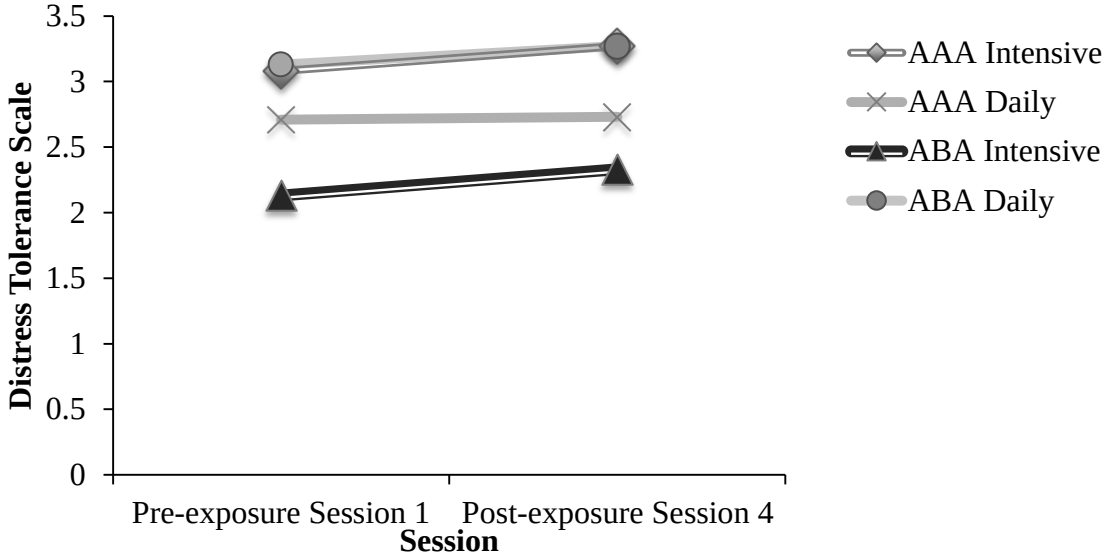


Figure 10. Total average distress tolerance scores from the Distress Tolerance Scale in Session 1 and Session 4 for all conditions.

The MTPT-C was used in Session 1 and Session 4 as a behavioural measure of distress tolerance. The time taken to terminate the MTPT-C task can be observed in Figure 11. The graph indicates that the AAA Daily group spent more time on the MTPT-C in Session 4. The AAA Intensive and ABA Intensive groups spent less time on the distressing task in Session and the time taken to terminate the task in the ABA Daily group appears to be stable across sessions. Furthermore, the average number of errors committed during the MTPT-C in Session 1 and Session 4 can be seen in Figure 12. The AAA Daily and AAA Intensive condition appeared to commit a similar number of errors in Session 1 and Session 4. Those in the ABA Intensive condition committed more errors in Session 4, and the ABA Daily condition committed fewer errors in Session 4.

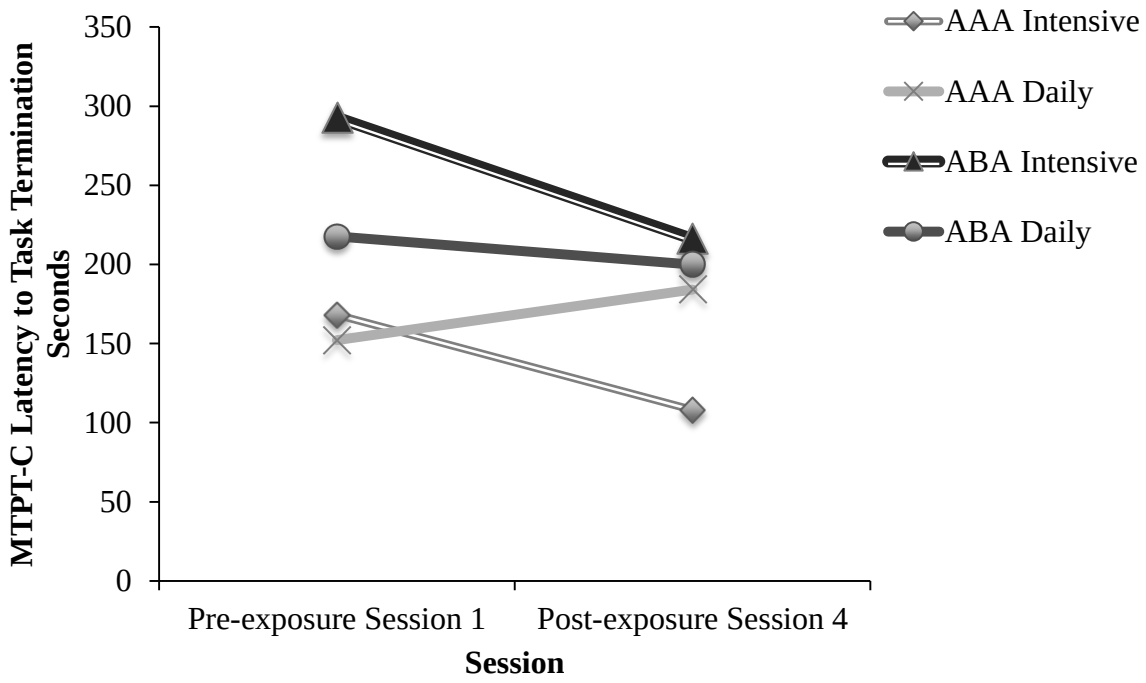


Figure 11. Average latency to task termination on the MTPT-C at Session 1 and Session 4 for each condition.

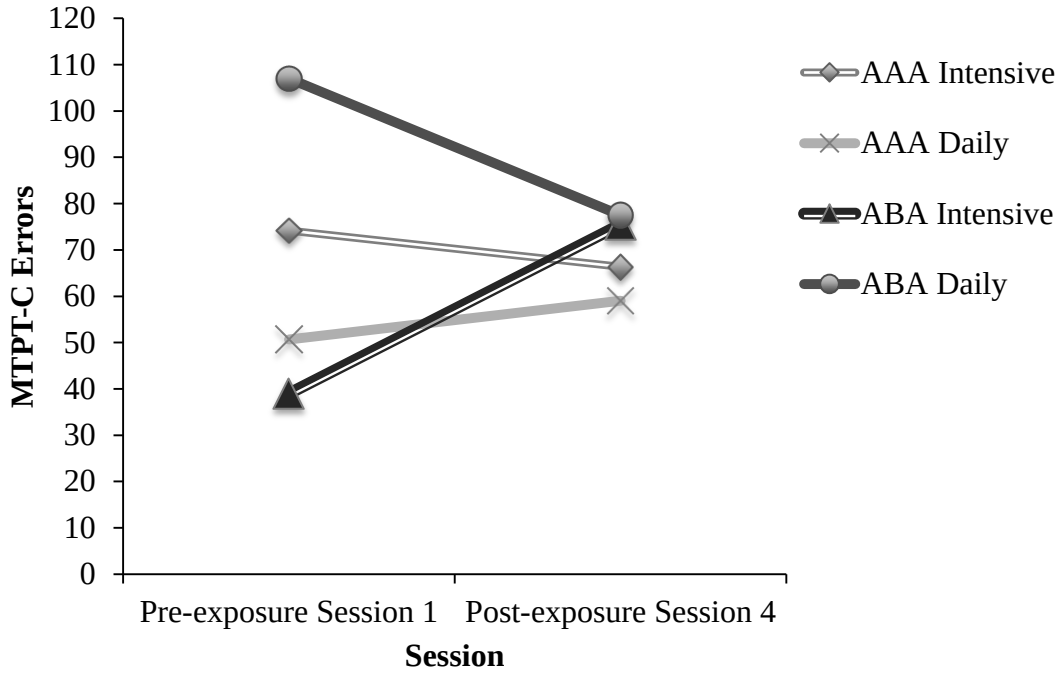


Figure 12. Average errors committed on the MTPT-C at Session 1 and Session 4 for each condition.

3.5 Contexts and Cue Information

Information was collected from participants about paraphernalia and the context. Nine participants indicated a preference to smoke cannabis with the laboratory's paraphernalia as opposed to their own. Table 5 indicates answers to the questions on the Study Context Questionnaire. All groups reported feeling moderately comfortable in the lounge room but said it was only mildly similar to their own smoking environment. Those in the ABA group reported almost no similarity between their own smoking environment and the therapist office. The ABA group also reported almost no similarity between the lounge room and therapist office.

Table 5

Study Context Questionnaire

	AAA M [95% CI] N=9	AAA Intensive M [95% CI] N=6	AAA Daily M [95% CI] N=3	ABA M [95% CI] N=6	ABA Intensive M [95% CI] N=2	ABA Daily M [95% CI] N=4
% similarity of Lounge room to own smoking environment	[a]39.67 [21.48, 57.85]	[a]43.40 [25.08, 61.72]	30.00 [-68.59, 128.59]	35.00 [11.53, 58.47]	42.50 [-179.86, 264.86]	31.25 [-6.84, 69.34]
% of comfort in the lounge room	[a]44.00 [15.67, 72.33]	[a]44.40 [9.46, 79.34]	43.33 [-79.21, 165.87]	58.33 [38.51, 78.15]	75	50.00 [21.68, 78.32]
% of comfort in the therapist office	-	-	-	17.50 [10.27, 24.73]	22.50 [-9.27, 54.27]	15.00 [3.75, 26.25]
% similarity of therapist office to own smoking environment	-	-	-	1.67 [-2.62, 5.95]	5.00 [-58.53, 68.53]	0
% similarity of therapist office to lounge room	-	-	-	33.33 [-0.95, 7.62]	2.50 [-29.27, 34.27]	3.75 [-3.87, 11.37]

Note: [a] = 1 missing case.

Discussion

This pilot study sought to investigate the role of context in cue-exposure therapy in a cannabis using population. Further, this pilot study sought to examine overall craving and tolerance for cravings across four sessions. Additionally, the current study was designed to examine changes in symbolic-expressive cue reactivity (e.g. cravings), physiological cue reactivity (e.g. EDA and HR), and tolerance for cravings, by comparing reactivity from the neutral cue to the cannabis cue, pre and post exposure. The results from this study provide preliminary support for the effect of context and renewal following cue-exposure therapy.

Findings indicate that cue-exposure therapy is most effective when given in the same context daily. This condition showed little to no change in symbolic-expressive cue reactivity and intolerability of cravings to the cannabis cues following cue-exposure therapy. Results indicate that those who receive massed cue-exposure in the same context decline in cravings overall, but show only slight improvements in symbolic-expressive cue reactivity and tolerance of cravings. Furthermore, evidence suggests that self-reported cravings renew from cue exposure to post-exposure assessment in those who received cue-exposure in a different context daily. Finally, it does not appear that cue exposure was effective in those who received massed cue exposure in a different context, as they increased in self-reported cravings and intolerability of cravings between cue exposure sessions. Support for the effect of context on cue exposure and tolerance of cravings highlights that cue-exposure therapy may not be beneficial if provided in arbitrary contexts.

4.1 Cue Exposure and Cravings

4.1.1 Craving and Cue Reactivity in the Same Context. Evidence for the role of context in the efficacy of cue-exposure therapy in drug using populations is unclear (Conklin & Tiffany, 2002). When observing self-reported cravings across all four sessions it appears

that the AAA Daily group has the greatest reduction in cravings, and a similar trend is observed in the AAA Intensive condition. Furthermore, examining cue reactivity by comparing the mean difference in cravings from the neutral to the cannabis cue pre and post exposure there was a slight decreasing trend across all conditions. The greatest decrease was in the AAA Daily condition, which evidenced almost no symbolic-expressive cue reactivity post exposure. This suggests that daily participation and cue-exposure in the same context as the assessment context was the most effective condition. This is consistent with research suggesting that exposure in the same context can effectively reduce cue reactivity to drug related paraphernalia (Collins & Brandon, 2002; Conklin & Tiffany, 2002; Perry et al., 2014; Thewissen et al., 2006). Perhaps research about massed and spaced extinction learning may explain why the daily condition was the most effective.

Information is remembered better when practice is spaced, compared to massed (Ebbinghaus 1885; Rescorla 1988). Bouton (1993) proposed that during extinction, subjects form a new inhibitory memory about the CS-US association. Therefore, spaced extinction trials may similarly strengthen inhibitory learning. Urcelay, Wheeler and Miller (2009) demonstrated that extinction was more effective when trials were spaced using animal models in a fear-conditioning paradigm. In this experiment, rats received either spaced or massed extinction trials, and each group spent the same total amount of time in extinction trials. Results indicated that the benefits of receiving spaced over massed extinction were small when the CS-US association was tested in the same context following extinction (Urcelay, Wheeler, & Miller, 2009). Similar findings have been observed in humans. However, massed and spaced cue exposure has been defined inconsistently in the literature. For example, cue exposure has been described as massed if the sessions are intensive over one day, and spaced as if the sessions are daily (Tsao & Craske, 2000). Alternatively, cue exposure has been described as massed when sessions are daily, and spaced when sessions are weekly (Foa,

Jameson, Turner, & Paynes, 1980). Though these terms have been used inconsistently when treating fear through exposure therapy, both spaced and massed exposure to the feared stimuli have been effective at reducing fear short-term (immediately following exposure). However, intensive cue exposure sessions over one day are observed as the least effective in preventing return of fear long-term, and daily sessions have been efficacious in reducing maintaining fear reduction at follow up. While this has not been examined in drug using populations, these findings are similarly observed in the current study. Both AAA conditions received the same total amount of time in exposure, and both decreased in their cravings across all sessions. However, the greatest reduction in cue reactivity was in the AAA condition that received daily exposure.

4.1.2 Renewal of Craving and Cue Reactivity. Evidence for renewal in drug using populations is inconsistent (Collins & Brandon, 2002; MacKillop & Lisman, 2008; Stasiewicz et al., 2007; Thewissen et al., 2006). In the current study there was some evidence of renewal of cravings following cue-exposure therapy. In the ABA Daily condition cravings renewed from the last cue-exposure session to the post-exposure assessment. This evidence of renewal is consistent with past research that demonstrated a return of responding due to a context change following extinction in animal models (Bouton, 1994; Bouton & Bolles, 1979; Bouton & King, 1983; Crombag & Shaham, 2002). This finding is not as clear in the ABA Intensive condition. The ABA Intensive group evidenced an increase in cravings during the cue-exposure therapy sessions, and this increase in cravings continued in assessment post exposure. Therefore, it is unclear whether this group evidenced renewal, or whether the increase occurred due to the previous trend where cravings may be arising naturally. Additionally, there was almost no evidence of a change in symbolic-expressive cue reactivity from pre to post exposure across the ABA conditions. The reason therapy was ineffective in

the ABA Intensive group may have something to do with the expectancy violation that occurs during exposure.

During the acquisition of a CS-US association participants have been seen to develop a temporal expectation about when the US will occur following the CS (Prenoveau et al., 2013). The, temporal expectation about when the CS will be delivered may potentially explain why cue-exposure was ineffective in the ABA Intensive group. For example, someone who uses a bong to smoke cannabis, but upon seeing that bong does not smoke for a few hours, would have the expectation that they smoke cannabis a few hours after seeing the bong. Since the ABA Intensive condition encountered their paraphernalia almost constantly when not smoking cannabis in the previous month, exposure may not have been long enough to violate the temporal association, and could therefore explain the increase in cravings across all sessions. Overall, the daily condition seems to provide evidence for the effect of context within the ABA group.

Furthermore, daily extinction may allow the violation of the CS-US association to be more effectively remembered since the inhibitory memory is consolidated (Bouton et al., 2006). Sleep plays a role in regulating emotions after stressful events and those who exhibit disturbance in sleep have trouble consolidating memories (Lavie, 2001). Sleep following exposure therapy has increased the efficacy of therapy by improving stimulus generalisation (Pace-Schott, Verga, Bennett, & Spencer, 2012). Furthermore, REM sleep has been considered critical for the consolidation of extinction memories (Datta & O'Malley, 2013). Therefore, those who participated daily may have the opportunity to consolidate the extinction memories between sessions. This may explain why the daily conditions provide evidence for the effect of context in this study.

4.2 Physiological Responses

4.2.1 Reactivity From Neutral to Cannabis Cues. Cue reactivity studies involving cannabis users have also observed increases in physiological measures of GSR, but no change in HR to cannabis related cues when compared to baseline or a neutral cue (Gray et al., 2008; Gray et al., 2011; Lundahl & Johanson, 2011; Wölfling et al., 2008). Similar trends are observed in the current study. Consistent with previous literature, GSR was consistently seen to increase from the neutral cue to the cannabis cue across conditions (Gray et al., 2008; Gray et al., 2011; Wölfling et al., 2008). This is consistent with incentive sensitisation theory that suggests physiological changes in response to stimuli occur because of the incentive salience attributed to stimuli (Robinson & Berridge, 1993).

There was a change in HR during Session 1 form the neutral cue to the cannabis cue in all ABA groups. This same reactivity was not observed across the AAA group. This suggests that the groups may respond differently to stimuli. However, this would be inconsistent with previous literature that has suggested that HR does not change in response to cannabis cues (Gray et al., 2008; Gray et al., 2011; Lundahl & Johanson, 2011; Wölfling et al., 2008).

According to models of conditioning, when individuals are presented with drug related stimuli, drug like or withdrawal like symptoms are experienced (Siegel, 1983; Stewart et al., 1984; Wikler, 1948). Tolerance to the increase in heart rate that results from cannabis use develops rapidly in chronic cannabis users (Benowitz & Jones, 1975; Benowitz & Jones, 1981; Jones, 2002). However, this tolerance is lost shortly after cessation, and HR during cannabis use will increase when cannabis smoking begins again (Jones, 2002). Furthermore, research on cannabis users has revealed no effect of withdrawal on heart rate (Budney et al., 2003)**.** While these findings provide a weak case for drug like and withdrawal like effects of cannabis on HR, participants may be experiencing somewhat drug like reactivity to cannabis cues in the ABA group since HR increases in response to cannabis paraphernalia**.**

4.2.2 Physiological Responding Following Cue-Exposure. Currently, there is no evidence for the effect of context on physiological responding in a cannabis using population. The evidence available for renewal of physiological cue reactivity has been mixed in alcohol users (Collins & Brandon, 2002; MacKillop & Lisman, 2008; Stasiewicz et al., 2007). In the current study, mean difference in EDA from pre and post exposure between the neutral and cannabis cue evidenced a decreasing trend across the AAA Daily, AAA Intensive and ABA intensive conditions. However, the AAA Daily condition evidenced no cue reactivity to the cannabis cues post exposure. This suggests that daily participation and cue-exposure in the same context as the assessment context was the most effective condition. In addition, the ABA Daily group evidenced more EDA to the cannabis cue post exposure. While this trend suggests that the ABA Daily condition reacted more to the cannabis cues following cue-exposure, it is difficult to say whether this is evidence of renewal because EDA was not recorded at the end of cue exposure. This appears to be consistent with literature suggesting that context plays a role in cue reactivity following exposure (Collins & Brandon, 2002; Thewissen et al., 2006).

Currently, there is no research about HR in a cannabis using population following cue-exposure therapy. Furthermore, past research has demonstrated that no changes in HR are evident in response to cannabis related cues (Gray et al., 2008; Gray et al., 2011; Lundahl & Johanson, 2011). The mean difference in HR pre and post exposure between the neutral and cannabis cue evidenced almost no change in HR in the daily conditions. Interestingly, the ABA Intensive group showed less reactivity in post exposure and the AAA Intensive group showed more reactivity in post exposure. Given that some evidence suggests that HR increases following cannabis use (Benowitz & Jones, 1975; Benowitz & Jones, 1981; Jones, 2002) These findings do not appear consistent with theory, which would suggest that HR in the AAA group would reduce following cue exposure since there would be less drug like cue

reactivity as a result of repeated cue exposure. Overall, HR appears to be an unreliable measure of cue reactivity in cannabis using individuals.

