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Graduate Education Office (A 1045), 4301 Jones Bridge Road, Bethesda, MD 20814

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APPROVAL SHEET

Title of Thesis: **"Mindfulness, Craving, & Cognition in Relapse to Alcohol: A Pilot Ecological Momentary Assessment Study"**

Name of Candidate: **Edwin Szeto**, Master of Science **in Medical and Clinical Psychology,**

Date: 04/07/16

THESIS AND ABSTRACT APPROVED:

DATE:

_____ _____
Andrew J. Waters
DEPARTMENT OF MEDICAL & CLINICAL PSYCHOLOGY
Committee Chairperson

_____ _____
David S. Krantz
DEPARTMENT OF MEDICAL & CLINICAL PSYCHOLOGY
Committee Member

[redacted] 4/6/16
Mark L. Ettenhofer
DEPARTMENT OF MEDICAL & CLINICAL PSYCHOLOGY
Committee Member

UNIFORMED SERVICES UNIVERSITY, SCHOOL OF MEDICINE GRADUATE PROGRAMS
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DATE:

[redacted]
4/7/16

Andrew J. Waters
DEPARTMENT OF MEDICAL & CLINICAL PSYCHOLOGY
Committee Chairperson

[redacted]
4-6-16

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DEPARTMENT OF MEDICAL & CLINICAL PSYCHOLOGY
Committee Member

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Committee Member

[redacted] 4/6/16

Mark L. Ettenhofer
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Committee Member

A PILOT ECOLOGICAL MOMENTARY ASSESSMENT STUDY OF MINDFULNESS, CRAVING, AND COGNITION IN ALCOHOL RELAPSE

by

Edwin H. Szeto

Thesis submitted to the Faculty of the
Medical and Clinical Psychology Graduate Program
Uniformed Services University of the Health Sciences
In partial fulfillment of the requirements for the degree of
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DEDICATION

I dedicate this thesis, and my commitment to the evolution of health research and systems, to every person who deserved particular support for their mental and/or physical experiences required certain support, but instead received care and reactions that were suboptimal, unjust, and/or persecutory. I dedicate this thesis to the advocates, pioneers, and visionaries, who recognized that mental and physical wellness are interlocked, and that even our best evidence and practices right now may not do our suffering justice in "reality." I dedicate this thesis to those who believe that our true strengths as individuals and groups do not falter because of suffering. I dedicate this thesis to those who guide our sciences and discourses to evolve how we see and help each other, so that we compassionately recognize how our limited available knowledge makes us and our societal systems consciously and unconsciously helpless, ignorant, and even unjust at times. Finally, I dedicate this thesis to the journey of the human race to understand wellness, health, and care from the anchor points of whole-person, integrated, and client-centered perspectives.

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Edwin H. Szeto

April 8, 2016

ABSTRACT

A Pilot Ecological Momentary Assessment Study of Mindfulness, Craving, and Cognition in Alcohol Relapse

Edwin Szeto, B.S., 2016

Thesis directed by: Andrew J. Waters, Associate Professor, Medical and Clinical Psychology

Excessive alcohol use remains a significant public health problem worldwide. A better understanding of relapse is needed. In an Ecological Momentary Assessment (EMA) study, Dutch alcohol dependent patients (n=11) carried around a personal digital assistant for 4 weeks while trying to maintain abstinence. They completed assessments at random times 3 times/day, and when they felt a strong urge to drink or came to the brink of drinking without doing so. Negative affect, "tempted now" ratings, recent drinking, and attentional or approach bias were assessed at each EMA assessment. Participants completed 70.2% of presented random assessments (RAs). Participants with higher trait mindfulness (measured by the Mindful Attention Awareness Scale (MAAS) scores) reported lower tempted-now ratings and less drinking. MAAS also moderated the association between tempted-now ratings and drinking, such that the association only occurred in those with low, but not high, MAAS participants. Further research should examine trait mindfulness in alcohol use and dependence.

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CHAPTER 1: INTRODUCTION

Excessive alcohol use remains a significant public health problem worldwide. A better understanding of relapse is needed so that more effective interventions can be developed. This 4-week ecological momentary assessment (EMA) study investigated relapse processes in Dutch persons who recently finished residential treatment for alcohol dependence in the Netherlands. The study focused specifically on the role of trait mindfulness in craving and use.

ALCOHOL MISUSE AND RELAPSE

In the United States, nationally representative studies estimated that 23% of persons over 12 years-old reported behaviors that qualified for binge drinking, and 4.7% qualified for alcohol abuse (Substance Abuse and Mental Health Services Administration, 2014). The World Health Organization (WHO; 2015b) defines excessive alcohol use as binge drinking, heavy drinking, any alcohol use by people under the minimum drinking age, and any alcohol use by pregnant women. Excessive alcohol use accounted for approximately 88,000 deaths annually from 2006 to 2010, and 10% of deaths in adults from ages 20 to 64 (Centers for Disease Control and Prevention, 2015). The rates were more alarming in the U.S. military. For instance, in 2008, 47% active duty service members reported behaviors that qualified for binge drinking (Institute of Medicine, 2013). About 20% of military personnel, and 27% of those with combat exposure, reported binge drinking every week in the past month (Institute of Medicine, 2013).

The economic cost of excessive alcohol consumption in the U.S. was $223.5 billion in 2006, an equivalent of $1.90 per drink, or about $746 per person. Such cost was

primarily due to losses in workplace productivity (72% of the total cost) and health care expenses (11%). Other costs (17%) were the result of criminal justice expenses, motor vehicle crash costs, and property damage (Division of Population Health, 2014). Moreover, it was estimated that 40% of the economic costs of excessive alcohol use in 2006 were paid by federal, state, and local governments (Sacks et al., 2013). Alcohol misuse, or the use of alcohol for a purpose not consistent with legal or medical guidelines, poses an immense burden on American health, economy, and healthcare and legal policies (World Health Organization, 2015a). The World Health Organization indicated that the 12-month prevalence estimates of alcohol use disorder (AUD) and dependence in the U.S. was 7.4% and 4.7%, respectively, in 2010 (World Health Organization, 2014).