4.3 Intolerance

4.3.1 Self-Reported Intolerance of Cravings. Those tolerant of distress may cope with negative state of withdrawal and cravings evoked by drug cues (Baker et al., 2004). Since extinction and inhibitory learning are believed to be a form of emotion regulation, exposure to the CS in the absence of the US directly teaches individuals how to cope with not using (Craske et al., 2008; Quirk & Beer, 2006; Quirk & Mueller, 2007). The AAA Daily group evidences the greatest decrease in intolerance of cravings across all sessions, with a similar trend observed in the AAA Intensive and ABA Daily condition. In these groups the intolerability of cravings appears to remain stable from cue exposure to post-exposure assessment. Therefore, it appears that both daily cue exposure, and cue exposure in the same context may improve tolerability of cravings across all sessions. Additionally, the ABA Intensive group exhibits greater intolerability of cravings between the cue-exposure sessions and this increase continues into the post-exposure session. Again this suggests that exposure may have been ineffective in the ABA Intensive condition. This increase may occur since participants in this condition are exposed to their paraphernalia almost constantly when they are not smoking cannabis. As aforementioned, participants develop a temporal expectation about when the US will occur following the CS during acquisition (Bouton et al., 2006; Prenoveau et al., 2013). Therefore, cue-exposure may not be effective if it does not last long enough to violate the temporal expectation(Bouton et al., 2006; Prenoveau et al., 2013).

The mean difference in self-reported tolerance for cravings between the neutral and cannabis cue evidenced a slight decreasing trend in all conditions across all sessions. The greatest improvement in tolerance of cravings was evident in the AAA Daily condition. In the AAA Daily condition self-reported cravings post-exposure were rated equally tolerable to the

cannabis cue as to the neutral cue. This finding suggests that daily participation and cue-exposure in the same context as the assessment context improves tolerability of cravings to the point where they do not change when presented with cannabis cues (no reactivity). Overall, when observing changes in tolerance it appears that the tolerance of cravings was best learned through spaced exposure, and best retrieved when the cue-exposure context was the same as the post exposure assessment context.

4.3.2 Intolerance of Distress. When examining overall tolerability for aversive states it appears that distress tolerance remains stable pre and post exposure. This finding suggests that distress tolerance, as a construct, may not be as amenable to change. This finding may occur because cue-exposure to drug paraphernalia may only require the tolerance of cravings. Therefore, specific improvements in distress tolerance may not generalise. Since distress tolerance has not been examined in the context of cue exposure and substance use, it is difficult to make further inferences from these preliminary findings (Tiffany & Wray, 2011). Furthermore, these findings are inconsistent with performance on the MTPT-C, which is a behavioural measure of distress tolerance.

Participants in the AAA Daily condition persisted on the MTPT-C longer post-exposure than they did pre exposure, despite committing the same number of errors. Since this group spent more time persisting on the distressing task, they exhibited more distress tolerance. This may suggest that cue exposure was effective at improving tolerance in this group. However, those in the ABA Daily group committed fewer errors post exposure, but spent the same amount of time persisting on the task. This suggests the group did not improve in tolerating distress and did not benefit from cue exposure in a different context. Furthermore, both of the intensive conditions exhibit less tolerance for the distressing task following cue exposure. The AAA Intensive condition committed the same number of errors post exposure, but terminated the task more quickly. Those in the ABA Intensive condition

terminated the task more quickly post-exposure, and committed many more errors. Making the task more frustrating, as the participant hears the loud buzzer and restarts the task more frequently. Fatigue arising due to self-control may explain why participants lacked the capacity to continue with the MTPT-C, even when fewer errors occurred (Muraven & Baumeister, 2000; Muraven & Shmueli, 2006).

Self-control involves the inhibition of behaviours, impulses, and urges that would occur automatically (Barkley, 1997). Often people exert self-control to follow a rule or delay gratification (Barkley, 1997). Restraint to use substances creates a conflict between an individual's desire to use and their resistance of these impulses (Bensley, 1989). The self-control strength model posits that individuals have a limited reserve of self-control which can be used for things such as resisting temptation (Muraven & Baumeister, 2000). Exerting self-control depletes this reserve, leaving individuals to perform more poorly on future tasks that require self-control (Muraven & Baumeister, 2000; Muraven & Shmueli, 2006). This has been demonstrated in a substance using population using a cue-exposure paradigm. For example, Muraven and Shmueli (2006) revealed that social drinkers who were asked to resist drinking when exposed to the sight and smell of their favourite alcoholic beverage performed more poorly on a self-stopping reaction time task and a handgrip task, compared to their performance after resisting a neutral water cue. This is believed to occur because participants are unable to drink and need to override the temptation. Thus, they exert self-control, which leads to a loss of self-control strength. A similar phenomenon appears to have occurred in the current study. Those who experienced massed cue-exposure therapy, perform worse on the MTPT-C post exposure. In the intensive condition, cue exposure occurred on the same day as the post-exposure assessment. Participants spent about 3 hours in cue exposure sessions and completed the study over 7.5 hours. Therefore, participants may have exhibited less tolerance for the task because they were required to exert self-control over their urge and desire to use

cannabis during cue exposure, leading to a loss of self-control strength post exposure. Consequently, their self-control reserve may have been depleted when they completed the MTPT-C.

4.4 Strengths, Limitations, and Future Directions.

Renewal studies in drug using individuals have often been limited in similar ways. First, previous renewal studies employing daily sessions have not required continuous abstinence between sessions (MacKillop & Lisman, 2008; Stasiewicz et al., 2007). Therefore, the current study required abstinence throughout the study. As previously discussed this allows the CS-US assumption to be more effectively violated throughout the study since the CS-US association cannot strengthen further (Bouton et al., 2006; Conklin & Tiffany, 2002; Wölfling et al., 2008). Second, previous studies have either provided massed exposure, or spaced cue exposure (Collins & Brandon, 2002; MacKillop & Lisman, 2008; Stasiewicz et al., 2007; Thewissen et al., 2006). By providing the option to complete the study daily or intensively, the current study provides data on the differences between massed and spaced cue exposure. However, participants were not randomly allocated to massed or spaced conditions so the variation observed could be due to individual differences. Nonetheless, this has not been examined before and provides insight when designing future studies. Finally, this study sought to include contexts similar to the conditioning environment, and is the first to examine cue exposure and renewal in a cannabis using population. However, this study is not without its limitations.

As a pilot study, the current investigation is limited by the sample size, which does not allow for inferences to be made about the population. In particular the ABA Intensive group is very small, which makes it difficult to draw conclusions about massed cue exposure in the ABA condition. Furthermore, this group encountered their paraphernalia almost constantly when not smoking cannabis before the study. Therefore, exposure may not have

violated temporal expectation about when the US will occur following the CS. Despite this, the current investigation provides some needed preliminary data for a future study to examine renewal and distress tolerance in a population with cannabis use disorder. The current study has demonstrated that examining renewal in cannabis using individuals incurs great costs, by being both time consuming and financially expensive. As with many studies that utilise substance-using populations we had great difficulty with recruitment and attrition (Jacobson, 2004). Research suggests that higher levels of intrinsic motivation relative to extrinsic motivation have been associated with readiness to cease drug use and successful cessation (Curry, Grothaus, & McBride, 1997). Therefore, it may have been useful in the current study to recruit treatment-seeking individuals.

Future studies using an in-patient setting could assist with recruitment and attrition. This is because individuals who are seeking treatment and may be more compliant and willing to engage in cue-exposure therapy (Curry et al., 1997). In-patient facilities may also maximise exposure to paraphernalia and allow for greater expectancy violations to occur, as they may be able to expose individuals to paraphernalia in settings similar to where drug taking occurs. For example, if a cannabis using individual typically smokes cannabis in a lounge room, placing personal paraphernalia in these kinds of rooms in the facility may provide prolonged exposure, allowing the CS-US expectancy to be effectively violated

A future study should replicate the current study on a larger scale in an in-patient setting. Additional research is needed to determine whether renewal occurs in cannabis using population and whether tolerance can be improved as a direct result of cue-exposure therapy. Furthermore, there is currently a gap in the use of theoretically driven research directly comparing different schedules of exposure trials (Craske et al., 2008). The current study suggests that daily cue-exposure therapy may be the most beneficial. Additionally, findings in the current study suggest that the self-control required during cue-exposure may deplete

resources. Therefore, cue-exposure therapy for substance use disorder should consider the risk of relapse immediately following therapy. If resources are depleted following cue exposure, individuals may be less able to resist using drugs. Research is therefore needed to determine the parameters of cue-exposure therapy in drug using populations.

4.5 Conclusions

The preliminary findings in the current study suggest that spaced exposure therapy in the same context is the most effective in reducing cravings and improving tolerability of cravings at test. Furthermore, the trend of renewal of self-reported cravings highlights that extinction following cue-exposure therapy is limited, and may not generalise to different contexts. This pilot study is the first of its kind to examine cue-exposure therapy and tolerance of cravings in a cannabis using population, and while the sample is small, the data provide a good foundation for future studies.

Cue-exposure therapy has re-emerged as an area of interest in the literature. However, it is still unclear whether renewal occurs in substance using individuals or whether this can be attenuated. If cue-exposure therapy in familiar contexts can help to reduce cue reactivity and prevent relapse, it would provide much needed treatment for those with substance use disorders (Tiffany & Wray, 2011). Future research should therefore attempt to clearly demonstrate the effect of context in cannabis using individuals, and perhaps using an in-patient setting and daily exposure would be most beneficial.

References

Abrams, D. B., Monti, P. M., Carey, K. B., Pinto, R. P., & Jacobus, S. I. (1988). Reactivity to smoking cues and relapse: Two studies of discriminant validity. *Behaviour Research and Therapy*, *26*(3), 225–233. doi:10.1016/0005-7967(88)90003-4

Allsop, D. J., Copeland, J., Norberg, M. M., Fu, S., Molnar, A., Lewis, J., & Budney, A. J. (2012). Quantifying the clinical significance of cannabis withdrawal. *PLoS ONE, 7*(9), e44864. doi:10.1371/journal.pone.0044864.t006

Andrews, G., & Slade, T. (2001). Interpreting scores on the Kessler Psychological Distress Scale (K10). *Australian and New Zealand Journal of Public Health*, *25*(6), 494–497. doi:10.1111/j.1467-842X.2001.tb00310.x

Arch, J. J., & Craske, M. G. (2011). Addressing relapse in cognitive behavioral therapy for panic disorder: Methods for optimizing long-term treatment outcomes. *Cognitive and Behavioral Practice*, *18*(3), 306–315. doi:10.1016/j.cbpra.2010.05.006

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5 (5th ed.).* Arlington, VA: American Psychiatric Publishing.

American Psychiatric Association. (2013). *Highlights of Changes from DSM-IV-TR to DSM-5*. Arlington, VA: American Psychiatric Publishing.

Australian Institute of Health and Welfare. (2013). National Drug Strategy Household Survey detailed report: 2013. Canberra, Australia

Baker, T. B., Piper, M. E., McCarthy, D. E., Majeskie, M. R., & Fiore, M. C. (2004). Addiction Motivation Reformulated: An Affective Processing Model of Negative Reinforcement. *Psychological review*, *111*(1), 33–51. doi:10.1037/0033-295X.111.1.33

Barkley, R. A. (1997). ADHD and the nature of self-control. New York: Guilford Press.

Bastle, R. M., Kufahl, P. R., Turk, M. N., Weber, S. M., Pentkowski, N. S., Thiel, K. J., & Neisewander, J. L. (2012). Novel cues reinstate cocaine-seeking behavior and induce fos

protein expression as effectively as conditioned cues. *Neuropsychopharmacology*, *37*(9), 2109–2120. doi:10.1038/npp.2012.60

Bensley, L. S. (1989). The heightened role of external responsiveness in the alcohol consumption of restrained drinkers. *Cognitive Therapy and Research*, *13*(6), 623–636. doi:10.1007/BF01176072

Bentowitz, N. L., & Jones, R. T. (1975). Cardiovascular effects of prolonged delta-9-tetrahydrocannabinol ingestion. *Clinical Pharmacology and Therapeutics, 18*(3), 287-297. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1164818

Bentowitz, N. L., & Jones, R. T. (1981). Cardiovascular and metabolic considerations in prolonged cannabinoid administration in man. *The Journal of Clinical Pharmacology, 21*(S1), 214S-223S. 10.1002/j.1552-4604.1981.tb02598.x

Biernacki, P., & Waldorf, D. (1981). Snowball sampling: Problems and techniques of chain referral sampling. *Sociological Methods Research, 10*(2), 141–163. doi:10.1177/004912418101000205

Bonn-Miller, M. O., Vujanovic, A. A., & Zvolensky, M. J. (2008). Emotional dysregulation: Association with coping-oriented marijuana use motives among current marijuana users. *Substance Use & Misuse*, *43*(11), 1653–1665. doi:10.1080/10826080802241292

Bornovalova, M. A., Gratz, K. L., Daughters, S. B., Hunt, E. D., & Lejuez, C. W. (2012). Initial RCT of a distress tolerance treatment for individuals with substance use disorders. *Drug and Alcohol Dependence*, *122*(1-2), 70–76. doi:10.1016/j.drugalcdep.2011.09.012

Bouton, M. E. (1993). Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. *Psychological Bulletin*, *144*(1), 80–99. doi: 10.1037/0033-2909.114.1.80

Bouton, M. E. (1994). Conditioning, remembering, and forgetting. *Journal of Experimental Psychology: Animal Behavior Processes*, *20*(3), 219–231. doi: 10.1037/0097-

7403.20.3.219

Bouton, M. E. (2004). Context and behavioral processes in extinction. *Learning & Memory*, *11*(5), 485–494. doi:10.1101/lm.78804

Bouton, M. E., & Bolles, R. C. (1979). Contextual control of the extinction of conditioned fear. *Learning and Motivation*, *10*(4), 445–466. doi: 10.1016/0023-9690(79)90057-2

Bouton, M. E., & King, D. A. (1983). Contextual control of the extinction of conditioned fear: Tests for the associative value of the context. *Journal of Experimental Psychology: Animal Behavior Processes*, *9*(3), 248–265. doi: 10.1037/0097-7403.9.3.248

Bouton, M. E., Nelson, J. B., & Rosas, H. D. (1999). Stimulus generalization, context change, and forgetting. *Psychological Bulletin*, *125*(2), 171–186. doi: 10.1037/0033-2909.125.2.171

Bouton, M. E., Westbrook, R. F., Corcoran, K. A., & Maren, S. (2006). Contextual and temporal modulation of extinction: Behavioral and biological mechanisms. *Biological Psychiatry*, *60*(4), 352–360. doi:10.1016/j.biopsych.2005.12.015

Brandon, T. H., Herzog, T. A., Juliano, L. M., Irvin, J. E., Lazev, A. B., & Simmons, V. N. (2003). Pretreatment task persistence predicts smoking cessation outcome. *Journal of Abnormal Psychology*, *112*(3), 448–456. doi:10.1037/0021-843X.112.3.448

Budney, A. J., Moore, B. A., Vandrey, R. G., & Hughes, J. R. (2003). The time course and significance of cannabis withdrawal. *Journal of Abnormal Psychology*, *112*(3), 393–402. doi:10.1037/0021-843X.112.3.393

Bujarski, S. J., Norberg, M. M., & Copeland, J. (2012). The association between distress tolerance and cannabis use-related problems: The mediating and moderating roles of coping motives and gender. *Addictive Behaviors*, *37*(10), 1181–1184. doi:10.1016/j.addbeh.2012.05.014

Carter, B. L., & Tiffany, S. T. (1999). Meta-analysis of cue-reactivity in addiction research.

Addiction, *94*(3), 327–340. doi:10.1046/j.1360-0443.1999.9433273.x

Chaudhri, N., Sahuque, L. L., & Janak, P. H. (2008). Context-induced relapse of conditioned behavioral responding to ethanol cues in rats. *Biological Psychiatry*, *64*(3), 203–210. doi:10.1016/j.biopsych.2008.03.007

Cheer, J. F., Wassum, K. M., Heien, M. L. A. V., Phillips, P. E. M., & Wightman, R. M. (2004). Cannabinoids enhance subsecond dopamine release in the nucleus accumbens of awake rats. *Journal of Neuroscience*, *24*(18), 4393–4400. doi:10.1523/JNEUROSCI.0529-04.2004

Collins, B. N., & Brandon, T. H. (2002). Effects of extinction context and retrieval cues on alcohol cue reactivity among nonalcoholic drinkers. *Journal of Consulting and Clinical Psychology*, *70*(2), 390–397. doi:10.1037//0022-006X.70.2.390

Conklin, C. A., & Tiffany, S. T. (2002). Applying extinction research and theory to cue-exposure addiction treatments. *Addiction*, *97*(2), 155–167. doi:10.1046/j.1360-0443.2002.00014.x

Craske, M. G., & Barlow, D. H. (2008). Panic disorder and agoraphobia. *CBT for Anxiety Disorders*. doi: 10.1002/978111833004

Craske, M. G., Kircanski, K., Zelikowsky, M., Mystkowski, J., Chowdhury, N., & Baker, A. (2008). Optimizing inhibitory learning during exposure therapy. *Behaviour Research and Therapy*, *46*(1), 5–27. doi:10.1016/j.brat.2007.10.003

Crombag, H. S., & Shaham, Y. (2002). Renewal of drug seeking by contextual cues after prolonged extinction in rats. *Behavioral Neuroscience*, *116*(1), 169–173. doi:10.1037//0735-7044.116.1.169

Curry, S. J., Grothaus, L., & McBride, C. (1997). Reasons for quitting: Intrinsic and extrinsic motivation for smoking cessation in a population-based sample of smokers. *Psychology of Addictive Behaviors*, *22*(6), 729–739. doi:10.1016/S0306-4603(97)00059-2

Datta, S., & O'Malley, M. W. (2013). Fear extinction memory consolidation requires potentiation of pontine-wave activity during REM sleep. *Journal of Neuroscience, 33*(10), 4561–4569. doi:10.1523/JNEUROSCI.5525-12.2013

Daughters, S. B., Lejuez, C. W., Bornovalova, M. A., Kahler, C. W., Strong, D. R., & Brown, R. A. (2005a). Distress tolerance as a predictor of early treatment dropout in a residential Substance abuse treatment facility. *Journal of Abnormal Psychology, 114*(4), 729–734. doi:10.1037/0021-843X.114.4.729

Daughters, S. B., Lejuez, C. W., Kahler, C. W., Strong, D. R., & Brown, R. A. (2005b). Psychological distress tolerance and duration of most recent abstinence attempt among residential treatment-seeking substance abusers. *Psychology of Addictive Behaviors, 19*(2), 208–211. doi:10.1037/0893-164X.19.2.208

Davis, W. M., & Smith, S. G. (1978). Role of conditioned reinforcers in the initiation, maintenance and extinction of drug-seeking behavior. *Pavlovian Journal of Biological Science, 11*(4), 222–236. Retrieved from http://psycnet.apa.org/psycinfo/1977-12373-001

Dawe, S., Powell, J., Richards, D., Gossop, M., Marks, I., Strang, J., & Gray, J. A. (1993). Does post-withdrawal cue exposure improve outcome in opiate addiction? A controlled trial. *Addiction, 88*(9), 1233–1245. doi:10.1111/j.1360-0443.1993.tb02146.x

De Vries, T. J., Schoffelmeer, A. N. M., Binnekade, R., Mulder, A. H., & Vanderschuren, L. J. M. J. (1998). Drug-induced reinstatement of heroin- and cocaine- seeking behaviour following long-term extinction is associated with expression of behavioural sensitization. *European Journal of Neuroscience, 10*(11), 3565–3571. doi:10.1046/j.1460-9568.1998.00368.x

Donovan, D. M., Bigelow, G. E., Brigham, G. S., Carroll, K. M., Cohen, A. J., Gardin, J. G., Hamilton, J. A., et al. (2011). Primary outcome indices in illicit drug dependence treatment research: Systematic approach to selection and measurement of drug use end-

points in clinical trials. *Addiction*, *107*(4), 694–708. doi:10.1111/j.1360-0443.2011.03473.x

Drobes, D. J., & Tiffany, S. T. (1997). Induction of smoking urge through imaginal and in vivo procedures: Physiological and self-report manifestations. *Journal of Abnormal Psychology*, *106*, 15–25. doi: 10.1037/0021-843X.106.1.15

Drummond, C. D. (2000). What does cue-reactivity have to offer clinical research? *Addiction, 29*, s129–s144. doi:10.1046/j.1360-0443.95.8s2.2.x

Drummond, C. D., & Glautier, S. (1994). A controlled trial of cue exposure treatment in alcohol dependence. *Journal of Consulting and Clinical Psychology*, *62*(4), 809–817. doi: 10.1037/0022-006X.62.4.809

Drummond, C. D., Troy, C., & Glautier, S. P. (1990). Conditioned learning in alcohol dependence: Implications for cue exposure treatment. *British Journal of Addiction*, *85*(6), 725–743. doi:10.1111/j.1360-0443.1990.tb01685.x

Ebbinghaus, H. (1885). *Über das Gedächtnis: Untersuchungen zur Experimentellen Psychologie.* Berlin: Duncker & Humblot.

Egstrom, G. G., Weltman, G., Baddeley, A. D., Cucaro, W. J., & Willis, M. A. (1972). Underwater work performance and work tolerance. Los Angeles: University of California.

Fant, R. V., Heishman, S. J., Bunker, E. B., & Pickworth, W. B. (1998). Acute and residual effects of marijuana in humans, *60*(4), 777–784. doi:10.1016/S0091-3057(97)00386-9

Fassaert, T., de Wit, M. A. S., Tuinebreijer, W. C., Wouters, H., Verhoeff, A. P., Beekman, A. T. F., & Dekker, J. (2009). Psychometric properties of an interviewer-administered version of the Kessler Psychological Distress scale (K10) among Dutch, Moroccan and Turkish respondents. *International Journal of Methods in Psychiatric Research*, *18*(3), 159–168. doi:10.1002/mpr.288

Fatseas, M., Serre, F., Alexandre, J.-M., Debrabant, R., Auriacombe, M., & Swendsen, J. (2015). Craving and substance use among patients with alcohol, tobacco, cannabis or heroin addiction: A comparison of substance- and person-specific cues. *Addiction*, *110*(6), 1035–1042. doi:10.1111/add.12882

Filbey, F. M., Schacht, J. P., Myers, U. S., Chavez, R. S., & Hutchison, K. E. (2009). Marijuana craving in the brain. *Neuroscience*, *106*(31), 13016–13021. doi:10.1073/pnas.0903863106

First, M. B., Williams, J. B. W., Spitzer, Robert. L., & Gibbon, Miriam. (2007). *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Clinical Trials Version (SCID-CT*). New York: Biometrics Research, New York State Psychiatric Institute.

Foa, E. B., Jameson, J. S., Turner, R. M., & Paynes, L. L. (1980). Massed vs. spaced exposure sessions in the treatment of agoraphobia. *Behaviour Research and Therapy*, *18*(4), 333–338. doi:10.1016/0005-7967(80)90092-3

Gray, K. M., LaRowe, S. D., & Upadhyaya, H. P. (2008). Cue reactivity in young marijuana smokers: A preliminary investigation. *Psychology of Addictive Behaviors*, *22*(4), 582–586. doi:10.1037/a0012985

Gray, K. M., LaRowe, S. D., Watson, N. L., & Carpenter, M. J. (2011). Reactivity to in vivo marijuana cues among cannabis-dependent adolescents. *Addictive Behaviors*, *36*(1-2), 140–143. doi:10.1016/j.addbeh.2010.08.021

Hart, C. L., van Gorp, W., Haney, M., Foltin, R. W., & Fischman, M. W. (2001). Effects of acute smoked marijuana on complex cognitive performance. *Neuropsychopharmacology*, *25*(5), 757–765. doi:10.1016/S0893-133X(01)00273-1

Haughey, H. M., Marshall, E., Schacht, J. P., Louis, A., & Hutchison, K. E. (2008). Marijuana withdrawal and craving: Influence of the cannabinoid receptor 1 (CNR1) and fatty acid amide hydrolase (FAAH) genes. *Addiction*, *103*(10), 1678–1686.

doi:10.1111/j.1360-0443.2008.02292.x

Heatherton, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerstrom, K. (1991). The Fagerström test for nicotine dependence: A revision of the Fagerstrom Tolerance Questionnaire. *British Journal of Addiction*, *86*(9), 1119–1127. doi: 10.1111/j.1360-0443.1991.tb01879.x

Heishman, S. J., Evans, R. J., Singleton, E. G., Levin, K. H., Copersino, M. L., & Gorelick, D. A. (2009). Reliability and validity of a short form of the Marijuana Craving Questionnaire. *Drug and Alcohol Dependence*, *102*(1-3), 35–40. doi:10.1016/j.drugalcdep.2008.12.010

Heishman, S. J., Stitzer, M. L., & Yingling, J. E. (1989). Effects of tetrahydrocannabinol content on marijuana smoking behavior, subjective reports, and performance. *Pharmacology Biochemistry and Behavior*, *34*(1), 173–179. doi:10.1016/0091-3057(89)90369-9

Henry, E. A., Kaye, J. T., Bryan, A. D., Hutchison, K. E., & Ito, T. A. (2014). Cannabis cue reactivity and craving among never, infrequent and heavy cannabis users. *Neuropsychopharmacology*, *39*(5), 1214–1221. doi:10.1038/npp.2013.324

Jacobson, J. O. (2004). Place and Attrition from Substance Abuse Treatment. *Journal of Drug Issues*, *34*, 23–49. doi:10.1177/002204260403400102

Jones, R. T. (2002). Cardiovascular system effects of marijuana. *The Journal of Clinical Pharmacology*, *42*(S1), 58S–63S. doi:10.1177/0091270002238795

Kessler. R., & Mroczek, D. (1994). Final versions of our non-specific psychological distress scale. Survey Research Center of the Institute for Social Research. University of Michigan

Kalivas, P. W., & Volkow, N. D. (2005). The neural basis of addiction: A pathology of motivation and choice. *Reviews and Overviews*, *162*(8), 1403–1413.

doi:10.1016/j.addbeh.2010.08.021

Karschner, E. L., Schwilke, E. W., Lowe, R. H., Darwin, W. D., Herning, R. I., Cadet, J. L., & Huestis, M. A. (2009). Implications of plasma Δ-tetrahydrocannabinol, 11-hydroxy-THC, and 11-nor-9-carboxy-THC concentrations in chronic cannabis smokers. *Journal of Analytical Toxicology*, *33*(8), 469–477. doi:10.1093/jat/33.8.469

Kavanagh, D. J., Sitharthan, G., Young, R. M., Sitharthan, T., Saunders, J. B., Shockley, N., & Giannopoulos, V. (2006). Addition of cue exposure to cognitive-behaviour therapy for alcohol misuse: a randomized trial with dysphoric drinkers. *Addiction*, *101*(8), 1106–1116. doi:10.1111/j.1360-0443.2006.01488.x

Kolb, B. (1984). Functions of the frontal cortex of the rat: A comparative review. *Brain Research Reviews*, *8*, 65–98. doi: 10.1016/0165-0173(84)90018-3

Larimer, M. E., Palmer, R. S., & Marlatt, G. A. (1999). Relapse prevention: An overview of Marlatt's cognitive-behavioral model. *Alcohol research & health: The journal of the National Institute on Alcohol Abuse and Alcoholism*, *23*(2), 151–160. Retrieved from http://thegoalgroup.co.uk/static/pdf/Relapse%20Prevention.pdf

Lavie, P. (2001). Sleep disturbances in the wake of traumatic events. *The New England Journal of Medicine, 345*(25), 1825-1832. doi:10.1056/NEJMra012893

Lejuez, C., Kahler, C., & Brown, R. (2003). A modified computer version of the Paced Auditory Serial Addition Task (PASAT) as a laboratory-based stressor. *The Behavior Therapist, 26*(4), 290–293. Retrieved from http://psycnet.apa.org/psycinfo/2003-06608-006

Leon, A. C., Davis, L. L., & Kraemer, H. C. (2011). The role and interpretation of pilot studies in clinical research. *Journal of Psychiatric Research*, *45*(5), 626–629. doi:10.1016/j.jpsychires.2010.10.008

Lewis, J., Molnar, A., Allsop, D., Copeland, J., & Fu, S. (2015). Rapid elimination of

Carboxy-THC in a cohort of chronic cannabis users. *International Journal of Legal Medicine*, 1–6. doi:10.1007/s00414-015-1241-z

Loeber, S., Croissant, B., Heinz, A., Mann, K., & Flor, H. (2010). Cue exposure in the treatment of alcohol dependence: Effects on drinking outcome, craving and self-efficacy. *British Journal of Clinical Psychology*, *45*(4), 515–529. doi:10.1348/014466505X82586

Lundahl, L. H., & Johanson, C. E. (2011). Cue-induced craving for marijuana in cannabis-dependent adults. *Experimental and Clinical Psychopharmacology*, *19*(3), 224–230. doi:10.1037/a0023030

MacKillop, J., & Lisman, S. A. (2008). Effects of a context shift and multiple context extinction on reactivity to alcohol cues. *Experimental and Clinical Psychopharmacology*, *16*(4), 322–331. doi:10.1037/a0012686

Magill, M., & Ray, L. (2009). Cognitive-behavioral treatment with adult alcohol and illicit drug users: A meta-analysis of randomized controlled trials. *Journal of Studies on Alcohol and Drugs*, *70*(4), 516–527. doi: 10.15288/jsad.2009.70.516

Marijuana Treatment Project Research Group. (2004). Brief treatments for cannabis dependence: Findings from a randomized multisite trial. *Journal of Consulting and Clinical Psychology 72*, 455-466. doi:10.1037/0022-006X.72.3.455

Marlatt, G. A., & Gordon, J. R. (1985). Relapse prevention: Maintenance strategies in the treatment of addictive behaviors. New York: Guilford.

Martin, T., LaRowe, S. D., & Malcolm, R. (2010). Progress in cue exposure therapy for the treatment of addictive disorders: A review update. *The Open Addiction Journal*, *3*, 92–101. doi:10.2174/1874941001003010092

McClure, S. M., Daw, N. D., & Read Montague, P. (2003). A computational substrate for incentive salience. *Trends in Neurosciences*, *26*(8), 423–428. doi:10.1016/S0166-2236(03)00177-2

McLellan, T. A., Childress, A. R., Ehrman, R., O'Brien, C. P., & Pashko, S. (1986). Extinguishing conditioned responses during opiate dependence treatment turning laboratory findings into clinical procedures. *Journal of Substance Abuse Treatment*, *3*, 1–8. doi:10.1016/0740-5472(86)90006-1

Meneses-Gaya, I. C., Zuardi, A. W., Loureiro, S. R., & Crippa, J. A. (2009). Psychometric properties of the Fagerström Test for Nicotine Dependence. *Jornal Brasileiro de Pneumologia*, *35*(1), 73–82. doi:10.1590/S1806-37132009000100011

Milad, M. R., & Quirk, G. J. (2002). Neurons in medial prefrontal cortex signal memory for fear extinction. *Nature*, *420*(6911), 70–74. doi:10.1038/nature01138

Muraven, M., & Baumeister, R. F. (2000). Self-regulation and depletion of limited resources: Does self-control resemble a muscle? *Psychological Bulletin*, *126*(2), 247–259. doi:10.1037/0033-2909.126.2.247

Muraven, M., & Shmueli, D. (2006). The self-control costs of fighting the temptation to drink. *Psychology of Addictive Behaviors*, *20*(2), 154–160. doi:10.1037/0893-164X.20.2.154

Myers, K. M., & Carlezon, W. A., Jr. (2010). Extinction of drug- and withdrawal-paired cues in animal models: Relevance to the treatment of addiction. *Neuroscience and Biobehavioral Reviews*, *35*(2), 285–302. doi:10.1016/j.neubiorev.2010.01.011

Norberg, M. M., Mackenzie, J., & Copeland, J. (2012). Quantifying cannabis use with the Timeline Followback approach: A psychometric evaluation. *Drug and Alcohol Dependence*, *121*(3), 247–252. doi:10.1016/j.drugalcdep.2011.09.007

Norton, P. J., & Price, E. C. (2007). A meta-analytic review of adult cognitive-behavioral treatment outcome cross the anxiety disorders. *The Journal of Nervous and Mental Disease*, *195*(6), 521–531. doi:10.1097/01.nmd.0000253843.70149.9a

O'Brien, C. P. (2005). Anticraving medications for relapse prevention: A possible new class

of psychoactive medications. *The American Joural of Psychiatry*, *162*(8), 1423–2431. doi:10.1176/appi.ajp.162.8.1423

Pace-Schott, E. F., Verga, P. W., Bennett, T. S., & Spencer, R. M. C. (2012). Sleep promotes consolidation and generalization of extinction learning in simulated exposure therapy for spider fear. *Journal of Psychiatric Research*, *46*(8), 1036–1044. doi:10.1016/j.jpsychires.2012.04.015

Paliwal, P., Hyman, S. M., & Sinha, R. (2008). Craving predicts time to cocaine relapse: Further validation of the Now and Brief versions of the cocaine craving questionnaire. *Drug and Alcohol Dependence*, *93*(3), 252–259. doi:10.1016/j.drugalcdep.2007.10.002

Panlilio, L. V., Goldberg, S. R., & Justinova, Z. (2015). Cannabinoid abuse and addiction: Clinical and preclinical findings. *Clinical Pharmacology & Therapeutics, 97*(6), 616-627. doi:10.1002/cpt.118

Papachristou, H., Nederkoorn, C., Giesen, J. C. A. H., & Jansen, A. (2014). Cue reactivity during treatment, and not impulsivity, predicts an initial lapse after treatment in alcohol use disorders. *Addictive Behaviors*, *39*(3), 737–739. doi:10.1016/j.addbeh.2013.11.027

Pavlov, I. P. (1927). *Conditional Reflexes*. New York: Dover Publications

Perry, C. J., Zbukvic, I., Kim, J. H., & Lawrence, A. J. (2014). Role of cues and contexts on drug-seeking behaviour. *British Journal of Pharmacology*, *171*(20), 4636–4672. doi:10.1111/bph.2014.171.issue-20

Phan, K. L., Fitzgerald, D. A., Nathan, P. J., Moore, G. J., Uhde, T. W., & Tancer, M. E. (2005). Neural substrates for voluntary suppression of negative affect: A functional magnetic resonance imaging study. *Biological Psychiatry*, *57*(3), 210–219. doi:10.1016/j.biopsych.2004.10.030

Prenoveau, J. M., Craske. M. G., Liao, B., & Ornitz, E. M. (2013). Human fear conditioning and extinction: Timing is everything…or is it?. *Biological Psychology*, *92*(1), 59–68.

doi:10.1016/j.biopsycho.2012.02.005

Quirk, G. J. (2002). Memory for extinction of conditioned fear is long-lasting and persists following spontaneous recovery. *Learning & Memory*, *9*(6), 402–407. doi:10.1101/lm.49602

Quirk, G. J., & Beer, J. S. (2006). Prefrontal involvement in the regulation of emotion: Convergence of rat and human studies. *Current Opinion in Neurobiology*, *16*(6), 723–727. doi:10.1016/j.conb.2006.07.004

Quirk, G. J., & Mueller, D. (2007). Neural mechanisms of extinction learning and retrieval. *Neuropsychopharmacology*, *33*(1), 56–72. doi:10.1038/sj.npp.1301555

Ramo, D. E., Anderson, K. G., Tate, S. R., & Brown, S. A. (2005). Characteristics of relapse to substance use in comorbid adolescents. *Addictive Behaviors*, *30*(9), 1811–1823. doi:10.1016/j.addbeh.2005.07.021

Rescorla, R. A. (1988) Behavioral studies of Pavlovian conditioning. *Annual Review of Neuroscience, 11,* 329–352. doi:10.1146/annurev.ne.11.030188.001553

Rescorla, R. A. (2006). Deepened extinction from compound stimulus presentation. *Journal of Experimental Psychology: Animal Behavior Processes*, *32*(2), 135–144. doi:10.1037/0097-7403.32.2.135

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

Robinson, S. M., Sobell, L. C., Sobell, M. B., & Leo, G. I. (2014). Reliability of the Timeline Followback for cocaine, cannabis, and cigarette use. *Psychology of Addictive Behaviors*, *28*(1), 154–162. doi:10.1037/a0030992

Robinson, T. E., & Berridge, K. C. (1993). The neural basis of drug craving: An incentive-

sensitization theory of addiction. *Brain Research Reviews*, *18*(3), 247–291. doi:10.1016/0165-0173(93)90013-P

Robinson, T. E., & Berridge, K. C. (2008). The incentive sensitization theory of addiction: Some current issues. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *363*(1507), 3137–3146. doi:10.1016/0166-4328(95)00131-C

Salkovskis, P. M. (2008). The importance of behaviour in the maintenance of anxiety and panic: A cognitive account. *Behavioural Psychotherapy*, *19*, 1–14. doi:10.1017/S0141347300011472

Siegel, S. (1983). Classical conditioning, drug tolerance and drug dependence. In: Smart, R., Glaser, F., Israel, Y., Kalant, H., Popham, R., Schmidt, W. E. (Eds.), Research advances in alcohol and drug problems. Plenum Press, New York.

Siegel, S. (2005). Drug tolerance, drug addiction, and drug anticipation. *Current Directions in Psychological Science*, *14*(6), 96–300. doi:10.1111/j.0963-7214.2005.00384.x

Siegel, S., Baptista, M. A., Kim, J. A., McDonald, R. V., & Weise-Kelly, L. (2000). Pavlovian psychopharmacology: The associative basis of tolerance. *Experimental and Clinical Psychopharmacology*, *8*(3), 276–293. doi:10.1037/1064-1297.8.3.276

Simons, J. S., & Gaher, R. M. (2005). The Distress Tolerance Scale: Development and validation of a self-report measure. *Motivation and Emotion*, *29*(2), 83–102. doi:10.1007/s11031-005-7955-3

Simons, J. S, Correia, C. J., Carey, K. B., & Borsari, B. E. (1998). Validating a five-factor Marijuana Motives Measure: Relations with use, problems, and alcohol motives. *Journal of Counseling Psychology*, *45*(3), 265–273. doi:10.1037/0022-0167.45.3.265

Simons, J. S., Dvorak, R. D., Merrill, J. E., & Read, J. P. (2012). Dimensions and severity of marijuana consequences: Development and validation of the Marijuana Consequences Questionnaire (MACQ). *Addictive Behaviors*, *37*(5), 613–621.

doi:10.1016/j.addbeh.2012.01.008

Singleton, E. G., Trotman, A. J. M., Zavahir, M., Taylor, R. C., & Heishman, S. J. (2002). Determination of the reliability and validity of the Marijuana Craving Questionnaire using imagery scripts. *Experimental and Clinical Psychopharmacology*, *10*(1), 47–53. doi:10.1037//1064-1297.10.1.47

Sinha, R., & Li, C. S. R. (2007). Imaging stress- and cue-induced drug and alcohol craving: Association with relapse and clinical implications. *Drug and Alcohol Review*, *26*(1), 25–31. doi:10.1080/09595230601036960

Sitharthan, T., Sitharthan, G., Hough, M. J., & Kavanagh, D. J. (1997). Cue exposure in moderation drinking: A comparison with cognitive-behavior therapy. *Journal of Consulting and Clinical Psychology*, *32*(5), 878–882. doi:10.1037/0022-006X.65.5.878

Skinner, M. D., & Aubin, H.-J. (2010). Craving's place in addiction theory: Contributions of the major models. *Neuroscience and Biobehavioral Reviews*, *34*(4), 606–623. doi:10.1016/j.neubiorev.2009.11.024

Sobell, L. C., & Sobell, M. (1996). *Timeline Followback: A calendar method for assessing alcohol and drug use.* Toronto: Addiction Research Foundation.