Similar to the misuse of most psychoactive substances, the U.S. is not the only nation plagued by this preventable public health issue. According to the WHO (2014), 3.3 million deaths in 2012 were attributable to harmful use of alcohol. In 2012, 139 million disability-adjusted life years (DALYs), or 5.1% of the global burden of disease and injury, were attributable to alcohol consumption. There is also wide geographical variation in the proportion of alcohol-attributable deaths and DALYs, with the highest alcohol-attributable fractions reported in the WHO European Region. The WHO's 2014 report pointed out such variation was likely due to the diverse history, attitude, and practices of producing and consuming different forms of alcohol.

One scientific consensus that has emerged is that substance misuse can be characterized as a chronic disease (McKay, 2011). However, the triggers and the relapse process likely differ from other chronic illnesses, because of its distinct motivational and

appetitive mechanisms (McKay, 2011). One study found that, within recently treated persons with AUD, 64% relapsed within the first 12 months. Of those who were abstinent at 12 months, 34% relapsed in the next two years (Dennis, Foss, & Scott, 2007). The long term relapse rates in persons who were recently treated for AUD ranged from 20 to 80% (Jin, Rourke, Patterson, Taylor, & Grant, 1998; Moyer & Finney, 2002; Weisner, Matzger, & Kaskutas, 2003). In people treated for AUD for the first time, the relapse rate at 3-year follow-up was 43.4% for those who sought help, and 62.4% in those who did not (Moos & Moos, 2006). The 16-year follow-up of those who were abstinent at 3-year follow-up also revealed that 42.9% of the help-seeking persons relapsed, compared to 60.5% in the non-help-seeking persons (Moos & Moos, 2006). The relapse rates also varied from 22% in those with no psychosocial risk factors to 45% in those with one risk factor, 70% in those with two, and 86% in those with three or four (Moos & Moos, 2006).

ALCOHOL MISUSE AND RELAPSE IN THE NETHERLANDS

As noted earlier, the current study was conducted in the Netherlands. In the population of the current study, the Netherlands, the rates of alcohol use disorder and dependence were 1.2% and 0.7% in 2010 (World Health Organization, 2014) However, The Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2), a nationally representative sample of 18 to 64 year-old Dutch adults, also reported prevalence in a Dutch sample from 2007 to 2009 (de Graaf, Ten Have, & van Dorsselaer, 2010) and reported higher prevalence estimates. An estimated 5.4% of the population qualified for AUD under the DSM-IV criteria, and 4.4% under the DSM-5 criteria (Tuithof, ten Have, van den Brink, Vollebergh, & de Graaf, 2014b). In addition, the NEMESIS-2 study also examined the proportion of individuals with AUD who qualified

for Excessive Alcohol Consumption (EAC). Only 17.7% of those with AUD under DSM-IV criteria qualified for EAC, defined as consuming more than14 drinks weekly for women, 21 drinks for men, *and* at least three 5+ drinking days weekly. Similarly, only 25.3% of those with EAC qualified for AUD (Tuithof et al., 2014b). Compared to non-problematic drinkers, AUD-only and EAC-only groups had worse mental health problems, but the AUD+EAC group had the worst outcomes. The DSM-5 criteria increased the AUD+EAC overlap slightly for the same sample. In other words, alcohol misuse research need to recognize that individuals have varied consumption threshold (i.e., EAC) for functional impairment (i.e., AUD) (Tuithof et al., 2014b).

Within those who have been remitted of AUD under DSM-5 for more than 12 months at baseline of NEMESIS 2.0, the retrospective relapse rates were 5.6% 5 years since the last remission, 9.1% after 10 years, and 12% after 20 years (Tuithof, ten Have, van den Brink, Vollebergh, & de Graaf, 2014a). For those who qualified for AUD under DSM-5 at baseline of NEMESIS 2.0, the overall prospective relapse rate was 29.5% (Tuithof et al., 2014a). Remission was associated with a reduction of six drinks per week between baseline and 3-year follow-up. In addition, 35.8% of those in remission at 3-year follow-up consumed more than the recommended maximum seven drinks weekly for women, and 14 for men (Tuithof et al., 2014a).

The findings from the three NEMESIS 2.0 studies provided two significant implications for understanding alcohol misuse and its disease course. First, context matters. The Netherlands differs from the U.S. in approaching etiology and recovery, both culturally and scientifically. Many Dutch studies of substance abuse reflect a harm reduction approach, as opposed to the abstinence-based approach often seen in American

studies. Second, the diagnosis of AUD only partially predicts outcomes and more focus on drinking behaviors within their context is warranted. That is, drinking behaviors, whether excessive or not, may predict the occurrences and severity of clinical impairment. Similarly, the markers of clinical impairment related to alcohol use may be hidden in mundane daily activities, or masked by cultural and individual differences. One person's protective factor against relapse may be another's risk factor. For instance, having a glass of wine at a family dinner at home may invite supportive interactions. The same wine may invite craving and self-medication if it occurred at a contentious high school reunion. There remains much to be explored how the links between intention, behaviors, and the consequences of behaviors.

There are some advantages in conducting an EMA study of alcohol dependence such as the current one in the Netherlands. In the United States only a quarter of people with lifetime alcohol dependence seek treatment (Rusch, Angermeyer, & Corrigan, 2005), whereas in the Netherlands one third of people do (Corrigan, Rafacz, & Rusch, 2011). Therefore it may be easier to obtain a larger and more representative sample in the Netherlands. In addition, in a survey study Dutch respondents were more sympathetic toward alcoholism than respondents from North America and some other European countries (Room, 2005). Therefore heavy drinking may be less stigmatized in the Netherlands (van Boekel, Brouwers, van Weeghel, & Garretsen, 2013), and participants may be more willing to participate in the study and give valid responses. Finally, perceived financial barriers to mental health treatment are less significant for low income persons in Dutch than the US (Sareen et al., 2007).