Sotres-Bayon, F., Cain, C. K., & LeDoux, J. E. (2006). Brain mechanisms of fear extinction: Historical perspectives on the contribution of prefrontal cortex. *Biological Psychiatry*, *60*(4), 329–336. doi:10.1016/j.biopsych.2005.10.012

Stasiewicz, P. R., Brandon, T. H., & Bradizza, C. M. (2007). Effects of extinction context and retrieval cues on renewal of alcohol-cue reactivity among alcohol-dependent outpatients. *Psychology of Addictive Behaviors*, *21*(2), 244–248. doi:10.1037/0893-164X.21.2.244

Stewart, J., de Wit, H., & Eikelboom, R. (1984). Role of unconditioned and conditioned drug effects in the self-administration of opiates and stimulants. *Psychological Review*, *91*(2),

251–268. doi:10.1037/0033-295X.91.2.251

Strong, D. R., Lejuez, C. W., Daughters, S. B., Marinello, M., Kahler, C. W., & Brown, R. A. (2003). The computerized mirror tracing task version 1. Unpublished manuscript.

Tanda, G., & Goldberg, S. R. (2003). Cannabinoids: Reward, dependence, and underlying neurochemical mechanisms? A review of recent preclinical data. *Psychopharmacology*, *169*(2), 115–134. doi:10.1007/s00213-003-1485-z

Teesson, M., Slade, T., Swift, W., Mills, K., Memedovic, S., Mewton, L., Grove, R., et al. (2012). Prevalence, correlates and comorbidity of DSM-IV cannabis use and cannabis use disorders in Australia. *Australian and New Zealand Journal of Psychiatry*, *46*(12), 1182–1192. doi:10.1177/0004867412460591

Thewissen, R., Snijders, S. J. B. D., Havermans, R. C., van den Hout, M., & Jansen, A. (2006). Renewal of cue-elicited urge to smoke: Implications for cue exposure treatment. *Behaviour Research and Therapy*, *44*(10), 1441–1449. doi:10.1016/j.brat.2005.10.010

Tiffany, S. T. (1990). A cognitive model of drug urges and drug-use behavior: Role of automatic and nonautomatic processes. *Psychological review*, *97*(2), 147–168. doi:10.1037/0033-295X.97.2.147

Tiffany, S. T. (1999). Cognitive concepts of craving. *Alcohol research & health: The journal of the National Institute on Alcohol Abuse and Alcoholism*, *23*(3), 215–224. Retrieved from https://secure.ce-credit.com/articles/100624/215-224.pdf

Tiffany, S. T., & Wray, J. M. (2011). The clinical significance of drug craving. *Annals of the New York Academy of Sciences*, *1248*(1), 1–17. doi:10.1111/j.1749-6632.2011.06298.x

Tiffany, S. T., Friedman, L., Greenfield, S. F., Hasin, D. S., & Jackson, R. (2011). Beyond drug use: A systematic consideration of other outcomes in evaluations of treatments for substance use disorders. *Addiction*, *107*(4), 709–718. doi:10.1111/j.1360-0443.2011.03581.x

Todd, T. P., Winterbauer, N. E., & bouton, M. E. (2012). Contextual control of appetite. Renewal of inhibited food-seeking behavior in sated rats after extinction. *Appetite*, *58*(2), 484–489. doi:10.1016/j.appet.2011.12.006

Tsao, J. C. I., & Craske, M. G. (2000). Timing of treatment and return of fear: Effects of massed, uniform-, and expanding-spaced exposure schedules. *Behavior Therapy*, *31*(3), 479–497. doi:10.1016/S0005-7894(00)80026-X

Urcelay, G. P., Wheeler, D. S., & Miller, R. R. (2009). Spacing extinction trials alleviates renewal and spontaneous recovery. *Learning & Behavior*, *37*(1), 60–73. doi:10.3758/LB.37.1.60

Urry, H. L., van Reekum, C. M., Johnstone, T., Kalin, N. J., Thurow, M. E., Schaefer, H. S., Jackson, C. A., et al., (2006). Amygdala and ventromedial prefrontal cortex are inversely coupled during regulation of negative affect and predict the diurnal pattern of cortisol secretion among older adults. *Journal of Neuroscience*, *26*(16), 4415–4425. doi:10.1523/JNEUROSCI.3215-05.2006

Vervoort, E., Vervliet, B., Bennett, M., & Baeyens, F. (2014). Generalization of human fear acquisition and extinction within a novel arbitrary stimulus category. *PLoS ONE*, *9*(5), e96569. doi:10.1371/journal.pone.0096569.g006

Vijanovic, A. A., & Zcolensky, M. J. (2009) Anxiety sensitivity, acute nicotine withdrawal symptoms, and anxious and fearful responding to bodily sensations: A laboratory test. *Experimental and Clinical Psychopharmacology, 17*(3), 181-190. doi: 10.1037/a0016266

Weiss, R. D., Griffin, M. L., Mazurick, C., Berkman, B., Gasfriend, D. R., Frank, A., Barber, J. P., et al. (2003). The relationship between cocaine craving, psychosocial treatment, and subsequent cocaine use. *The American Journal of Psychiatry*, *160*(7), 1320–1325. doi:10.1016/S0376-8716(00)90011-5

Wikler, A. (1948). Recent progress in research on the neurophysiologic basis of morphine

addiction. *The American Journal of Psychiatry*, *105*(5), 329–338. doi:10.1176/ajp.105.5.329

Wölfling, K., Flor, H., & Grüsser, S. M. (2008). Psychophysiological responses to drug-associated stimuli in chronic heavy cannabis use. *European Journal of Neuroscience*, *27*(4), 976–983. doi:10.1111/j.1460-9568.2008.06051.x

Wolpe. J, (1969). *The Practice of Behavior Therapy*. New York: Pergamon Press,

Appendix A

Eligibility Checklist

Inclusion Criteria

Between 18 and 65 years of age	Yes	No	Unsure
Uses cannabis at least 5 days a week	Yes	No	Unsure
Reports at least a "somewhat intense" craving or urge for cannabis	Yes	No	Unsure
Always or almost always mulls tobacco with cannabis or smokes a tobacco cigarette within 15 minutes of smoking cannabis	Yes	No	Unsure
Primarily uses cones/bongs to smoke cannabis	Yes	No	Unsure
Reports smoking cannabis in a living room or lounge-like environment	Yes	No	Unsure
Willing to abstain from cannabis for 1 week	Yes	No	Unsure
Willing to bring in paraphernalia and other drug cues and leave them in the laboratory during the course of the study	Yes	No	Unsure

Exclusion Criteria

Currently receiving treatment for substance use	Yes	No	Unsure
Past history of substantial adverse events during abstinence	Yes	No	Unsure
A current state of acute psychiatric distress	Yes	No	Unsure
Consumed alcohol on more than 10 of the past 30 days and total quantity exceeded 50 standard drinks	Yes	No	Unsure
Use of any drug (besides tobacco) on more than 4 of the past 30 days	Yes	No	Unsure
History of heart disease or other cardiovascular problems	Yes	No	Unsure
No increase in craving in response to cannabis cues on Day 1 in comparison to neutral cues (less than 10-pt self-reported increase)	Yes	No	Unsure

Appendix B

Phone Screen

Hello! Thank you for your interest in our study. As explained in the ad, we are looking for cannabis users who are willing to abstain from using cannabis for 5 days. We are conducting a study to discover how drug paraphernalia influences cravings. The study requires individuals to come into our laboratory at Macquarie University. There are two options for participation in the study, you may come into Macquarie every day for 5 days (Monday to Friday) where the appointments will last from 75 minutes to 2 hours each day. Or you may come in only twice, once for 2 hours on Monday, and a whole day on Friday.

In order to participate, you must regularly smoke cannabis, but be willing to abstain from cannabis and other drugs for one week, restrict your caffeine and tobacco use prior to appointments, provide urine drug screens to verify your abstinence, and bring in your cannabis paraphernalia to our laboratory. This includes your cones, bongs, lighters, mullers, grinders, stash jars and any storage boxes. You will NOT bring in any cannabis to our lab. If eligible, you will be asked to store these things in our lab during your week of participation.

In summary, we are looking for:

- People who use cannabis.

- People who are willing to abstain and verify their abstinence.

- People who are willing to bring in their cannabis paraphernalia and store these items in our lab for the week of participation

-People are able to come into our lab at Macquarie University daily for one week.

-People who are unlikely to experience extreme distress from withdrawing for cannabis for one week. If you are likely to experience extreme withdrawal symptoms, it might be better for you to seek treatment rather than participate in our study.

Do you have any questions? **NO** **YES**

Do you remain interested in this study? **NO** **YES**

I would like conduct a 20-25 minute interview with you to determine if you might be eligible for our study. The information obtained from you will remain confidential and securely stored. In other words, your responses will be stored separately from your name. Everything you say will remain confidential unless you report instances of illegal behaviour that may result in 5 or more years of imprisonment. Such behaviours include giving cannabis to a young person or dealing commercial quantities of cannabis. We do not ask you about such behaviours in the phone interview. We will ask you about your mental health during the interview. We do not directly ask you if you are a danger to yourself or others, but if it becomes apparent through our discussion, we may break confidentiality in order to help you.

Do I have your consent to conduct this interview? **NO** **YES**

1. What is your gender?

(0) ☐ Male

(1) ☐ Female

(2) ☐ Other

2. How old are you? _____ years

3. On how many days have you used cannabis in the last 90 days? _____ /90 (13 weeks)

4. On how many days have you used cannabis in the past week? _____ /7

If no use in the past week, end the interview. Thank the participant and tell him/her we are looking for people who currently use cannabis.

I am now going to ask you questions about craving. A craving is a desire or urge to use cannabis. Cravings can range from a subtle belief that it would be pleasant to smoke cannabis to an intense urge that you need to smoke in order to alleviate a concern, such as tension or the inability to sleep.

5. I want you to think about this past week. Think about the time you wanted to smoke cannabis the most. At that time, how much did you crave cannabis?

(0) ☐ None

(1) ☐ A little

(2) ☐ Somewhat

(3) ☐ A lot

6. How intense was your urge to smoke cannabis at the time?

(0) ☐ Not at all

(1) ☐ A little intense

(2) ☐ Somewhat intense

(3) ☐ Very intense

7. a) In the past 90 days, where did you most often smoke cannabis? Describe this place. (e.g., where in the home, colour of walls, furniture.)

_____

_____

_____

b) What percentage of your smoking occurred there, during the past 90 days? _____%

8. *[Ask this follow up question about living room ONLY if they do not mention the lounge room as their primary smoking environment]*

a) In the past 90 days, have you smoked in a living room or a lounge-like environment?

(0) ☐ No

(1) ☐ Yes

Describe this place. (e.g., colour of walls, furniture.)

_____

_____

_____

b) What percentage of your smoking occurred there, during the past 90 days? _____%

9. In the past 90 days, did you ever smoke at the beach or immediately prior to going to the beach?

(0) ☐ No

(1) ☐ Yes, if so how many days in the last 90 days? _____

10. At what times of days do you always or almost always smoke cannabis?

(0) ☐ between 7am and 10am

(1) ☐ between 10am and 1pm

(2) ☐ between 1pm and 4pm

(3) ☐ between 4pm and 7pm

(4) ☐ between 7pm and 7am

11. How do you usually smoke cannabis? Choose the best option.

(0) ☐ via cones/bongs

(1) ☐ via joints

(2) ☐ via pipes

(3) ☐ via vaporiser

(4) ☐ other

12. Do you always or almost always mull cannabis with tobacco or smoke a tobacco cigarette within

15 minutes of smoking cannabis?

(0) ☐ No

(1) ☐ Yes

13. If yes, how much of your mix is tobacco? _____%

14. Do you smoke tobacco cigarettes at times when you are not smoking cannabis?

(0) ☐ No

(1) ☐ Yes

15. If yes, how many days did you smoke cigarettes during the past month? _____/ 30 days

16. How many cigarettes did you smoke per day of use? _____cigarettes

17. On how many days did you use the following drugs during the past month?

17a. Alcohol _____/30 days (if more than 0 drinks:) Approximately how many drinks have you had each day for the last month? _____

(Total:_____ Drinks/30Days)

17b. Sedative/Hypnotics/Anxiolytics (e.g., Xanax, sleeping pills) _____/30 days

17c. Stimulants (e.g., speed, meth, ice, diet pills) _____/30 days

17d. Opioids (e.g., heroin, codeine, opium) _____/30 days

17e. Cocaine _____/30 days

17f. Hallucinogens (e.g., ecstasy, LSD, ketamine) _____/30 days

17g. Other (e.g, steroids, nitrous oxide) _____/30 days

18. Since you began regularly smoking cannabis, have you ever abstained from cannabis for at least a week?

(0) ☐ No

(1) ☐ Yes

19. [If yes] What sorts of difficulties did you experience? [Ask about a "bong snap" if person does not spontaneously report on it.]

(Note: write "no violent episodes after cessation" if true)

_____

_____

_____

_____

20. [If yes] Have you ever failed an abstinence attempt? If so, how did you react?

_____

_____

_____

_____

_____

21. Are you currently receiving any form of treatment for cannabis use? (Or any other treatment that targets cannabis use? E.g. for anxiety)

(0) ☐ No

(1) ☐ Yes

22. Have you received any form of treatment for your cannabis use in the last 3 months?

(0) ☐ No

(1) ☐ Yes

Now, I am going to ask you some questions about your physical and mental health.

23. How many days a week do you exercise for at least 20 minutes? /7 days

24. Have you had a history of heart disease, high blood pressure, mitral valve prolapse, or other cardiovascular problems?

(0) ☐ No

(1) ☐ Yes

25. For the next series of questions, please answer regarding how you felt in the past 4 weeks. For each question, please respond with "none of the time", "a little of the time", "some of the time", "most of the time", or "all of the time".

	None of the time	**A little of the time**	**Some of the time**	**Most of the time**	**All of the time**
K10.01 In the past four weeks, how often did you feel worn out for no real reason?	1☐	2☐	3☐	4☐	5☐
K10.02 In the past 4 weeks, how often did you feel nervous?	1☐	2☐	3☐	4☐	5☐
K10.03 In the past 4 weeks, how often did you feel so nervous that nothing could calm you down?	1☐	2☐	3☐	4☐	5☐
K10.04 In the past 4 weeks, how often did you feel hopeless?	1☐	2☐	3☐	4☐	5☐
K10.05 In the past 4 weeks, how often did you feel restless or fidgety?	1☐	2☐	3☐	4☐	5☐
K10.06 In the past 4 weeks, how often did you feel so restless you could not sit still?	1☐	2☐	3☐	4☐	5☐
K10.07 In the past 4 weeks, how often did you feel depressed? _	1☐	2☐	3☐	4☐	5☐
K10.08 In the past 4 weeks, how often did you feel that everything was an effort?	1☐	2☐	3☐	4☐	5☐
K10.09 In the past 4 weeks, how often did you feel so sad that nothing could cheer you up?	1☐	2☐	3☐	4☐	5☐
K10.10 In the past 4 weeks, how often did you feel worthless?	1☐	2☐	3☐	4☐	5☐

Total Score: _____

Criteria for eligibility:	
<25	Eligible
25-29	Caution
≥30	Exclude

26. This study requires continuous abstinence from cannabis as well as synthetic cannabis (herbal blends) use and all other drugs besides tobacco and caffeine. Additionally, participants must not drink caffeine or smoke cigarettes for at least two hours prior to all appointments. Are you willing to abstain from cannabis and other drugs for one week, and restrict your caffeine and tobacco use prior to appointments?

(0) ☐ No

(1) ☐ Yes

26. This study requires daily visits to Macquarie University over the course of one week. Appointments will last between 75 minutes and 2 hours. Appointments must occur between the hours of 10am and 7pm. There is not flexibility to reschedule or to miss a day. In the next two weeks, are you able to commit to this schedule?

(0) ☐ No

(1) ☐ Yes

27. What would be the best time of day for you to participate? (time of day when you would normally smoke cannabis)

_____

28. This study requires you to bring in your cannabis paraphernalia to Macquarie University and leave it with us during your week-long participation. Are you willing to commit to this?

(0) ☐ No

(1) ☐ Yes

Thank you for answering all my questions. We will make a decision regarding your eligibility within the next 3 business days. So that I or someone else on the study team may call you back to let you know about your eligibility, may I get your full name and contact information?

Appendix C

Demographic Questions

1. What is your gender?

   0 ☐Male
   1 ☐ Female
   2 ☐ Transgender or Intersex

2. How old are you? _____ years

3. What is your marital status?

   0 ☐ Never married
   1 ☐ Married, or living with someone in a committed relationship
   2 ☐ Separated/Divorced/Annulled/Widowed

4. Are you of Aboriginal or Torres Strait Islander origin?

   0 ☐ No
   1 ☐ Yes, Aboriginal or Torres Strait Islander or both

5. Were you born in Australia?

   0 ☐ No, I was born overseas
   1 ☐ Yes, I was born in Australia

6. What is your main source of income?

   0 ☐ Full-time employment
   1 ☐ Part-time employment
   2 ☐ Temporary benefit, pension, retirement fund, student allowance
   3 ☐ Dependant on others

7. What is the highest level of education that you have completed?
   0 ☐ Up to and including year 10
   1 ☐ Years 11 or 12
   2 ☐ Diploma or trade certificate
   3 ☐ Completed undergraduate degree
   4 ☐ Completed postgraduate degree

8. How many times have you tried to abstain from cannabis, for at least one week, in the past? _____

9. For how many years have you been regularly smoking cannabis? _____

10. When was the last time you smoked cannabis? Date: _____
    Time: _____

11. Are you currently taking any psychotropic medication?
    0 ☐ No
    1 ☐ Yes. If yes, what kind? _____

Appendix D

K-10

Please answer regarding how you felt in the past 4 weeks. For each question, please respond with "none of the time", "a little of the time", "some of the time", "most of the time", or "all of the time".

	None of the time	**A little of the time**	**Some of the time**	**Most of the time**	**All of the time**
K10.01 In the past four weeks, how often did you feel worn out for no real reason?	1☐	2☐	3☐	4☐	5☐
K10.02 In the past 4 weeks, how often did you feel nervous?	1☐	2☐	3☐	4☐	5☐
K10.03 In the past 4 weeks, how often did you feel so nervous that nothing could calm you down?	1☐	2☐	3☐	4☐	5☐
K10.04 In the past 4 weeks, how often did you feel hopeless?	1☐	2☐	3☐	4☐	5☐
K10.05 In the past 4 weeks, how often did you feel restless or fidgety?	1☐	2☐	3☐	4☐	5☐
K10.06 In the past 4 weeks, how often did you feel so restless you could not sit still?	1☐	2☐	3☐	4☐	5☐
K10.07 In the past 4 weeks, how often did you feel depressed? _	1☐	2☐	3☐	4☐	5☐
K10.08 In the past 4 weeks, how often did you feel that everything was an effort?	1☐	2☐	3☐	4☐	5☐
K10.09 In the past 4 weeks, how often did you feel so sad that nothing could cheer you up?	1☐	2☐	3☐	4☐	5☐
K10.10 In the past 4 weeks, how often did you feel worthless?	1☐	2☐	3☐	4☐	5☐

Criteria for eligibility:	
<25	Eligible
25-29	Caution
≥30	Exclude

Total Score: _____

Appendix E

The Brief Marijuana Consequences Questionnaire

The following is a list of things that sometimes happen to people either during, or after they have been using marijuana. Select either **YES** or **NO** to indicate whether that item describes something that has happened to you **IN THE PAST MONTH**.