PSYCHOLOGICAL PROCESSES UNDERLYING ALCOHOL ADDICTION

Given the societal and economic costs described above, it is critical to understand the psychological processes underlying relapse to alcohol so that more effective interventions can be developed. A recent conceptualization of Alcohol Use Disorder described addiction as a three-stage process (see Litten et al., 2015), binge-intoxication, withdrawal-negative affect, and preoccupation-anticipation. The psychological processes examined in the current study include negative affect, craving, and cognitive biases. The latter two are important in preoccupation-anticipation. Each of these processes is described in more detail below.

Negative Affect

Both theory and data suggest that negative affect and stress can provoke alcohol craving and consumption through a number of mechanisms (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Litten et al., 2015). For example, Baker et al. argue that "the escape and avoidance of negative affect is the prepotent motive for addictive drug use". A detailed review of their model is beyond the scope of the current manuscript. Stated briefly, increases in negative affect are thought to influence information processing in a way that promotes drug use motivation, to include increases in craving. Negative affect can also elicit craving through classical conditioning (Siegel, 1983; Wikler, 1948).

Pertinent to the current study, empirical data also suggest that negative affect can cause craving. Laboratory studies have examined the effect of stress and negative affect on craving (though not temptation episodes). Studies have reported that acute stress (vs. no stress) increases craving for alcohol in alcohol-dependent patients in the laboratory (Fox, Bergquist, Hong, & Sinha, 2007; Sinha et al., 2008) . In a EMA study, Krahn et al. (2005) measured both negative affect and craving with Alcohol Urge Questionnaire,

(AUQ) in the field. Their cluster analysis showed that two clusters emerged, low negative affect and low craving, and high negative affect and high craving (Krahn et al., 2005). Thus, negative affect and craving appear to be associated in the field.

Craving

Craving has been defined as "a strong desire or sense of compulsion to take the drug" by the International Classification of Diseases (ICD-10; Schmidt & Room, 1999). A recent study reported that the majority of studies examining the relationship between craving and substance use reported a positive relationship between craving and substance use. Therefore craving remains a target for interventions (Serre, Fatseas, Swendsen, & Auriacombe, 2015). However, only nine of the 92 selected studies concerned alcohol use, and of these nine studies, only five included alcohol-dependent patients (Cooney et al., 2007; Litt, Cooney, & Morse, 2000). Therefore, the evidence for the association between craving and use is less robust in this population. In addition, in studies with alcohol-dependent individuals, overall craving ratings are often low and seem to show very little variation over time compared with craving in other substance use disorder (SUD) patients (Tiffany, 1990).

Cognitive Biases and Addiction

Another line of research has focused on drug cue reactivity. According to this view, drug-related cues provoke craving and other responses which maintain drug use and promote relapse (Niaura et al., 1988; Robinson & Berridge, 1993). Incentive-sensitization theory (IST; Robinson & Berridge, 2008) provided a detailed account for how drug cues might control behavior. IST suggests that persistent drug use causes changes in the brain circuits that regulate the attribution of incentive salience to stimuli.

This process causes "pathological" levels of incentive salience to be assigned with drugs and drug-related cues (Robinson & Berridge, 1993). Robinson and Berridge (1993, p. 267) used "pathological" to indicate excessive levels of incentive salience assigned to mental representation of drug cues that is disproportionate to the pleasures obtained from drug taking and that results in dysfunctional behavior. Over time, drug-related cues become highly attractive and provoke drug taking. Berridge et al. (2009) described this phenomenon in the following statement:

> "When attributed to a stimulus representation, incentive salience transforms the mere sensory shape, smell or sound into an attractive and attention-riveting incentive. Once attributed, the incentive percept becomes difficult to avoid noticing, the eyes naturally move toward the incentive, it captures the gaze and becomes motivationally attractive, and the rest of the body may well follow to obtain it." (p. 2)

The statement above indicates that the processing of drug cues has at least two consequences. First, drug users will preferentially attend to drug cues. An "attentional bias" is said to have formed when a person's attention is captured by, and maintained on, drug-related cues more than neutral cues (Field & Cox, 2008). Second, drug users may tend to automatically approach drug cues. An "approach bias" refers to the tendency to automatically approach drug-related stimuli more than neutral stimuli. Both attentional bias and approach bias are assessed in the current study.

Much recent research, in part inspired by IST described above, has focused on the cognitive processes underlying addiction in the hope of identifying cognitive targets for intervention. Much research has been grounded in the dual-process theory (Wiers &

Stacy, 2006). Dual process theories propose that there are two distinct types of cognitive processes (Shiffrin & Schneider, 1977). Automatic or implicit processes are fast, parallel, and effortless processes that are often outside of one's conscious awareness. Conversely, non-automatic or explicit processes are slow, reflexive, and serial processes which are sometimes referred to as controlled processes (Kahneman, 2003). Recent research has emphasized the importance of automatic processes in underlying health behaviors (Marteau, Hollands, & Fletcher, 2012), including the addictions (Wiers & Stacy, 2006).

Attentional bias and approach bias are part of a broader literature of cognitive psychological theories that have been applied to addiction. Attentional bias is an automatic process. For example, a smoker may attend to a smoking-related cue without making the conscious decision to do so (Field & Cox, 2008; Field, Duka, Tyler, & Schoenmakers, 2009), and others specifically examined the role of attentional bias (Field & Cox, 2008; Franken, 2003) and approach bias (Field, Wiers, Christiansen, Fillmore, & Verster, 2010) in drug addiction.

Attentional bias can be assessed by reaction time tasks such as the modified Stroop task. In a modified Stroop task, participants are asked to indicate the color of neutral words and drug-related words. Slowed responding on the drug-related words (vs. neutral words) is indicative of attentional bias. Research suggests that drug users exhibit an attentional bias to drug cues, whereas non-drug users do not (Cox, Pothos, & Hosier, 2007).

Approach bias can also be assessed with computerized reaction time tasks (Cousijn, Goudriaan, & Wiers, 2011; Schoenmakers, Wiers, & Field, 2008). Some tasks require that participant make an actual movement (e.g., moving a joystick) whereas

others do not. Approach bias has been assessed using the Implicit Association Test (IAT), described later.