1. The quality of my work or schoolwork has suffered because of my marijuana use.
   (0) _____ No
   (1) _____ Yes

2. I have driven a car when I was high.
   (0) _____ No
   (1) _____ Yes

3. I have felt in a fog, sluggish, tired, or dazed the morning after using marijuana.
   (0) _____ No
   (1) _____ Yes

4. I have been unhappy because of my marijuana use.
   (0) _____ No
   (1) _____ Yes

5. I have gotten into physical fights because of my marijuana use.
   (0) _____ No
   (1) _____ Yes

6. I have spent too much time using marijuana.
   (0) _____ No
   (1) _____ Yes

7. I have felt like I needed a hit of marijuana after I'd gotten up.
   (0) _____ No
   (1) _____ Yes

8. I have become very rude, obnoxious, or insulting after using marijuana.
   (0) _____ No
   (1) _____ Yes

9. I have been less physically active because of my marijuana use.
   (0) _____ No
   (1) _____ Yes

10. I have had trouble sleeping after stopping or cutting down on marijuana use.
    (0) _____ No
    (1) _____ Yes

11. I have neglected obligations to family, work, or school because of my marijuana use.
    (0) _____ No
    (1) _____ Yes
12. When using marijuana I have done impulsive things that I regretted later.

(0) _____ No
(1) _____ Yes

13. I have awakened the day after using marijuana and found I could not remember a part of the evening before.
(0) _____ No
(1) _____ Yes

14. I have been overweight because of my marijuana use.
(0) _____ No
(1) _____ Yes

15. I haven't been as sharp mentally because of my marijuana use.
(0) _____ No
(1) _____ Yes

16. I have received a lower grade on an exam or paper than I ordinarily could have because of marijuana use.
(0) _____ No
(1) _____ Yes

17. I have tried to quit using marijuana because I thought I was using too much.
(0) _____ No
(1) _____ Yes

18. I have felt anxious, irritable, lost my appetite or had stomach pains after stopping or cutting down on marijuana use.
(0) _____ No
(1) _____ Yes

19. I have often thought about needing to cut down or to stop using marijuana.
(0) _____ No
(1) _____ Yes

20. I have less energy or felt tired because of my marijuana use.
(0) _____ No
(1) _____ Yes

21. I have lost motivation to do things because of my marijuana use.
(0) _____ No
(1) _____ Yes

The Fagerstrom Test for Nicotine Dependence

Please answer the following questions in regard to tobacco smoking only. Please consider the last month.

1. How soon after you wake up do you smoke your first cigarette?

(3)_____ 5 minutes or less

(2)_____ 6 to 30 minutes

(1)_____ 31 to 60 minutes

(0)_____ After 60 minutes

2. Is it hard for you to not smoke in places where it is not allowed like in church, at the library, or at the movies?

(1)_____ Yes

(0)_____ No

3. Which cigarette would you hate to give up the most?

(1)_____ The first one in the morning

(o)_____ All others

4. How many cigarettes per day do you smoke?

(0)_____ 10 or less

(1)_____ 11 to 20

(2)_____ 21 to 30

(3)_____ 31 or more

5. Do you smoke more during the first few hours after you wake up than during the rest of the day?

(1)_____ Yes

(0)_____ No

6. Do you smoke if you are so sick that you are in bed most of the day?

(1)_____ Yes

(0)_____ No

Appendix G

Marijuana Motives Measure

Please consider all of the times that you have smoked cannabis in the past month. Using the following scale, indicate how often you smoked cannabis for each of the below reasons

1----------2----------3----------4----------5

Almost Never /Never — About half the time — Almost Always /Always

1.	To forget my worries	_____
2.	Because my friends pressured me to use marijuana	_____
3.	To help me enjoy a party	_____
4.	To help me when I felt depressed or nervous	_____
5.	To be sociable	_____
6.	To cheer me up when I was in a bad mood	_____
7.	Because I liked the feeling	_____
8.	So that others wouldn't kid me about not using marijuana	_____
9.	Because it was exciting	_____
10.	To get high	_____
11.	To make a social gathering more fun	_____
12.	To fit in with the group I like	_____
13.	To give me a pleasant feeling	_____
14.	To improve parties and celebrations	_____
15.	To feel more self-confident and sure of myself	_____
16.	To forget about my problems	_____
17.	Because it was fun	_____
18.	To be liked	_____
19.	So I wouldn't feel left out	_____
20.	To know myself better	_____
21.	To be more creative and original	_____
22.	To understand things differently	_____
23.	To expand my awareness	_____
24.	To be more open to experiences	

Appendix H

The Structured Clinical Interview for DSM Disorders modified for the DSM-5

LIFETIME CANNABIS USE	**CANNABIS USE DISORDER CRITERIA**				
Now I'd like to ask you some questions about your cannabis use in the last year. During the last year…	A problematic pattern of substance use leading to clinically significant impairment or distress, as manifested by at least two of the following occurring within a 12-month period:				
(Did you often find/*Have you often found)* that when you started using cannabis you ended up using much more of it than you were planning to? (Tell me about it.) IF NO: What about using it over a much longer period of time than you were planning to?	(1) substance is often taken in larger amounts OR over a longer period than was intended	?	1	2	3
(Did you try/*Have you tried*) to cut down or stop using cannabis? IF YES: Did you ever actually stop using cannabis altogether? (How many times did you try to cut down or stop altogether?) IF NO: Did you want to stop or cut down? (Is this something you kept worrying about?)	(2) there is a persistent desire OR unsuccessful efforts to cut down or control substance use	?	1	2	3
(Did you spend/*Have you spent*) a lot of time using cannabis or doing whatever you had to do to get it? Did it take you a long time to get back to normal? (How much time?)	(3) a great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects	?	1	2	3
(Did you spend/Have you spent) a lot of time <u>thinking</u> about using cannabis or how you were going to get it? Were these thoughts accompanied by strong urges or desires to use cannabis? IF YES: Did these desires or urges feel out of your control? Did you feel like you would be more content if you were using cannabis?	(4) craving or a strong desire or urge to use substance	?	1	2	3

(Did you miss/*Have you ever missed*) work or school because you were very high or very hung over? What about doing a bad job at work or failing courses at school because you used cannabis? IF NO: What about not keeping your house clean [IF CHILDREN: or not taking proper care of your children] because of using cannabis? IF YES TO EITHER: How often? (Over what period of time?)	(5) recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)	?	1	2 3
IF NOT ALREADY KNOWN: (Did your use of cannabis cause/*Has your use of cannabis caused*) problems with other people, such as with family members, friends, or people at work? Did you get into physical fights or bad arguments about your cannabis use? IF YES: Did you keep on using cannabis anyway? (Over what period of time?)	(6) continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with spouse about consequences of intoxication, physical fights)	?	1	2 3
(Did you often have/*Have you often had*) times when you would use cannabis so often that you used cannabis instead of working or spending time with your family or friends or engaging in other important activities, such as sports, gardening, or playing music?	(7) important social, occupational, or recreational activities given up or reduced because of substance use	?	1	2 3
(Did you ever use/*Have you ever used*) cannabis in a situation in which it might have been dangerous to be using cannabis at all? ([Did you ever drive/*Have you ever driven*] while you were really too high to drive?) (What about surfing or swimming?) IF YES AND UNKNOWN: How many times? (When?)	(8) recurrent substance use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use)	?	1	2 3
IF NOT ALREADY KNOWN: (Did cannabis cause/*Has cannabis caused*) any psychological problems like making you depressed, agitated, or paranoid? (Did cannabis cause/*Has cannabis caused*) any significant physical problems or made physical problems worse? IF YES TO EITHER OF ABOVE: Did you keep on using cannabis anyway?	(9) substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., recurrent cocaine use despite recognition of cocaine-related depression)	?	1	2 3

(Did you find/*Have you found*) that you needed to use a lot more cannabis in order to get the feeling you wanted than you did when you first started using it? IF YES: How much more? IF NO: What about finding that when you used the same amount, it had much less effect than before?	(10) tolerance, as defined by either of the following: (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect (b) markedly diminished effect with continued use of the same amount of the substance	?	1	2 3
(Did you have/*Have you ever had*) any withdrawal symptoms, that is, felt sick when you cut down or stopped using cannabis? IF YES: What symptoms did you have? IF NO: After not using cannabis for a few hours or more, did you sometimes use it to keep yourself from getting sick with (WITHDRAWAL SYMPTOMS)? Possible cannabis withdrawal symptoms: Sleeping difficulties, including vivid dreams Appetite changes Nausea, stomach aches	(11) withdrawal, as manifested by either of the following: (a) the characteristic withdrawal syndrome for the substance (b) the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms Mood changes Lethargy Increase in cravings	?	1	2 3

IF UNKNOWN: When did (SXS CODED "2" ABOVE) occur? (Did they all happen around the same time?)

AT LEAST TWO SYMPTOMS CODED "2" AND ITEMS OCCURRED WITHIN THE SAME 12-MONTH PERIOD

1 3

CANNABIS USE DISORDER GO TO *CHRONOLOGY*

CHRONOLOGY FOR CANNABIS USE DISORDER

How old were you when you first had these problems associated with cannabis?

Age at onset of Non-Alcohol Substance Use Disorder (CODE 99 IF UNKNOWN) ___ ___

IF UNCLEAR: During the past month, have you used cannabis at all?

IF YES: Tell me more about it. (Has your [DRUG] use caused you any problems?)

Full criteria for Cannabis Use Disorder met at any time in past month (or no month without any symptoms)?

? 1 3

GO TO ***REMISSION SPECIFIERS***

CURRENT CANNABIS USE DISORDER

NOTE CURRENT SEVERITY:

0 Mild: Presence of 2-3 symptoms

1 Moderate: Presence of 4-5 symptoms

2 Severe: Presence of 6 or more symptoms

REMISSION SPECIFIERS

THE FOLLOWING REMISSION SPECIFIERS CAN BE APPLIED ONLY AFTER NO CRITERIA FOR CANNABIS USE DISORDER HAVE BEEN MET FOR AT LEAST 1 MONTH.

Note: These specifiers do not apply if the individual is In a Controlled Environment (below).

Number of months prior to interview when last had some problems with drug _____months

1 **Early Remission:** For at least 3 months, but less than 12 months, no criteria for Substance Use Disorder have been met (with the exception of Criterion A4, "Craving, or a strong desire or urge to use substance", may be present)

2 **Sustained Full Remission:** None of the criteria for a Substance Use Disorder have been met at any time during a period of 12 months or longer (with the exception of "Craving, or a strong desire or urge to use substance")

3 **Check ___ if In a Controlled Environment:** The individual is in an environment where access to alcohol and controlled substances is restricted and no criteria for a Substance Use Disorder have been met for at least the past month. Examples are closely supervised and substance-free jails, therapeutic communities, and locked hospital units.

Appendix I

Timeline Followback Interview

Using the calendar below, please indicate how many joints or cones you had on the days that you used cannabis in the last 30 days. Also indicate use of alcohol, sedatives, stimulants, opioids, cocaine, and hallucinogen use.

Mon	Tue	Wed	Thur	Fri	Sat	Sun
Example: ☑ 4 joints	☐	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	☐	☐

Appendix J

Subjective Units of Cannabis Withdrawal (Past 24 Hours)

[Responses should be based on a comparison between the last 24 hours and when participants were smoking cannabis regularly]

In the past 24 hours:

1. How intensely did you think about smoking cannabis? _____

0----------25----------50----------75----------100
Not at all Mildly Moderately Very Extremely

2. How intense was your anger and/or irritability? _____

0----------25----------50----------75----------100
Not at all Mildly Moderately Very Extremely

3. How much trouble did you have sleeping last night? _____

0----------25----------50----------75----------100
Not at all Mildly Moderately Very Extremely

4. How intense or strange were your dreams or nightmares? _____

0----------25----------50----------75----------100
Not at all Mildly Moderately Very Extremely

5. How tense or anxious did you feel? _____

0----------25----------50----------75----------100
Not at all Mildly Moderately Very Extremely

6. How much did life feel like an uphill struggle? _____

0----------25----------50----------75----------100
Not at all Mildly Moderately Very Extremely

7. Did your appetite change? _____

0----------25----------50----------75----------100
Not at all Mildly Moderately Very Extremely

Appendix K

Contextual Cue Assessment

1. In the past month, what percentage of cannabis smoking occasions involved another person? _____%

2. In the past month, with whom did you usually use cannabis with?
   - 0☐ Flatmate
   - 1☐ Friends
   - 2☐ Family members
   - 3☐ Co-workers
   - 4☐ Dealer

3. In the past month, when you smoked with other people, how many people usually smoked cannabis with you? _____people

4. Do you currently live with someone who uses cannabis?
   - 0☐ No
   - 1☐ Yes

5. Are the people you are emotionally closest to cannabis smokers?
   - 0☐ No
   - 1☐ Yes

6. How do you use marijuana? Tell me about the objects you touch in order to use cannabis.

_____

_____

_____

_____

_____

_____

7. In the past month, how often did you encounter the objects identified above?
   - 0☐ Every other day
   - 1☐ Once a day
   - 2☐ A few times each day
   - 3☐ Approximately half the time each day
   - 4☐ Almost constantly each day

8. In the past month, how often did you encounter these objects when you were not using cannabis?
   - 0☐ Never. I only encounter these items when I use them to smoke cannabis.
   - 1☐ Less than half of the time.
   - 2☐ About half of the time I encounter these objects I am not using cannabis.
   - 3☐ More than half of the time.
   - 4☐ Almost constantly. I encounter these items almost constantly when I'm not using cannabis.

9. In the past month, where did you most often smoke cannabis?
   - 0☐ My own living room
   - 1☐ My own bedroom
   - 2☐ Someone else's living room
   - 3☐ Someone else's bedroom
   - 4☐ Outside
   - 5☐ Other_____

10. What activities do you usually engage in while smoking cannabis? (e.g. play video games, watch movies etc…)

_____

_____

_____

_____

_____

_____

_____

11. Describe the thoughts that you frequently have prior to and during cannabis use.

_____

_____

_____

_____

_____

_____

12. In the past month, how often have you smoked cannabis to get rid of disturbing feelings as quickly as possible (does not include cravings)?

0☐ Never
1☐ very little of my use was for this reason, but it did happen
2☐ less than half of my use was for this reason
3☐ half my use was for this reason
4☐ more than half of my use was for this reason
5☐ most of my use was for this reason, but not quite all
6☐ all of my use was for this reason

13. In the past month, how often have you smoked cannabis to deal with uncomfortable situations or places you did not want to be?

0☐ Never
1☐ very little of my use was for this reason, but it did happen
2☐ less than half of my use was for this reason
3☐ half my use was for this reason
4☐ more than half of my use was for this reason
5☐ most of my use was for this reason, but not quite all
6☐ all of my use was for this reason

14. In the past month, how often have you smoked cannabis to specifically get rid of cravings?

0☐ Never
1☐ very little of my use was for this reason, but it did happen
2☐ less than half of my use was for this reason
3☐ half my use was for this reason
4☐ more than half of my use was for this reason
5☐ most of my use was for this reason, but not quite all
6☐ all of my use was for this reason

15. What is the worst that might happen if you never smoked cannabis again?

_____

_____

_____

_____

_____

16. What is the most likely outcome of never smoking cannabis again?

17. Rank the cannabis paraphernalia items that you brought in with you today. Please use a 0 to indicate that if you were abstinent, the object would not lead you to experience any craving or urge to use cannabis, and 100 to indicate that the object would lead you to experience immense cravings that would nearly impossible or impossible to alleviate without using cannabis. 50 indicates a moderate degree of craving is produced by the object.

Object	**Subjective Units of Craving**
1.	
2.	
3.	
4.	
5.	

Appendix L

Quit Session

This session is meant to assist participants in successfully remaining abstinent from cannabis and other drugs over the next week. The clinician should begin by asking the participant how they are feeling about not smoking cannabis over the next week. The clinician should explain that (even if the participant feels confident about maintaining abstinence), it is a requirement of our study that they go through some basic quitting techniques and information with them now, as all participants are treated equally.

The clinician should specifically highlight the issue of withdrawal – and explain to the participant that withdrawal can make it difficult to stop smoking, and can often cause people to return to cannabis use, even when symptoms are mild.

Motivational Interviewing

Motivational Interviewing (MI) principles should be used throughout this session. These principles can be viewed as a general strategy for discussion.

1. *Express Empathy*. Empathy is expressed using reflective listening to direct the client toward motivation for change.

2. *Reflective listening*

    a. Ask open-ended questions
    b. Reflect what you think the client means, using statements (not questions)
    c. Reflect what the client seems to be feeling (e.g., "Right now you seem pretty frustrated; do I have that right?"). Selectively emphasise certain aspects of what the client says, particularly when he/she appears to be expressing self-motivational statements
    d. Use compliments and statements of appreciation and understanding
    e. Use summary statements to link together material that has been discussed, particularly where the client makes self-motivational statements

3. *Support Self-Efficacy*

    a. Look for signs of readiness to change, such as Decreased resistance, Decreased questions about the problem, Resolve, Self-motivational statements, Increased questions about change, Envisioning, and Experimenting.

    b. Move the client toward making a decision. Doing so may include:

        1. Recapitulation: Summarise the client's situation. This should include a summary of the client's perceptions of the problem, including what remains positive or attractive about cannabis use; any indications the client has offered of wanting, intending, or planning to change; and your own assessment of the client's situation, particularly at points where it meets with the client's own concerns.

        2. Key questions: Ask the client what he/she wants to do. This should be asked using open-ended questions, which selectively reinforce self-motivational statements and emphasize personal choice.

        3. Information and advice: you can give advice if the client asks for it, but take care not to offer advice when the client isn't ready to hear it. Ways to avoid this include

waiting for the request, qualifying your suggestions (e.g., presenting them as data), and offering multiple options.

Self-efficacy

Have the participant answer the following questions in order to assess how confident he/she is in resisting the urge to use cannabis during various potential situations.

0% confident could resist using cannabis - 100% confident could resist using

1. If you feel angry or frustrated _____

2. If you have trouble sleeping _____

3. If something good happens and you want to celebrate _____

4. If you unexpectedly find some cannabis or see something that reminds you of using cannabis _____

5. If you see others smoking cannabis _____

6. If other people treat you unfairly or interfere with your plans _____

7. If you are out with friends and they keep suggesting you smoke cannabis _____

8. If you have to do monotonous work _____

9. If you feel depressed or worried _____

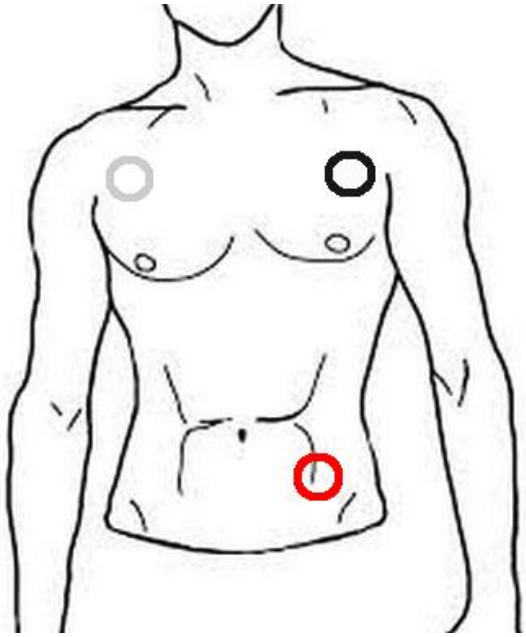
10. If you have free time _____

Ask participants why they feel as confident as they do in each situation. Develop strategies in an attempt to have participants feel at least 80% confident in each situation. General strategies to avoid use include:

Avoid stimuli and people that remind you of using
Think about other things when you get an urge
Do something else that prevents you from smoking
Find other ways to calm down
Engage in relaxing and enjoyable activities each day
Tell people directly when you feel upset
Call the investigator or the Cannabis Information Helpline

Appendix M

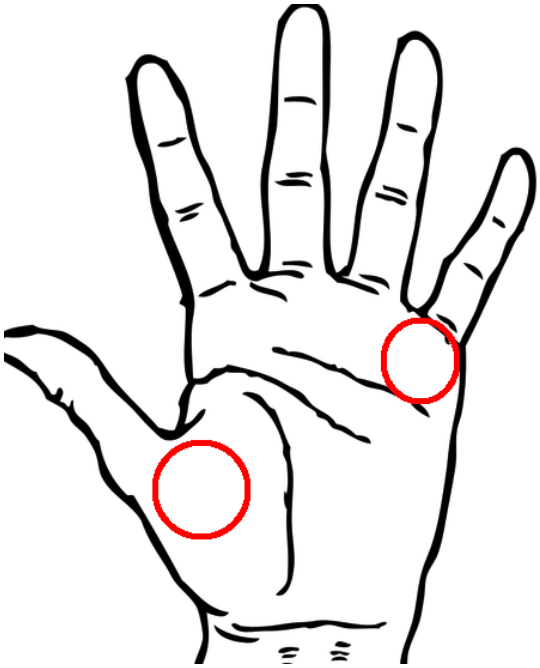
Electrode Placement in Einthovens Triangle



Appendix N

Skin Conductance Electrode Placement

Placement on the palm of the hand.



Appendix O

Subjective Units of Craving and Tolerance

1. Right now, how intense is your current craving and urge to use cannabis? _____

0----------25----------50----------75----------100

No urge or craving	Mild urges/cravings	Moderate urges/cravings	Intense urges/cravings	Very Intense urges/cravings

2. Right now, how pleasant would it be to use cannabis? _____

0----------25----------50----------75----------100

No at all pleasant	Mildly pleasant	Moderately pleasant	Very pleasant	Incredibly pleasant

3. Right now, how UNacceptable is this current level of craving and urge to use cannabis? _____

0----------25----------50----------75----------100

Completely acceptable	Mildly unacceptable	Moderately unacceptable	Very unacceptable	Completely unacceptable

4. Right now, how unbearable or intolerable is your level of craving and urge to use cannabis? _____

0----------25----------50----------75----------100

Completely tolerable	Mildly intolerable	Moderately intolerable	Very intolerable	Completely intolerable

5. If you were at home and not in this study, how likely would it be that you would use cannabis when experiencing this level of craving and urge to use cannabis? _____

0----------25----------50----------75----------100

Completely unlikely	Somewhat likely	Moderately likely	Very likely	Extremely likely

Appendix P

Subjective Units of Craving and Tolerance Progression Form

How intense is your current craving and urge to use cannabis right now?

0----------25----------50----------75----------100

No urge or craving	Mild urges/cravings	Moderate urges/cravings	Intense urges/cravings	Very Intense urges/cravings

How unbearable or intolerable is this level of craving and urge to use cannabis?

0----------25----------50----------75----------100

Completely tolerable	Mildly intolerable	Moderately intolerable	Very intolerable	Completely intolerable

Day 2

Item 1 (Lowest Craving) _____
Pre - craving ____ - intolerability ____
Mid - craving ____ - intolerability ____
Post - craving ____ - intolerability ____

Item 2_____
Pre - craving ____ - intolerability ____
Mid - craving ____ - intolerability ____
Post - craving ____ - intolerability ____

Item 3_____
Pre - craving ____ - intolerability ____
Mid - craving ____ - intolerability ____
Post - craving ____ - intolerability ____

Item 4 _____
Pre - craving ____ - intolerability ____
Mid - craving ____ - intolerability ____
Post - craving ____ - intolerability ____

Item 5 (Highest Craving) _____
Pre - craving ____ - intolerability ____
Mid - craving ____ - intolerability ____
Post - craving ____ - intolerability ____

All 5 Items combined
Pre - craving ____ - intolerability ____
Mid - craving ____ - intolerability ____
Post - craving ____ - intolerability ____

Day 3

Item 1 (Lowest Craving) _____
Pre - craving ____ - intolerability ____
Mid - craving ____ - intolerability ____
Post - craving ____ - intolerability ____

Item 2 _____
Pre - craving ____ - intolerability ____
Mid - craving ____ - intolerability ____
Post - craving ____ - intolerability ____

Item 3 _____
Pre - craving ____ - intolerability ____
Mid - craving ____ - intolerability ____
Post - craving ____ - intolerability ____

Item 4 _____
Pre - craving ____ - intolerability ____
Mid - craving ____ - intolerability ____
Post - craving ____ - intolerability ____

Item 5 (Highest Craving) _____
Pre - craving ____ - intolerability ____
Mid - craving ____ - intolerability ____
Post - craving ____ - intolerability ____

All 5 Items combined
Pre - craving ____ - intolerability ____
Mid - craving ____ - intolerability ____
Post - craving ____ - intolerability ____

Appendix Q

Audio Script

Baseline 1 Script

Over the next few minutes, you will be provided with two different scenarios. Your only task is to listen carefully to the descriptions and follow any instructions that are provided to you.

For now, we would like you to get comfortable in your chair. Please try not to move during the next few minutes as your physiological responses are being recorded. Now that you are comfortable, please pay attention to your surroundings. Until you are given your next set of instructions, please continue to take notice of what is around you.

Baseline 2 Script

While you wait for the next scenario description please remember to sit still but comfortably in your chair. Your physiological responses are continuing to be recorded. While you wait, please pay attention to your surroundings. Please take notice of where you are at and what is around you, until you are given your next set of instructions.

Baseline 3 Script

Please remember to sit still but comfortably in your chair. Your physiological responses are continuing to be recorded. While you wait, please pay attention to your surroundings. Please take notice of where you are at and what is around you, until you are given your next set of instructions.

Neutral Script

You're at the beach lying on a towel. Your good friends are lying next to you. The warm sun penetrates your skin, while a fresh breeze blows over your body, completely relaxing you. Some people are playing in the water, others are surfing, and kids are playing with beach balls and making sand castles. As you lay there, you listen to the sounds around you. You hear the sounds of rolling waves splashing rhythmically against the shore. You're feeling relaxed and at ease. As the sun beats down on your skin, you think about how satisfying it would be to cool yourself off in the ocean. You don't want to get up because you are feeling so relaxed, yet, it would be great to feel the cold water against your body. You walk to the shore, gently easing yourself into the water. As you walk deeper and deeper into the ocean, waves crash against your body. You're enjoying this day completely.

Wait 5 seconds then say: Now keep imagining you're at the beach. (Run beach audio for 30 seconds).

Cannabis Script

You're at home sitting in a comfortable chair. You have friends over that you've known a long time and you're enjoying yourself very much. You're feeling relaxed and totally at ease. Many of your friends are passing the bong around. As you sit there listening to the conversation and the gurgling of the bong water, you begin to think about how enjoyable a cone would be. The smoke begins to fill the room and you think about how satisfying it would be to hold a bong in your hands. The more you think about smoking a cone, the stronger you desire becomes. You

think that because you're at home and having a good time with your friends it might be okay to get stoned. How could you really enjoy yourself fully unless you smoke a cone? Your desire to smoke becomes really intense and you think there's no good reason not to smoke a cone while the bong is being passed around.

Wait 5 seconds then say: Now keep imagining you're at home, watching the bong being passed around. (Run bong for 30 seconds).

Neutral Beach Cue

Appendix S

Cannabis Cue

Appendix T

Distress Tolerance Scale

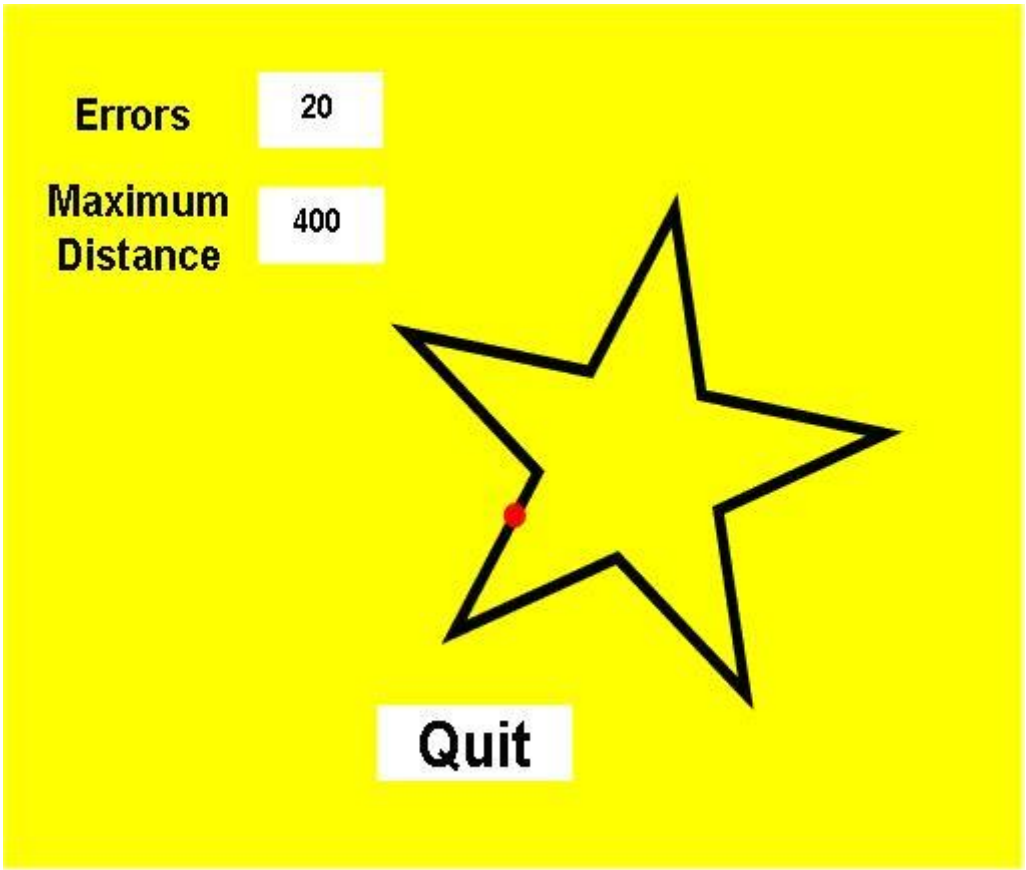
Think of times that you feel distressed or upset. Circle the number from the menu that best describes your beliefs about feeling distressed or upset.

1 Strongly agree	2 Mildly agree	3 Agree & disagree equally	4 Mildly disagree	5 Strongly disagree

1. Feeling distressed or upset is unbearable to me.	1	2	3	4	5
2. When I feel distressed or upset, all I can think about is how bad I feel.	1	2	3	4	5
3. I can't handle feeling distressed or upset.	1	2	3	4	5
4. My feelings of distress are so intense that they completely take over.	1	2	3	4	5
5. There's nothing worse than feeling distressed or upset.	1	2	3	4	5
6. I can tolerate being distressed or upset as well as most people.	1	2	3	4	5
7. My feelings of distress or being upset are not acceptable.	1	2	3	4	5
8. I'll do anything to avoid feeling distressed or upset.	1	2	3	4	5
9. Other people seem to be able to tolerate feeling distressed or upset better than I can.	1	2	3	4	5
10. Being distressed or upset is always a major ordeal for me.	1	2	3	4	5
11. I am ashamed of myself when I feel distressed or upset.	1	2	3	4	5
12. My feelings of distress or being upset scare me.	1	2	3	4	5
13. I'll do anything to stop feeling distressed or upset.	1	2	3	4	5
14. When I feel distressed or upset, I must do something about it immediately.	1	2	3	4	5
15. When I feel distressed or upset, I cannot help but concentrate on how bad the distress actually feels.	1	2	3	4	5

Mirror Tracing Persistence Task

Computerised task. Participants are instructed to trace four stars backwards by using a mouse. Tolerance for distress is measured by the amount of time an individual takes to give up on the task. This task adapts to a participant's level of ability based on performance during three practice stars. Additionally, the task provides a small incentive to continue on with the final star (up to $3.50) despite distress in order to mimic real-life events that include both distressing and rewarding properties (e.g., completing a challenging work task).



Appendix V

Marijuana Craving Questionnaire

Circle the number that best corresponds to the degree to which you disagree or agree with each statement based on how you are thinking and feeling right now.

1. Smoking marijuana would be pleasant right now.
   Strongly disagree 1 2 3 4 5 6 7 Strongly agree

2. I could not easily limit how much marijuana I smoked right now.
   Strongly disagree 1 2 3 4 5 6 7 Strongly agree

3. Right now, I am making plans to use marijuana.
   Strongly disagree 1 2 3 4 5 6 7 Strongly agree

4. I would feel more in control of things right now if I could smoke marijuana.
   Strongly disagree 1 2 3 4 5 6 7 Strongly agree

5. Smoking marijuana would help me sleep better at night.
   Strongly disagree 1 2 3 4 5 6 7 Strongly agree

6. If I smoked marijuana right now, I would feel less tense.
   Strongly disagree 1 2 3 4 5 6 7 Strongly agree

7. I would not be able to control how much marijuana I smoked if I had some here.
   Strongly disagree 1 2 3 4 5 6 7 Strongly agree

8. It would be great to smoke marijuana right now.
   Strongly disagree 1 2 3 4 5 6 7 Strongly agree

9. I would feel less anxious if I smoked marijuana right now.
   Strongly disagree 1 2 3 4 5 6 7 Strongly agree

10. I need to smoke marijuana now.
    Strongly disagree 1 2 3 4 5 6 7 Strongly agree

11. If I were smoking marijuana right now, I would feel less nervous.
    Strongly disagree 1 2 3 4 5 6 7 Strongly agree

12. Smoking marijuana would make me content.
    Strongly disagree 1 2 3 4 5 6 7 Strongly agree

MCQ SCORING

Compulsivity = Q2 + Q7 + Q10 = _____

Emotionality = Q4 + Q6+Q9 = _____

Expectancy = Q5+Q11+Q12 = _____

Purposefulness = Q1 +Q3+Q8 = _____

Persons who score above 14 on any subscale will be asked to stay in the lab until their cravings reduce to a more manageable level.

Appendix W

Study Context Questionnaire

1. In how many rooms at Macquarie University were you exposed to cannabis paraphernalia (either your own or someone else's)? _____

2. Please describe the living room?

_____

_____

_____

3. How similar was this room to lounge or lounge-like environment where you use cannabis? _____

0%----------25%----------50%----- ----------75%----------100%

Not at all similar	Somewhat similar	Moderately similar	Very similar	Completely similar

4. How at home (comfortable) did you feel in the living room? _____

0%----------25%----------50%----- ----------75%----------100%

Not at all at home	Somewhat at home	Moderately at home	Very at home	Completely at home

5. What paraphernalia would you rather smoke cannabis with?

☐ The Lab's cannabis paraphernalia
☐ Your personal cannabis paraphernalia

(Only ask the following questions to those participants who were assigned to the ABA condition)

6. Please describe the therapist's office?

_____

_____

_____

7. How similar was the therapist's office to the living room in which you typically use cannabis? _____

0%----------25%----------50%----------75%----------100%

Not at all similar	Somewhat similar	Moderately similar	Very similar	Completely similar

8. How at home (comfortable) did you feel in the therapist's office? _____

0%----------25%----------50%----------75%----------100%

Not at all at home	Somewhat at home	Moderately at home	Very at home	Completely at home

9. How similar were the therapist's office and the living room to each other? _____

0%----------25%----------50%----------75%----------100%

Not at all similar	Somewhat similar	Moderately similar	Very similar	Completely similar