Some studies have reported that increased attentional bias to drug cues predicted lower rates of success in abstaining from drugs in persons with alcohol dependence (Cox, Brown, & Rowlands, 2003; Cox et al., 2007; Cox et al., 2002), cigarette smoking (Janes et al., 2010; Powell, Dawkins, West, Powell, & Pickering, 2010; H. Waters & Green, 2003), and cocaine use (Carpenter, Schreiber, Church, & McDowell, 2006). Similarly, an alcohol-approach bias has been found to be associated with alcohol use, and consumption level (Ostafin, Marlatt, & Greenwald, 2008; Ostafin & Palfai, 2006; Ostafin, Palfai, & Wechsler, 2003; Peeters et al., 2012). As noted in Snelleman et al. (2015), there is mixed evidence for an association between approach bias and relapse in alcohol use.

Most pertinent to the current study, meta-analyses of attentional bias and craving for various drugs have revealed that attentional bias is positively associated with craving (Field, Duka, et al., 2009), although the effect size is modest. Moreover, the association between attentional bias and craving can be affected by various moderating factors (Field, Munafo, & Franken, 2009). This study examined trait-mindfulness as one such variable, because the theories about incentive sensitization and attentional bias suggest that more "mindful" individuals should be less likely to be influenced by automatic processes. But first, a brief introduction to mindfulness and its influence in addictive behaviors will clarify what being mindful means in the psychology perspective.

Mindfulness in Substance Abuse

Historical Background

The mindfulness known in the practice and science of psychology today was first developed around 500 BCE by Siddhāttha Gautama, the founder of Buddhism. Gautama, commonly referred to as Buddha, organized his teaching about the nature and alleviation of suffering experienced by sentient beings into the Four Noble Truths: (1) suffering is universal and unavoidable; (2) suffering is caused not by experience, but by our need to have experience a certain way; (3) the cessation of suffering is possible; and (4) cessation can be achieved by practicing the Noble Eightfold Path. Right mindfulness is one element of the Noble Eightfold Path. Other elements include right view, right intention, right speech, right action, right livelihood, right effort, and right concentration (Kumar, 2002; Teasdale & Chaskalson, 2011). In Buddha's elaboration in Pali, mindfulness could be translated as the "right memory," "right awareness," or "right attention" focusing on the (1) body, (2) feelings, (3) mind, and (4) mental qualities (*dhammas*) in and of themselves, without reference to the world (Gautama). Moreover, Buddha further explained that these four elements of Right Mindfulness are first part of the thirty-seven *bodhipakkhiyā dhammā*, or Enlightenment Qualities. These Enlightenment Qualities were Buddha's explicit instruction for meditative and behavioral practices, which served as a template for the adaptation of mindfulness into psychological practice and science.

Modern Conceptualizations

Beginning around the 1960s, there has been increasing interest among psychologists in studying mindfulness in clinical and experimental settings. Such tradition has led to four layers of contemporary perspectives that build upon each other. First, Western practitioners and psychologists have repeatedly identified two psychological processes, attention and awareness, in theoretical definitions of

mindfulness (Bishop et al., 2004; K. W. Brown & Ryan, 2003; K. W. Brown, Ryan, & Creswell, 2007; Shapiro, Brown, Thoresen, & Plante, 2011; Shapiro, Carlson, Astin, & Freedman, 2006). Mindfulness has been defined as "a receptive attention to and awareness of present events and experiences" (K. W. Brown & Ryan, 2003; K. W. Brown et al., 2007). Awareness was described as the conscious registration of internal and external stimuli, while attention was referred to as the initial taking notice of or turning toward an object. Moreover, attention in mindfulness can also refer to the conscious direction of attention deployment during more elaborative processing.

Second, mindfulness has been defined as: "...the self-regulation of attention so that it is maintained on immediate experience, thereby allowing for increased recognition of mental events in the present moment" (the "Here and Now"), and "the… [adoption of] a particular orientation toward one's experiences in the present moment, …characterized by curiosity, openness, … acceptance" (Bishop et al., 2004). This definition emphasizes the importance of a non-judgmental attitude.

Trait Mindfulness

Most researchers believe that it is useful to treat mindfulness as a trait, in that it can vary greatly between persons and stay relatively stable within persons. Trait, or dispositional, mindfulness refers to an individual's natural level of trait mindfulness (K. W. Brown & Ryan, 2003). Many different assessments of trait mindfulness have been developed. Conceptualizations of mindfulness underlying self-report measures vary greatly from measure to measure (K. W. Brown et al., 2007; Grossman & Van Dam, 2011). Self-report measures are also based on the assumption that individuals can accurately report on their subjective experience (K. W. Brown et al., 2007).

The Mindful Attention Awareness Scale (MAAS), used in the current study, focuses on measuring a single factor that broadly captures the degree to which one is attentive and aware of one's experiences or surroundings regardless of conceptual or experiential exposure to mindfulness (e.g., "I tend to walk quickly to get where I'm going without paying attention to what I experience along the way"). A low mindful state is characterized by highly habitual, automatic, or injudicious patterns in thoughts and actions (K. W. Brown & Ryan, 2003).

Previous research has examined trait mindfulness in terms of its ability to predict alcohol outcomes (see Table 1 for review of alcohol and mindfulness studies). In persons recovering from alcohol dependence, those with high trait-mindfulness reported less craving than those with low trait-mindfulness (Garland, 2011). One study reported that trait mindfulness was negatively associated with alcohol attentional bias (Garland, Boettiger, Gaylord, Chanon, & Howard, 2012), while another reported no association between trait mindfulness attentional bias in smokers (A. J. Waters et al., 2009). Another study found that, compared to non-clinical social drinkers, persons undergoing residential treatment for substance dependence displayed low dispositional mindfulness (Lyvers et al., 2014). In men undergoing residential treatment, 61.4% of whom were alcohol-dependent, trait-mindfulness was positively correlated with spirituality and age, and negatively correlated with the affective, cognitive, and physical clusters of depression, and with alcohol consumption and drug use (Shorey, Gawrysiak, Anderson, & Stuart, 2015). In addition, trait-mindfulness accounted for unique variance in all three clusters of depressive symptoms, whereas spirituality only did so for the cognitive cluster (Shorey et al., 2015).

Trait mindfulness has been examined in other addictions. Research using the MAAS has reported associations between the MAAS and nicotine dependence (A. J. Waters et al., 2009). In abstinent methamphetamine-dependent persons, childhood maltreatment was found to be positively correlated with the at-rest functional connectivity of amygdala and various limbic structures (Dean, Kohno, Hellemann, & London, 2014). In addition, such connectivity was positively associated with trait-mindfulness (Dean et al., 2014). In persons undergoing acute detoxification or intensive outpatient treatment, those with lower dispositional mindfulness were reported to use opioids more frequently to self-medicate negative emotions, even after controlling for opioid use frequency and other clinical and sociodemographic covariates (Garland, Hanley, Thomas, Knoll, & Ferraro, 2015).

Trait mindfulness has also been examined as a moderator variable. A moderator variable is a variable that alters the strength of the causal relationship between an independent variable and a dependent variable (Baron & Kenny, 1986). In the current context, a moderator variable would influence the relationship between trait mindfulness and craving or alcohol use. The main hypothesis has been that higher levels of mindfulness weaken the association between cognitive biases (e.g., attentional and approach bias) and craving/drinking behavior. Pertinent to the current study, a high level of trait-acceptance was found to weaken the association between approach-bias and alcohol consumed (Ostafin et al., 2008). A high level of trait-mindfulness and executive control was also found to weaken the association between attentional bias and preoccupation with alcohol (Ostafin, Kassman, & Wessel, 2013).

In another perspective, one study examined the effect of interaction between trait-mindfulness factors, measured by the Five Facet Mindfulness Questionnaire (FFMQ), on substance abuse (Eisenlohr-Moul, Walsh, Charnigo, Lynam, & Baer, 2012). The FFMQ (Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006) is a self-report inventory the measures five factors of trait mindfulness, namely, *observing*, *describing*, *acting with awareness*, *non-judging* of inner experience, and *non-reactivity* to inner experience. The *observing* subscale was negatively associated with substance use at higher levels of *non-reactivity* but positively associated with periods of substance use at lower levels of *non-reactivity* (Eisenlohr-Moul et al.),. In other words, observing seemed to protect against substance use only when one is not reactive (but see Bowen et al., 2014).

In sum, in the current study, trait mindfulness will be examined both as a predictor variable and a moderator variable. Regarding the latter, trait mindfulness is expected to weaken the relationship between 1) negative affect and craving, 2) cognitive biases and craving, and 3) craving and drinking.

Clinical Interventions

Many clinical interventions have been developed that purport to increase mindfulness in various populations. There are many evidence-based therapies that incorporate mindfulness as a primary principle and technique. For example, Mindfulness-based Stress Reduction (MBSR), Dialectical Behavior Therapy (DBT), and Acceptance and Commitment Therapy (ACT), address one's ability to regulate emotions, stress, and automatic tendencies (Hayes, Masuda, Bissett, Luoma, & Guerrero, 2004; Linehan, 1993). Both DBT and ACT have strong clinical evidence to support their effectiveness to treat symptoms related to mood (Feldman, Harley, Kerrigan, Jacobo, & Fava, 2009;

Harley, Sprich, Safren, Jacobo, & Fava, 2008; Lynch, Morse, Mendelson, & Robins, 2003), anxiety (Panos, Jackson, Hasan, & Panos, 2014; Sarris et al., 2012; Swain, Hancock, Hainsworth, & Bowman, 2013), trauma (Bohus et al., 2013; Bohus, Dyer, Priebe, Kruger, & Steil, 2011; Steil, Dyer, Priebe, Kleindienst, & Bohus, 2011), personality disorders (Lynch et al., 2007), eating disorders (Juarascio, Forman, & Herbert, 2010), and substance abuse (De Groot, Morrens, & Dom, 2014; Lanza, Garcia, Lamelas, & Gonzalez-Menendez, 2014; Linehan et al., 1999; Luoma, Kohlenberg, Hayes, & Fletcher, 2012).

More recently, evidence has accumulated that mindfulness-based modalities, such as Mindfulness-based Relapse Prevention (MBRP), Mindfulness-based Cognitive Therapy (MBCT), and Mindfulness-oriented Recovery Enhancement (MORE), show efficacy in treating substance abuse. MBRP aims to "foster increased awareness of triggers, destructive habitual patterns, and "automatic" reactions (Witkiewitz & Bowen, 2010; Witkiewitz, Marlatt, & Walker, 2005). MBRP, and its treatment components, have been shown to be effective in improving short-term and long-term outcomes in craving and drug use (Bowen et al., 2006; Ostafin et al., 2006; Ostafin & Marlatt, 2008; Witkiewitz, Bowen, Douglas, & Hsu, 2013; Witkiewitz et al., 2005). MBCT was originally developed to prevent the relapse of depressive disorders (Bieling et al., 2012; Dimidjian et al., 2015; Rycroft-Malone et al., 2014; Teasdale et al., 2000), and recent studies showed that MBCT may be effective in treating co-occurring substance abuse and depression (Hoppes, 2006; Hosseinzadeh Asl & Barahmand, 2014). In addition, MORE (Mindfulness-oriented Recovery Enhancement) promoted self-awareness and impulse control in alcohol dependence (Garland, Schwarz, Kelly, Whitt, & Howard, 2012). For

persons with co-occurring chronic pain and opioid abuse, MORE led to decreased self-reported pain severity, decreased functional interference in daily activities, and craving for opioids (Garland, 2014; Garland & Howard, 2013).

ECOLOGICAL MOMENTARY ASSESSMENT

Use of EMA for Studying Alcohol Dependence

Most research on the psychological processes involved in relapse has involved the use of assessments administered in the laboratory. The same is true for research on the psychological processes underlying mindfulness. Increasingly, however, research is using Ecological Momentary Assessment (EMA) to study both alcohol relapse (see Table 2 for review of studies) and mindfulness.

EMA refers to the methodology of assessing phenomena at the moment they occur, and in their natural environment. Assessments may be done at random times ("random assessments"; RAs), and/or when participants experience heightened emotions or motivational states (e.g., temptations to use drugs), and/or immediately after encountering certain experiences (e.g., smoking or drinking).