Appendix X

Lounge Room

Appendix Y

Therapy Room

Appendix Z

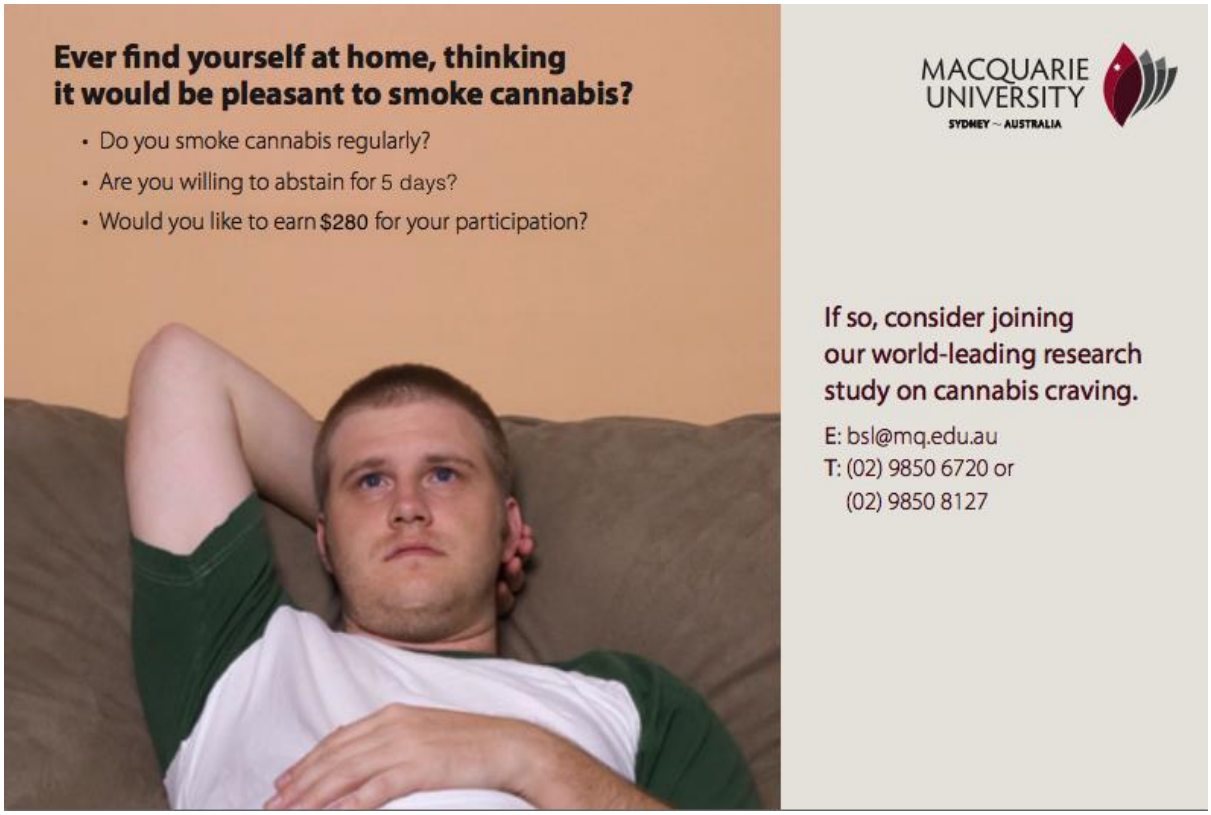
Advertisements

A world leading research study on cannabis craving

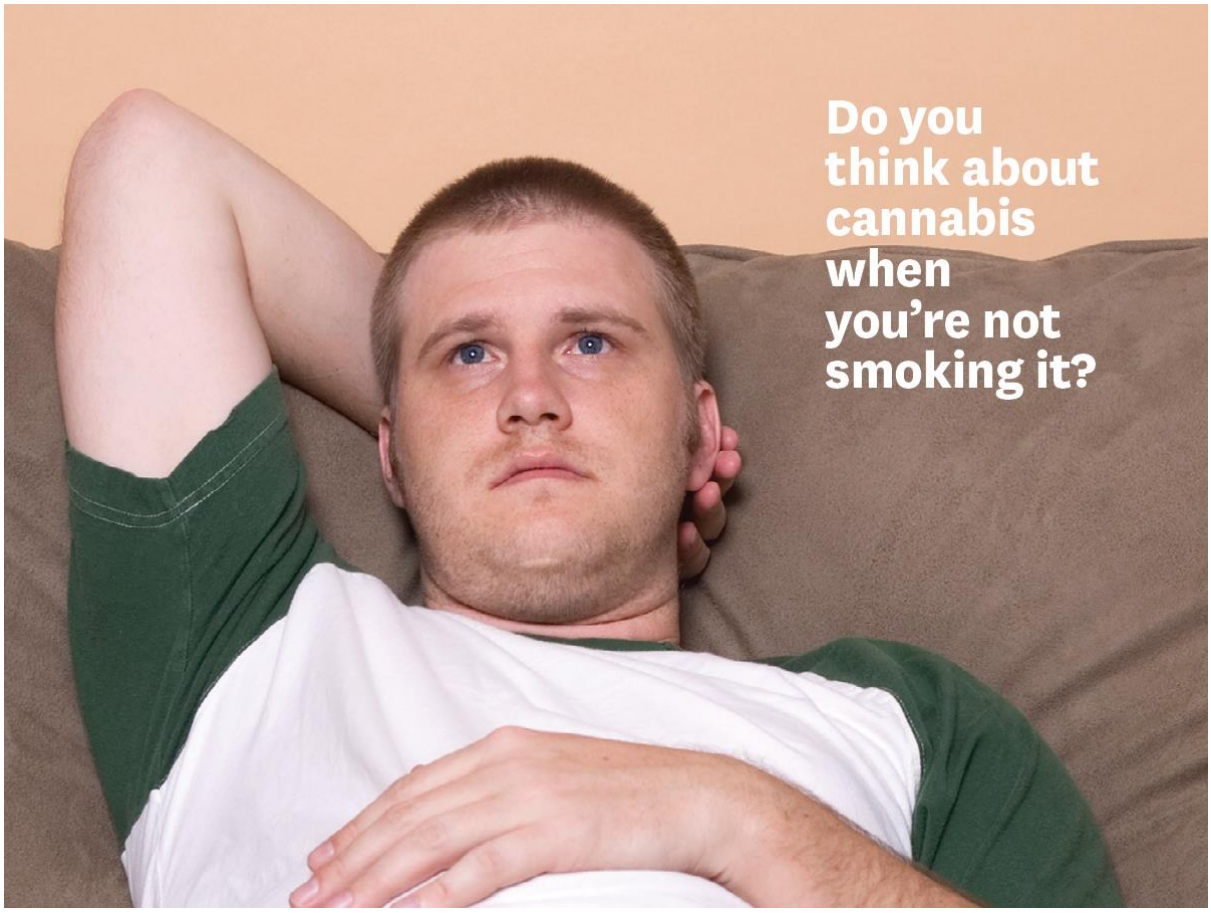
Macquarie University is seeking research participants over the age of 18, who regularly smoke cannabis, and are willing to abstain for 5 days. Participants will be reimbursed up to $280 for their time.

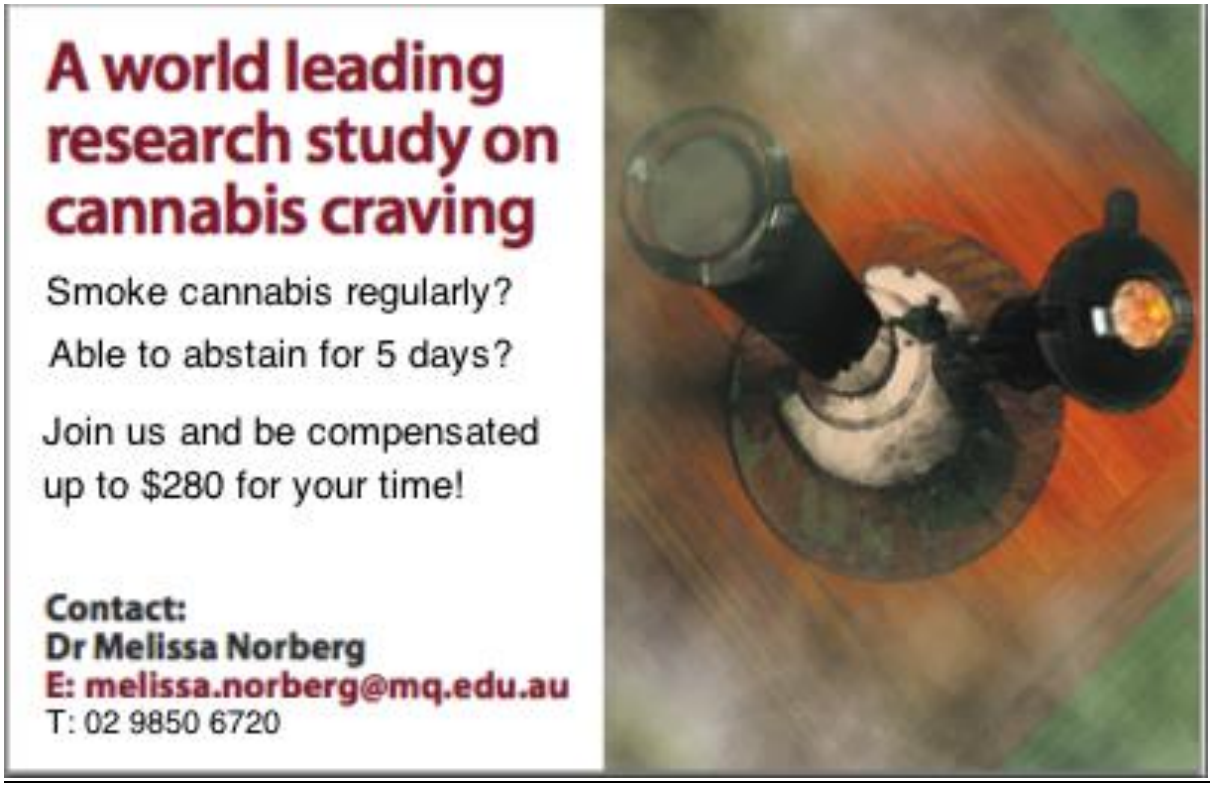
For information about this week-long study contact Dr Melissa Norberg
E: melissa.norberg@mq.edu.au
T: 02 9850 6720

Contact Dr Melissa Norberg
E: melissa.norberg@mq.edu.au
T: 02 9850 6720


Ever find yourself at home, thinking it would be pleasant to smoke cannabis?
• Do you smoke cannabis regularly?
• Are you willing to abstain for 5 days?
• Would you like to earn $280 for your participation?
MACQUARIE UNIVERSITY
SYDNEY ~ AUSTRALIA
If so, consider joining our world-leading research study on cannabis craving.
E: bsl@mq.edu.au
T: (02) 9850 6720 or
(02) 9850 8127


Smoke cannabis?
MACQUARIE University
• Willing to abstain for five days?
• Can you travel to Macquarie University?
• Want to earn $280 for your participation?
If so, consider joining our world-leading research study on cannabis craving.
T: (02) 9850 6720
E: bsl@mq.edu.au


Do you think about cannabis when you're not smoking it?


A world leading research study on cannabis craving
Smoke cannabis regularly?
Able to abstain for 5 days?
Join us and be compensated up to $280 for your time!
Contact:
Dr Melissa Norberg
E: melissa.norberg@mq.edu.au
T: 02 9850 6720


MACQUARIE
University
Smoke cannabis?
• Willing to abstain for five days?
• Can you travel to Macquarie University?
• Want to earn $280 for your participation?
If so, consider joining our world-leading research study on cannabis craving.
T: (02) 9850 6720
E: bsl@mq.edu.au
CRICOS Provider 00002J

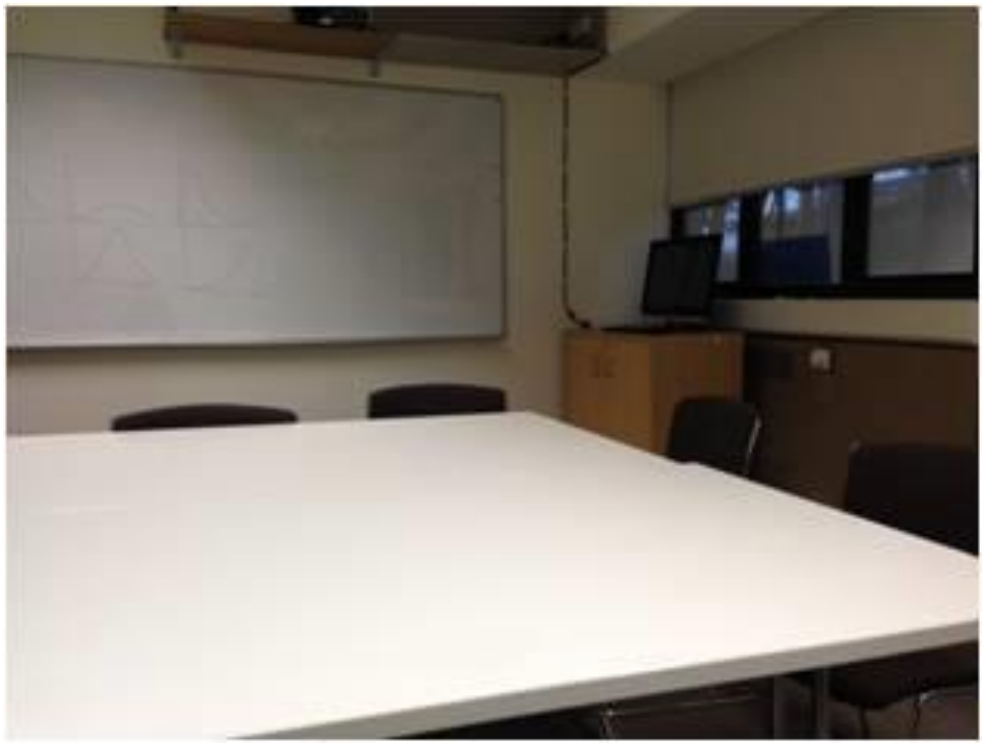

MACQUARIE
University
Smoke cannabis?
• Willing to abstain for five days?
• Can you travel to Macquarie University?
• Want to earn $280 for your participation?
If so, consider joining our world-leading research study on cannabis craving.
T: (02) 9850 6720
E: bsl@mq.edu.au
CRICOS Provider 00002J


MACQUARIE
University
Smoke cannabis?
• Willing to abstain for five days?
• Can you travel to Macquarie University?
• Want to earn $280 for your participation?
If so, consider joining our world-leading research study on cannabis craving.
T: (02) 9850 6720
E: bsl@mq.edu.au
CRICOS Provider 00002J


MACQUARIE
University
Smoke cannabis?
• Willing to abstain for five days?
• Can you travel to Macquarie University?
• Want to earn $280 for your participation?
If so, consider joining our world-leading research study on cannabis craving.
T: (02) 9850 6720
E: bsl@mq.edu.au
CRICOS Provider 00002J

Appendix AA

Consultation room



Appendix AB

Information and Consent Form

Participant Information Sheet/Consent Form

Short Title	***Examination of Craving for Cannabis (Daily Participation)***
Protocol Number	***5201300865***
Project Sponsor	***Macquarie University Research Development Grant***
Principal Investigator	***Dr Melissa Norberg***
Associate Investigators	***A/Prof Jennifer Cornish, Dr Carol Newall, Professor Ron Rapee, Dr Gabrielle Weidemann, & Professor Carl Lejuez***
Location	***Macquarie University, Department of Psychology***

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project, which is called ***Examination of Craving for Cannabis***. You have been invited because you regularly use cannabis and cannabis paraphernalia.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the processes involved with taking part. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or local health worker.

Participation in this research is voluntary. If you don't wish to take part, you don't have to.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to be involved in the research described
- Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

This project will examine how cravings for cannabis use change (or stay the same) over time. It is hoped that results from this study will be able to help people abstain from cannabis use, should they want that.

3 What does participation in this research involve?

This study consists of four phases: an Eligibility phase (Session 0; 2 hours), a Pre-Exposure Phase (Session 1; 75 minutes), a Cue Exposure phase (Sessions 2 and 3; 2 X 2 hours), and a Post-Exposure phase (Session 4; 90 minutes). You will be required to present to Macquarie University for each day of the study (Session 0-4) at approximately the same time each day. You will be expected to remain abstinent on all drugs, other than tobacco and caffeine, throughout the study. This includes synthetic cannabis, alcohol, opiates (e.g. Nurofen Plus), and benzodiazepines—even those which are prescribed (e.g., oxycodone , xanax). Your compliance with this requirement will be monitored via urine samples, which you must provide during Sessions 0 and 4. If you feel you cannot abstain from these drugs or that it will be detrimental to you (e.g., increase your anxiety or pain to an unmanageable level), then this study may not be appropriate for you.

You must also refrain from using tobacco and caffeine 2 hours prior to each appointment.

You will be reimbursed for your travel and for completing the study requirements, which includes abstinence throughout the study and engaging in a computerised task during Sessions 1 and 4. These payments will be paid in one installment into your bank account within two weeks of completion of your Session 4 appointment. You may also receive an additional payment within one month of study completion, if your urine drug screens demonstrate compliance with the abstinence requirements. You must provide us with your banking details if you wish to be reimbursed for your study participation.

Study Period	**Session 0**	**Session 1**	**Session 2**	**Session 3**	**Session 4**
Date	Monday	Tuesday	Wednesday	Thursday	Friday
Abstinence	12-hrs prior	Yes	Yes	Yes	Yes
Travel to MQ	Yes	Yes	Yes	Yes	Yes
Appt Duration	2 hrs	75 min	1hr 45min	1hr 45 min	90 min
Drug Screen	Yes	No	No	No	Yes
Payment	$50	$25	$50	$50	$50
Computer Task & Payment		Up to $3.50			Up to $3.50

Before completing any study procedures, you must sign the information and consent form. The procedures for each at phase are described below.

Session 0. Eligibility Phase (2 hours):

Prior to this appointment, you must have refrained from using any drug other than tobacco and caffeine for at least 12 hours. You must not have used caffeine or tobacco 2 hours prior to this appointment.

You must bring in your cannabis paraphernalia to this appointment. You will be asked to leave these items in our laboratory if you pass our initial eligibility criteria during this appointment. These items will be returned to you after study completion (i.e., Session 4). We will keep these items to assist you in remaining abstinent during the course of this study, and also because we will be using them during your appointments during session 2 and 3.

During this appointment, you will be required to complete interviews that assess basic characteristics such as your prior cannabis use and the characteristics of these cannabis use occasions. If you meet our initial eligibility criteria for continuing in our study, you will provide a urine sample and be scheduled for the session 1 appointment. To prepare you for remaining abstinent over the next week, we will review strategies and devise a plan for keeping you abstinent.

You will receive $50 for completing the requirements of this visit, to be paid after the completion of Session 4.

Session 1. Pre-Exposure Phase (75 minutes):

Prior to this appointment, you must have continued abstinence from drugs other than tobacco and caffeine. You must not have used caffeine or tobacco 2 hours prior to this appointment.

You will be required to listen to automated scripts during this appointment. These scripts will ask you to imagine a cannabis scenario and a day at the beach. During this visit we will measure how intense your urge is to use cannabis and how much you think you can tolerate that urge without using any cannabis. We will also assess your heart rate and how much you sweat when listening to these scripts. In order to do this, the experimenter (likely a female) will attach electrodes to your chest, lower abdomen, and the palm of your hand. If you are particularly hairy, the experimenter may ask you to shave a small portion of your hair in order for the electrodes to be attached. You will be given a new disposable razor to do so. Lastly, we will assess your performance on a computerised task. The computerised task is difficult; therefore, we will pay you for your effort. You can earn up to $3.50 on this task.

Based on how you respond during this visit (including your ability to maintain abstinence), you may be asked to continue in the study. If you are asked to continue in the study, you will be required to provide a urine specimen and to present to Macquarie University the following day.

You will receive $25 for completing the requirements of this visit, to be paid after Session 4.

Session 2 & 3. Cue Exposure Phase (1 hour and 45 minutes per appointment):

Prior to these appointments, you must have continued abstinence from drugs other than tobacco and caffeine. You must not have used caffeine or tobacco 2 hours prior to these appointments.

During these appointments you will be required to handle your cannabis paraphernalia without using any cannabis. When handling your paraphernalia you will be asked to imagine different scenarios. These scenarios may include a recent pleasant smoking occasion or times when you wish you could smoke, but can't. Similarly to the Pre-Exposure phase, you will be asked to report on your level of craving and tolerance of that craving.

You will receive $100 for completing the requirements of Sessions 2 and 3, to be paid after Session 4.

Session 4. Post-Exposure Phase (1 hour and 45 minutes):

Prior to this appointment, you must have continued abstinence from drugs other than tobacco and caffeine. You must not have used caffeine or tobacco 2 hours prior to this appointment.

This visit will be similar to the Pre-Exposure phase. Additionally, we will ask for your feedback about our study. You also will be asked for your permission to be contacted for participation in future research.

You will provide your final urine specimen. You will be provided with $50 for completing this appointment. Your bank details will be collected at this visit so that reimbursement for this visit and previous visits can be processed. You should receive the money in your bank account within two weeks of this visit.

You will be debriefed at the end of this visit. You also will be provided with information on where to receive treatment for cannabis use, upon request.

You will take your personal belongings with you when you leave.

Abstinence payment.

Within one month of completing the Day 4 visit your urine specimens will be analysed and assessed for compliance. If these results demonstrate that your cannabis levels decreased during the course of the study and that you abstained from other drug use, you will receive a $50 contingency-payment for successfully maintaining abstinence. Payment is solely based on the urine specimen results and does NOT depend on self-reported abstinence. In other words, if you self-report abstinence but your urine specimen does not support this, you will NOT be given the $50 contingency payment.

Referral payment.

After completing the study you may decide to refer your friends to the study. We would like to reimburse you $30 for EACH referral. To receive $30, the referred participant must complete Session 0 and nominate you as the person who referred them. If they fail to do so you will not be reimbursed.

4 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include satisfaction with contributing to research. If you have been thinking about abstaining from cannabis use, this study may assist you in those efforts.

5 What are the possible risks and disadvantages of taking part?

Cravings/Urges to Use Cannabis
Your participation in this study will likely lead to cravings to use cannabis. We expect that the level of these cravings will be similar to when you encounter your paraphernalia at home or other objects, situations, and people that remind you of cannabis. If you experience substantial cravings that do not easily dissipate and cause you significant psychological distress, your study participation will be ended. We will help you find an appropriate professional to manage your distress and/or cannabis use.

Withdrawal Symptoms
As a result of abstaining from cannabis, you are likely to experience withdrawal symptoms. The most common withdrawal symptoms include sleep difficulties, irritability, tension, and feeling like everything is a struggle. Usually these symptoms are mild in nature and do not substantially interfere with daily functioning. If you experience substantial withdrawal that significantly interferes with your life functioning, your study participation will be ended. We will help you find an appropriate professional to manage your withdrawal.

Mandatory Reporting of Illegal Behaviour
We are obligated by law to report the below instances of illegal behaviour.