The development of personal digital assistants (PDAs) and smartphones has facilitated the collection of EMA data. PDAs can be programmed to randomly prompt the person via sound and vibration. Compliance can be closely monitored (Stone, Shiffman, Schwartz, Broderick, & Hufford, 2003). The advent of mobile technology also meant that cognitive tasks, including those mentioned earlier, can now be administered on a PDA or smartphone in an EMA study (Shiffman, Paty, Gyns, Kassel, & Hickcox, 1996; A. J. Waters & Li, 2008; A. J. Waters, Marhe, & Franken, 2012; A. J. Waters, Miller, & Li, 2010). EMA studies provide highly detailed data, representative of a person's

functioning, and revealing of longitudinal patterns as well as acute fluctuations within the span of hours (e.g., Epstein et al., 2009; Shiffman & Waters, 2004).

For the purposes of studying alcohol abuse/dependence, EMA can provide detailed data on participants' mood, craving, and cognitive biases in the natural environment. In the current study, EMA will provide several measurements of key variables each day, resulting in a much more fine-grained "lens" through which to view processes as they are changing.

EMA Studies of Alcohol Use

As of late 2015, there were about 23 alcohol misuse studies that used an EMA approach, which was a relatively low number compared to over 60 studies that used EMA to examine cigarette smoking. The exact reasons for such a disparity are unclear. However, it is possible that the acute effects of alcohol may reduce the feasibility of EMA in heavy drinking populations. In addition, very few EMA studies have been conducted in alcohol dependent populations, and, of those, only two have used both random assessments and participant-initiated assessments (Cooney et al., 2007; Litt, Cooney, & Morse, 1998), and none have used both temptation assessments and random assessments on a PDA. Similarly, neither study used cognitive assessments, and the EMA protocols in Litt et al. (1998) and Cooney et al. (2007) were 14 and 21 days, respectively.

Therefore the current study will address the question as to whether EMA, using both random and temptation assessments, is a feasible methodology in individuals who have a history of alcohol abuse and dependence over the course of a 4-week EMA protocol. A central measure of feasibility in EMA studies is compliance on RAs, defined as the proportion of RAs that are presented to participants that are actually completed by

participants. If compliance is low, at a minimum both the statistical power of the study, as well as the generalizability of study findings, is reduced. A review of the literature yielded 23 empirical EMA studies that targeted people with past and current risks of misusing alcohol (Table 2). Out of the 23 studies, 12 administered RAs. Out of the 12 studies, 11 reported measures of compliance on RAs (Collins et al., 1998; Cooney et al., 2007; Dvorak, Pearson, & Day, 2014; Holt, Litt, & Cooney, 2012; Krahn et al., 2005; Litt et al., 1998, 2000; Ray, Miranda, et al., 2010; Tidey et al., 2008; Todd et al., 2005; Witkiewitz et al., 2014). Across these 11 studies, the median level of compliance was 80%, and 9 out of the 11 studies reported RA compliance greater than 70%.

A number of studies have examined changes in compliance over time in alcohol-dependent participants. Holt et al. (2012) reported that compliance on RAs did not significantly decline over time, and this was true for both lapsers and non-lapsers. Similarly, Serre et al. (2015) both reported that compliance on assessments at fixed times each day did not significantly decrease over time. Litt et al. (2000) investigated the effects of alcohol relapse and use on compliance with EMA protocol. They reported that 19 of 26 participants lapsed, but only 3 of the 19 were "non-compliant," defined as responding to <50% of RAs, for 1-3 days after their first lapse in the study. The other participants were determined to be compliant. In general, there is little evidence that compliance significantly decreases over time although it should be noted that most studies have not reported these data.

EMA Studies of Mindfulness

There is limited research using EMA methods to study mindfulness. In the development of the Mindfulness Attention and Awareness Scale (MAAS), Brown and

Ryan (2003) used a diary method in two samples of college students (see Table 1). Both samples carried pagers that beeped at quasi-random schedules. They also carried forms on a small note pad that assessed mindful behaviors at the moment when the pagers beeped (K. W. Brown & Ryan, 2003). MAAS scores were associated with positive emotional states assessed during EMA. Other studies reported that mindfulness was associated with increased self-reported inner peace (Liu et al., 2013), greater emotion differentiation and decreased emotional lability (Hill & Updegraff, 2012), and improved global emotional tone evidenced by trait-positive affect and momentary positive cognition (Garland et al., 2010).

Other studies have used EMA to study the effects of mindfulness-based interventions (MBI). Ruscio et al. (2015) reported that mindfulness-based practice reduced negative affect and craving assessed using EMA in non-treatment-seeking smokers. Another study reported that an 8-week group-based mindfulness treatment was effective in improving self-reported emotion dysregulation in adults with Attention Deficit/Hyperactivity Disorder (ADHD) (Mitchell et al., 2013). For adults with depression history, an EMA study found that MBCT led to increased reports of positive emotions, and enhanced responsiveness to pleasant daily-life activities, independent of decreased depression (Geschwind, Peeters, Drukker, van Os, & Wichers, 2011). One EMA study found that MBCT's effectiveness in improving positive affect were moderated by certain single-nucleotide polymorphisms (SNPs) underlying the brain-derived neurotrophic factor (BDNF) (Bakker et al., 2014).

STUDY RATIONALE

To summarize, alcohol misuse has remained a significant public health and economic problem worldwide, and relapse rates for treatment of alcohol dependence remain high. New treatment approaches are required. A greater understanding of the psychological processes underlying relapse to alcohol may lead to improved interventions.

Trait mindfulness is a potentially important risk factor for dependence and relapse in the addictions. However, the role of trait-mindfulness has been little investigated in alcohol dependence.

EMA has been used to study relapse processes in other addiction, and studies using cognitive tasks may be especially useful for tapping into automatic processes underlying drug use and relapse. However, data using EMA in alcohol dependent populations are sparse.