1. Any indictable offense that may result in 5 or more years of imprisonment.
2. Substance use of an adult that negatively impacts a person 16 years or younger.
3. Substance use that occurs during the course of a health professional's vocation.
4. Substance use of a student in clinical training that poses a risk to society.
5. Court Orders. If a court of law issues a subpoena, we must release our research records to the court.

In New South Wales, serious indictable offenses that may result in 5 or more years of imprisonment include (but are not limited to) possession of commercial quantities of cannabis, supplying cannabis to a person 16 years or younger, and manufacturing cannabis in the presence of young person.

Skin Irritation

You may experience minor skin irritation and/or itchiness after shaving or from the adhesive used to attach the electrodes to your skin for assessment of heart rate and sweatiness. If such discomfort occurs, it should only be temporary and may be reduced or alleviated by applying a cream or oil to the skin after the electrodes are removed.

6 What if I withdraw from this research project?

If you do consent to participate, you may withdraw at any time. If you decide to withdraw from the project, please notify a member of the research team before you withdraw. A member of the research team will inform you if there are any special requirements linked to withdrawing. If you do withdraw, you will be asked to complete and sign a 'Withdrawal of Consent' form; this will be provided to you by the research team.

If you decide to leave the research project, the researchers will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected up to the time you withdraw will form part of the research project results. If you do not want your data to be included, you must tell the researchers when you withdraw from the research project.

7 What happens when the research project ends?

After the completion of this project, a summary of the findings will be posted on Dr Melissa Norberg's webpage. This is expected to occur in early-mid 2016.

Part 2 How is the research project being conducted?

8 What will happen to information about me?

By signing the consent form you consent to the research team collecting and using personal information about you for this research project and related research. Any information obtained in connection with this research project that can identify you will remain confidential and securely stored. Only researchers involved in this project will have access to your data, although it may be made available in non-identifiable form to other researchers. Further, only Dr Melissa Norberg, and the research students will have access to your contact details as they will be involved with scheduling. Your contact details will not be linked to your data.

Your personal information will only be disclosed with your permission, except as required by law.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your express permission.

9 Ethics Clearance and Contacts

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the Macquarie University HREC. This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

If you have any complaints or concerns about any ethical aspects of your participation in this research, you may contact the Director of Macquarie University's HREC (02 9850 7854; ethics@mq.edu.au). Any complaint you make will be treated in confidence and investigated, and you will be informed of the outcome.

You may also contact the Principle Investigator, Dr Melissa Norberg (02 9850 8127; Melissa.norberg@mq.edu.au).

Consent Form

Short Title	***Examination of Craving for Cannabis (Daily Participation)***
Protocol Number	***5201300865***
Project Sponsor	***Macquarie University Research Development Grant***
Principal Investigator	***Dr Melissa Norberg***
Associate Investigators	***A/Prof Jennifer Cornish, Dr Carol Newall, Professor Ron Rapee, Dr Gabrielle Weidemann, & Professor Carl Lejuez***
Location	***Macquarie University, Department of Psychology***

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please _____

Signature _____ Date _____

Declaration by Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Researcher† (please print) _____

Signature _____ Date _____

† An appropriately qualified member of the research team must provide the explanation of, and information concerning, the research project.
Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation

Short Title	***Examination of Craving for Cannabis (Daily Participation)***
Protocol Number	***5201300865***
Project Sponsor	***Macquarie University Research Development Grant***
Principal Investigator	***Dr Melissa Norberg***
Associate Investigators	***A/Prof Jennifer Cornish, Dr Carol Newall, Professor Ron Rapee, Dr Gabrielle Weidemann, & Professor Carl Lejuez***
Location	***Macquarie University, Department of Psychology***

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine care, or my relationships with the researchers or Macquarie University.

Name of Participant (please _____

Signature _____ Date _____

In the event that the participant's decision to withdraw is communicated verbally, the Senior Researcher must provide a description of the circumstances below.

Declaration by Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Researcher (please print) _____

Signature _____ Date _____

† An appropriately qualified member of the research team must provide information concerning withdrawal from the research project.
Note: All parties signing the consent section must date their own signature.

MACQUARIE UNIVERSITY
SYDNEY ~ AUSTRALIA

FACULTY OF HUMAN SCIENCES

Participant Information Sheet/Consent Form

Short Title	***Examination of Craving for Cannabis (Bi-Weekly Participation)***
Protocol Number	***5201300865***
Project Sponsor	***Macquarie University Research Development Grant***
Principal Investigator	***Dr Melissa Norberg***
Associate Investigators	***A/Prof Jennifer Cornish, Dr Carol Newall, Professor Ron Rapee, Dr Gabrielle Weidemann, & Professor Carl Lejuez***
Location	***Macquarie University, Department of Psychology***

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project, which is called ***Examination of Craving for Cannabis***. You have been invited because you regularly use cannabis and cannabis paraphernalia.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the processes involved with taking part. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or local health worker.

Participation in this research is voluntary. If you don't wish to take part, you don't have to.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to be involved in the research described
- Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

This project will examine how cravings for cannabis use change (or stay the same) over time. It is hoped that results from this study will be able to help people abstain from cannabis use, should they want that.

3 What does participation in this research involve?

This study consists of four phases: an Eligibility phase (Session 0; 2 hours), a Pre-Exposure Phase (Session 1; 75 minutes), a Cue Exposure phase (Sessions 2 and 3; 2 X 105 mins), and a Post-Exposure phase (Session 4; 105 minutes). You will be required to present to Macquarie University on two days, four days apart. You will complete Session 0 on the first day, and Session 1-4 on the second day.

You will be expected to remain abstinent on all drugs, other than tobacco and caffeine, throughout the study. This includes synthetic cannabis, alcohol, opiates (e.g. Nurofen Plus), and benzodiazepines—even those which are prescribed (e.g., oxycodone , xanax). Your compliance with this requirement will be monitored via urine samples, which you must provide during sessions 0, and 4. If you feel you cannot abstain from these drugs or that it will be detrimental to you (e.g., increase your anxiety or pain to an unmanageable level), then this study may not be appropriate for you.

You must also refrain from using tobacco and caffeine 2 hours prior to each appointment.

You will be reimbursed for your travel and for completing the study requirements, which includes abstinence throughout the study *and engaging in a computerised task during sessions 1 and 4.* Reimbursement will be paid in one installment into your bank account within two weeks of completion of your Session4 appointment. You may also receive an additional payment of $50 within one month of study completion, if your urine drug screens demonstrate compliance with the abstinence requirements. You must provide us with your banking details if you wish to be reimbursed for your study participation.

Study Period	**Session 0**				**Sessions 1- 4**
Date	Monday	Tuesday	Wednesday	Thursday	Friday
Abstinence	12-hrs prior	Yes	Yes	Yes	Yes
Travel to MQ	Yes	No	No	No	Yes
Appt Duration	2 hrs				Approximately 6-7 hours
Drug Screen	Yes				Yes
Payment	$50				$175
Computer Task & Payment					Up to $7.00

Before completing any study procedures, you must sign the information and consent form. The procedures for each at phase are described below.

Example Timeline Options for Friday (please note this is an approximation):

Task	**Option 1 Early**	**Option 2 Later**
Session 1	75 min; 9:00-10:15am	75 min; 11:30am-12:45pm
Break	10-15 mins; 10:15-10:30am	10-15 mins; 12:45-1pm
Session 2	1hr 45min; 10:30am-12:15pm	1hr 45 min; 1:00pm-2:45pm
Break	22 min; 12:15-12:37pm	22 min; 2:45-3:07pm
Session 3	1hr 45min; 12:37-2:22pm	1hr 45min; 3:07-4:52pm
Meal Break	45 min; 2:22-3:07pm	45 min; 4:52- 5:37pm
Session 4	1 hr 45 min; 3:07-4:52pm	1hr 45 min; 5:37-7:07pm

Day 1

Session 0. Eligibility Phase (2 hours):

Prior to this appointment, you must have refrained from using any drug other than tobacco and caffeine for at least 12 hours. You must not have used caffeine or tobacco 2 hours prior to this appointment.

You must bring in your cannabis paraphernalia to this appointment. You will be asked to leave these items in our laboratory if you pass our initial eligibility criteria during this appointment. These items will be returned to you after study completion (i.e., Session 4). We will keep these items to assist you in remaining abstinent during the course of this study, and also because we will be using them during your appointments during Sessions 2 and 3.

During this appointment, you will be required to complete interviews that assess basic characteristics such as your prior cannabis use and the characteristics of these cannabis use occasions. If you meet our initial eligibility criteria for continuing in our study, you will provide a urine sample and be scheduled for the Session 1 appointment. To prepare you for remaining abstinent over the next week, we will review strategies and devise a plan for keeping you abstinent.

You will receive $50 for completing the requirements of this session, to be paid after the completion of Session 4.

Day 5

Session 1. Pre-Exposure Phase (75 minutes):

Prior to this appointment, you must have continued abstinence from drugs other than tobacco and caffeine. You must not have used caffeine or tobacco 2 hours prior to this appointment.

You will be required to listen to automated scripts during this appointment. These scripts will ask you to imagine a cannabis scenario and a day at the beach. During this session we will measure how intense your urge is to use cannabis and how much you think you can tolerate that urge without using any cannabis. We will also assess your heart rate and how much you sweat when listening to these scripts. In order to do this, the experimenter (likely a female) will attach electrodes to your chest, lower abdomen, and the palm of your hand. If you are particularly hairy, the

experimenter may ask you to shave a small portion of your hair in order for the electrodes to be attached. You will be given a new disposable razor to do so. Lastly, we will assess your performance on a computerised task. The computerised task is difficult; therefore, we will pay you for your effort. You can earn up to $3.50 on this task.

Based on how you respond during this session (including your ability to maintain abstinence), you may be asked to continue in the study. If you are asked to continue in the study, you will be required to provide a urine specimen and to present to Macquarie University the following day.

Session 2 & 3. Cue Exposure Phase (105 minutes each)

During these sessions you will be required to handle your cannabis paraphernalia without using any cannabis. When handling your paraphernalia you will be asked to imagine different scenarios. These scenarios may include a recent pleasant smoking occasion or times when you wish you could smoke, but can't. Similarly to the Pre-Exposure phase, you will be asked to report on your level of craving and tolerance of that craving.

Session 4. Post-Exposure Phase (90 minutes):

Prior to this appointment, you must have continued abstinence from drugs other than tobacco and caffeine. You must not have used caffeine or tobacco 2 hours prior to this appointment.

This session will be similar to the Pre-Exposure phase. Additionally, we will ask for your feedback about our study. You also will be asked for your permission to be contacted for participation in future research. You will provide your final urine specimen.

You will be provided with $175 for completing this appointment, which includes Sessions 1-4. Your bank details will be collected at this session so that reimburseyou. You should receive the money in your bank account within two weeks of this visit.

You will be debriefed at the end of this visit. You also will be provided with information on where to receive treatment for cannabis use, upon request.

You will take your personal belongings with you when you leave.

Abstinence payment.

Within one month of completing the study your urine specimens will be analysed and assessed for compliance. If these results demonstrate that your cannabis levels decreased during the course of the study and that you abstained from other drug use, you will receive a $50 contingency-payment for successfully maintaining abstinence. Payment is solely based on the urine specimen results and does NOT

depend on self-reported abstinence. In other words, if you self-report abstinence but your urine specimen does not support this, you will NOT be given the $50 contingency payment.

Earn More Money By Referring a Friend.

After completing the study you may decide to refer your friends to the study. We would like to reimburse you $30 for EACH referral. To receive $30, the referred participant must complete Session 0 and nominate you as the person who referred them. If they fail to do so you will not be reimbursed.

4 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include satisfaction with contributing to research. If you have been thinking about abstaining from cannabis use, this study may assist you in those efforts.

5 What are the possible risks and disadvantages of taking part?

Cravings/Urges to Use Cannabis
Your participation in this study will likely lead to cravings to use cannabis. We expect that the level of these cravings will be similar to when you encounter your paraphernalia at home or other objects, situations, and people that remind you of cannabis. If you experience substantial cravings that do not easily dissipate and cause you significant psychological distress, your study participation will be ended. We will help you find an appropriate professional to manage your distress and/or cannabis use.

Withdrawal Symptoms
As a result of abstaining from cannabis, you are likely to experience withdrawal symptoms. The most common withdrawal symptoms include sleep difficulties, irritability, tension, and feeling like everything is a struggle. Usually these symptoms are mild in nature and do not substantially interfere with daily functioning. If you experience substantial withdrawal that significantly interferes with your life functioning, your study participation will be ended. We will help you find an appropriate professional to manage your withdrawal.

Mandatory Reporting of Illegal Behaviour
We are obligated by law to report the below instances of illegal behaviour.

6. Any indictable offense that may result in 5 or more years of imprisonment.
7. Substance use of an adult that negatively impacts a person 16 years or younger.
8. Substance use that occurs during the course of a health professional's vocation.

9. Substance use of a student in clinical training that poses a risk to society.
10. Court Orders. If a court of law issues a subpoena, we must release our research records to the court.

In New South Wales, serious indictable offenses that may result in 5 or more years of imprisonment include (but are not limited to) possession of commercial quantities of cannabis, supplying cannabis to a person 16 years or younger, and manufacturing cannabis in the presence of young person.

Skin Irritation

You may experience minor skin irritation and/or itchiness after shaving or from the adhesive used to attach the electrodes to your skin for assessment of heart rate and sweatiness. If such discomfort occurs, it should only be temporary and may be reduced or alleviated by applying a cream or oil to the skin after the electrodes are removed.

6 What if I withdraw from this research project?

If you do consent to participate, you may withdraw at any time. If you decide to withdraw from the project, please notify a member of the research team before you withdraw. A member of the research team will inform you if there are any special requirements linked to withdrawing. If you do withdraw, you will be asked to complete and sign a 'Withdrawal of Consent' form; this will be provided to you by the research team.

If you decide to leave the research project, the researchers will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected up to the time you withdraw will form part of the research project results. If you do not want your data to be included, you must tell the researchers when you withdraw from the research project.

7 What happens when the research project ends?

After the completion of this project, a summary of the findings will be posted on Dr Melissa Norberg's webpage. This is expected to occur in early 2016.

Part 2 How is the research project being conducted?

8 What will happen to information about me?

By signing the consent form you consent to the research team collecting and using personal information about you for this research project and related research. Any information obtained in connection with this research project that can identify you will remain confidential and securely stored. Only researchers involved in this project will have access to your data, although it may be made available in non-identifiable form to other researchers. Further, only Dr Melissa Norberg, and the research students will have access to your contact details as they will be involved with scheduling. Your contact details will not be linked to your data.

Your personal information will only be disclosed with your permission, except as required by law.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your express permission.

9 Ethics Clearance and Contacts

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the Macquarie University HREC. This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

If you have any complaints or concerns about any ethical aspects of your participation in this research, you may contact the Director of Macquarie University's HREC (02 9850 7854; ethics@mq.edu.au). Any complaint you make will be treated in confidence and investigated, and you will be informed of the outcome.

You may also contact the Principle Investigator, Dr Melissa Norberg (02 9850 8127; Melissa.norberg@mq.edu.au).

Consent Form

Short Title	***Examination of Craving for Cannabis (Bi-Weekly Participation)***
Protocol Number	***5201300865***
Project Sponsor	***Macquarie University Research Development Grant***
Principal Investigator	***Dr Melissa Norberg***
Associate Investigators	***A/Prof Jennifer Cornish, Dr Carol Newall, Professor Ron Rapee, Dr Gabrielle Weidemann, & Professor Carl Lejuez***
Location	***Macquarie University, Department of Psychology***

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please _____

Signature _____ Date _____

Declaration by Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Researcher† (please print) _____

Signature _____ Date _____

† An appropriately qualified member of the research team must provide the explanation of, and information concerning, the research project.
Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation

Short Title	***Examination of Craving for Cannabis (Bi-Weekly Participation)***
Protocol Number	***5201300865***
Project Sponsor	***Macquarie University Research Development Grant***
Principal Investigator	***Dr Melissa Norberg***
Associate Investigators	***A/Prof Jennifer Cornish, Dr Carol Newall, Professor Ron Rapee, Dr Gabrielle Weidemann, & Professor Carl Lejuez***
Location	***Macquarie University, Department of Psychology***

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine care, or my relationships with the researchers or Macquarie University.

Name of Participant (please _____

Signature _____ Date _____

In the event that the participant's decision to withdraw is communicated verbally, the Senior Researcher must provide a description of the circumstances below.

Declaration by Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Researcher (please print) _____

Signature _____ Date _____

† An appropriately qualified member of the research team must provide information concerning withdrawal from the research project.
Note: All parties signing the consent section must date their own signature.

Appendix AC

Cue-Exposure Scene Description Script

The following script is read aloud to participants in exposure sessions.
"Imagine you are at home in your lounge room and you are having some friends over for a get together. You're all sitting around ... *[use personal information of what the person usually does before/while smoking here (E.g playing video games)]*.

One of your friends pulls out a cone and begins to smoke. The smell is wafting toward you. You can hear the lighter click as they light the cone and the slow exhale as they take their first drag. Your friend asks you if you want some. You feel …"

[Select two of the following 5 descriptive paragraphs to integrate into the story based on top two scoring motives in the MMM:]

1. [Social] "…like you want to enjoy yourself, and want to be more sociable. You want to feel more self-confident and sure of yourself and think that if you smoke cannabis it will make the party more fun."

2. [Coping] "… like you need a bit of help to cheer yourself out of a bad mood as you have been feeling depressed or nervous. You may want to forget your worries and problems and just want to rid yourself of these disturbing feelings quickly. Also, it could be that this isn't a place you want to be and so you may want to avoid dealing with this uncomfortable situation. Or maybe you just want to smoke to get rid of a craving."

3. [Expansion]"… the desire to be creative and original and expand your awareness. You want to feel more open to this experience and maybe want to get to know yourself better or want to understand things differently."

4. [Conformity] "… pressured to use and that you should smoke so that your friends won't make fun of you. That way you will feel like you fit in and are liked – not left out."

5. [Enhancement] "… like you want to be high because you like the feeling. It is exciting, fun and it gives you a pleasant feeling."

[Finish all stories with the following sentence:]
"… and you think that nothing would help quite like cannabis would."

Appendix AD

Debriefing

Many thanks for your participation in our cannabis craving study. Your involvement in our study has given us valuable information that will help us to understand why some people may have difficulty abstaining from cannabis.

We decided to carry out this study because some people have problems associated with cannabis use, which encourages them to abstain. These efforts are often short-lived. Many people resume smoking within six months of a quit attempt. There is some evidence that craving contributes to ongoing use, especially when individuals feel that they are unable to tolerate their feelings and urges to use cannabis.

Prior research has shown that exposure to cannabis paraphernalia increase's people's desire to smoke cannabis. Animal research and theory suggests that this occurs due to cannabis paraphernalia being repeatedly associated with using cannabis use. Thus, this study is examining if repeated exposure to cannabis paraphernalia, in the absence of smoking cannabis, reduces the amount of craving those objects produce.

In order to test this, we needed to make sure that you did not use cannabis outside of this experiment. Using cannabis outside of this experiment would prevent the experimental sessions from having any effect, as ongoing cannabis use would strengthen the relationship between cannabis paraphernalia and cannabis use.

Additionally, we tested whether place of exposure to cues is important. Some people received exposure to their cannabis cues in the living room, whereas others received exposure to their cues in a therapist's office. Everyone was tested for craving in the living room. It may be that one can only apply new skills in the same place as where they learned the new skill. This has been shown to be true for alcohol and cigarettes, but no one has ever tested this before for cannabis.

We hope you enjoyed our study and we welcome your feedback. We have a list of places where you may seek advice or treatment for cannabis use, if you are interested.