The current study had three specific aims. The first aim examined the feasibility of conducting a 4-Week EMA protocol with cognitive assessments in an alcohol dependent population attempting to maintain abstinence. The second aim examined whether trait-mindfulness was associated with ratings of temptation to drink (termed "tempted now" ratings) and relapse to alcohol. The third aim examined trait-mindfulness as a moderator variable in relapse to alcohol.

The specific aims and hypotheses were as follows:

SPECIFIC AIMS AND HYPOTHESES

Specific Aim 1: To examine the feasibility of a 4-Week EMA protocol with cognitive assessments in an alcohol relapse study.

Hypothesis 1.1: Compliance with random assessments will be greater than 70%.

Hypothesis 1.2: Compliance with random assessments will be stable over the study duration

Specific Aim 2*:* To examine whether trait mindfulness, as assessed by the MAAS at the baseline visit, is associated with tempted now ratings and drinking alcohol assessed during EMA

Hypothesis 2.1: More mindful individuals (assessed using the MAAS) will report lower tempted now ratings assessed during EMA (1-7 scale)

Hypothesis 2.2: More mindful individuals (assessed using the MAAS) will report less drinking as assessed during EMA using a single item

Specific Aim 3*:* To examine trait mindfulness, as assessed by the MAAS, as a moderator variable. Specifically, trait mindfulness is expected to <u>weaken</u> the relationship between 1) negative affect and craving, 2) cognitive biases and craving, and 3) craving and drinking.

Hypothesis 3.1: The association between negative affect (assessed during EMA with a short form of the Positive and Negative Affect scale) and tempted now ratings (1-7 scale), assessed during EMA, will be weaker in participants with higher (vs. lower) trait mindfulness (assessed using the MAAS).

Hypothesis 3.2: The association between cognitive biases (assessed during EMA using the alcohol Stroop task and IAT) and tempted now ratings, assessed during EMA (1-7 scale), will be weaker in participants with higher (vs. lower) trait mindfulness (assessed using the MAAS).

Hypothesis 3.3: The association between tempted now ratings (1-7 scale) and drinking, assessed during EMA (single item), will be weaker in participants with higher (vs. lower) trait mindfulness (assessed using the MAAS).

CHAPTER 2: METHOD

PARTICIPANTS

Participants were 11 Dutch outpatients recruited three locations of an addiction treatment facility in the Netherlands. The patients were completing a 6-week residential addition treatment and were screened and referred to the current study by the treatment staff (e.g., nurses and psychiatrists). The inclusion criteria were: (a) aged 18 years or older; (b) a current diagnosis of alcohol dependence as defined in the Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition (DSM-IV; American Psychiatric Association, 2000) and as determined by Section J of the Dutch version of the Composite International Diagnostic Interview (CIDI; Robins et al., 1988); (c) an eighth-grade literacy level; and (d) a period of abstinence of at least two weeks prior to the first appointment of the parent study (described later). Patients were excluded if they had one of the following: (a) were diagnosed with an Axis II disorder according to the DSM-IV; (b) were diagnosed with a disorder in the psychotic spectrum; or (c) used other addictive substances (except nicotine) on a regular basis.

PROCEDURE

This study was part of a larger parent study examining predictors of relapse (Fig. 1). For the parent study, participants (n = 59) were recruited from three locations of an addiction treatment facility in the Netherlands. Recruitment took place in an outpatient detoxification program. In the parent study, the participants went through two group therapy sessions per week for six weeks, in addition to pharmacotherapy. The group sessions were led by two counselors who employed cognitive behavioral therapy and motivational interviewing techniques during these sessions. After this six-week program,

patients continued with group therapy, terminated treatment, or started an individual treatment program. Both individual and group therapy consisted of a combination of CBT and motivational interviewing techniques. The choice for group or individual therapy was made by both the participant and their counselor. Additionally, participants either used disulfiram, acamprosate, naltrexone, or no medication.

As noted earlier, a minimum of 2 weeks abstinence was required for enrollment in the parent study. As the study progressed, the treatment goals could be modified, such that complete abstinence was not the goal and controlled drinking could be permitted. However, in the current report, all the subjects were trying to maintain completed abstinence during the study period.

Those who were close to finishing their treatment were screened for eligibility for the EMA study. At the orientation session for the EMA study, eligible participants were administered post-treatment assessments for the 4-week parent study (i.e., at the end of the 6-week treatment), and baseline assessments, including the MAAS, for the EMA study (Fig. 1). They were then trained on using the personal digital assistant (PDA, model HP1920) to respond to the EMA assessments.

Thereafter the four weeks of EMA started (Fig. 1). The PDA was programmed to signal three times a day at random times (random assessment; RA). Participants were also instructed to initiate an assessment themselves whenever they experienced an acute increase in the urge to drink or an occasion when they felt that they came to the brink of drinking without actually doing so (temptation assessment; TA). At each RA or TA assessment, participants responded to items assessing subjective variables (e.g., mood and craving) and drinking. Subsequently participants were presented with either an

alcohol Stroop task or an alcohol approach-avoidance IAT. The current study does not examine the effects of assessment type (TA vs. RA) on subjective or cognitive assessments (but see Snelleman et al., 2015, under review).

As noted earlier, the EMA program was programmed to present 3 RAs per day. These were presented between a wake-up time and a bed-time which were set by the subject. However, RAs were not presented if the power on the PDA was low, or if the program malfunctioned. Moreover, participants had the opportunity to prevent the device from presenting RAs (e.g., if they had an important meeting to attend) through the use of a "suspend" button. RAs scheduled during a "suspend" were not presented, and RAs could also be lost if the bed-time was changed.

During the 4-week EMA study, data were downloaded every week by the researcher during face-to-face appointments with the participants, who also checked the compliance with the protocol. Additionally, the researcher asked the participants whether they had consumed any alcohol in the preceding week. Participants continued the study even if they had relapsed. After four weeks participants handed in the PDA and received financial compensation for their participation (€ 4.45 per day, max € 125,-). The study was approved by the Medical Ethical Committee of the Erasmus Medical Center, Rotterdam, The Netherlands (registration number MEC-2012-346).

MEASURES

Laboratory Assessment

The Mindful Attention Awareness Scale (MAAS; Brown & Ryan, 2003) is a 15-item self-report survey that measures trait mindfulness on a 6-point Likert scale. This measure has been validated and normed in clinical and non-clinical samples, with

Cronbach's alpha ranging from .80 to .90 (K. W. Brown & Ryan, 2003; Carlson & Brown, 2005). The Dutch version of the MAAS (MAAS-D) also replicated the original measure's reliability (alpha ranging from .81 to .87), and one-factor structure (Schroevers, Nykliček, & Topman, 2008). Evidence suggest that the MAAS-Dutch is an appropriate measure of "…[the] attention, informed by a sensitive awareness of what is occurring in the present, simply observes what is taking place" (K. W. Brown & Ryan, 2003).

EMA Assessments

Self-Report Assessments

The Positive Affect & Negative Affect - Short Form (PANAS-SF; Mackinnon et al., 1999) is a 10-item self-report of five negative and five positive affective states. The PANAS consists of 10 items: five positive items (PANAS-NA) and five negative items (PANAS-NA). Participants indicated whether they agreed with a statement (e.g. I feel upset right now) on a 5-point scale (1 = not at all to 5 = extremely). In the current study, Cronbach's alpha was good for both PANAS-PA (alpha = .95) and PANAS-NA (alpha = .95).

An item assessed participants' current temptation to drink on a 7-point Likert scale; "I feel tempted to drink right now" ("Tempted Now"). Participants could indicate to what degree they agreed with this statement on a 7-point scale (1 = not at all to 7 = very much). Craving was assessed using the item "I feel the urge to drink right now" (Craving) on a 7-point scale (1 = not at all to 7 = very much). Responses to Tempted Now (M = 2.14, SD = 1.89) and Craving (M = 2.16, SD = 1.91) were highly correlated (r = .93) The current ms reports results from Tempted Now.

An Alcohol Consumption item ("Drinking") assessed number of drinks consumed since the previous assessment: 1 = no drinks; 2 = 1-2 glasses; 3 = 3-4 glasses; 4 = 5-6 glasses; 5 = 7 or more glasses.

Cognitive Assessments

The Alcohol Stroop task assessed the degree to which person's attention is captured by alcohol cues, or "attentional bias" to alcohol cues (Cox, Fadardi, & Pothos, 2006). Participants were presented with words in different colors on the PDA. The participants were instructed to respond by pressing a button that corresponded with the color of the word by pressing one of three buttons on the PDA (see A. J. Waters et al., 2012). They were instructed to respond as quickly as possible to the color, and to ignore the meaning of the words. Participants were presented with a block of 33 neutral words and a block of alcohol words, with randomized word order). The Dutch stimulus words are listed in Table 5 with their English translation. The Stroop task was scored by subtracting the median RT on neutral words from the median RT on alcohol words. The resulting difference score is the alcohol Stroop effect. A positive difference score reflects a slower response time on alcohol words, indicating an attentional bias to alcohol words.

The Approach-Avoidance Implicit Association Test (AA-IAT) is a computerized reaction task that assesses the degree to which a person associates drug cues with a tendency to approach them. Participants were presented with words from four different categories, e.g., alcohol-related, non-alcohol-related, approach-related, and avoid-related. The Dutch stimulus words are listed in Table 5 with their English translation.

On the AA-IAT, participants were asked to respond rapidly by pressing a certain PDA key for items representing two concepts (e.g., Alcohol + approach), and with a

different PDA key for items from two other concepts (e.g., Neutral + avoid) (Task 1). In Task 2, the assignment of one concept was switched such that "Neutral" + "approach" shared a common key-response, and "Alcohol" + "avoid" shared the other response. The idea underlying the IAT is that it is easier to perform the IAT when the two concepts are strongly associated in memory than when the two concepts are unrelated (De Houwer, 2002). The IAT effect is the difference in reaction times (RTs) on Task 1 vs. Task 2. It is considered an index of the relative strength of mental associations. In the example above, it indicates whether associations are stronger between Alcohol and approach, and Neutral and avoid, than between Neutral and approach, and Alcohol and avoid. Higher (more positive) scores (i.e., faster responses when "Alcohol" is paired with "approach" compared to when "Alcohol" is paired with "avoid") are interpreted as indicating an approach bias.

On each trial, a stimulus (word) was presented in the center of the PDA screen. On the top of the screen were labels (on each side of the screen) to remind participants of the categories assigned to each key for the current task. Participants were instructed to categorize each stimulus word into its respective category by pressing either an "L" key or the "R" key on the PDA as quickly and as accurately as possible. If the participant responded correctly the program proceeded to the next trial, with a 150 ms pause between trials. If the participant made an error, a red "X" appeared below the stimulus until the participant responded correctly. Participants were instructed to correct their errors as quickly as possible.

The AA-IAT was scored with the algorithm recommended by Greenwald et al. (2003) to derive the IAT effect. The scoring algorithm divides the difference score by the

pooled standard deviation of response times of all trials from Tasks 1 and 2. The algorithm also eliminates assessments with RTs less than 300 ms on more than 10% of the trials. In addition, any trials with RT greater than 10,000 ms were excluded, and RTs on incorrect responses were replaced by the mean RT from the correct responses of the block, plus 600 ms (Greenwald et al., 2003).

DATA ANALYSIS

Linear Mixed Models (LMMs) were used to address Specific Aims 1, 2, and 3. LMM is a common method used to analyze EMA data, because LMMs can handle the fact that assessments are nested within participants, and that participants have different numbers of assessments. Each LMM used a random intercept, and an autoregressive model of order 1 for the residuals within subjects. All models included Day of study as a covariate. For all models the parameter estimate is provided as an (unstandardized) measure of effect size. All tests used $\alpha = .05$, and were 2-tailed.

Compliance was defined as the proportion between the number of RAs participants completed and the number of RA prompts presented by the PDAs. Two of the 11 participants did not complete the 4-week study but provided partial data; their data were used in all analyses. To examine if compliance changed over time (Specific Aim 1), Day was entered as an independent variable in a LMM. The dependent variable was compliance (proportion of RAs completed) on each day. To test MAAS as a predictor variable (Specific Aim 2), MAAS was entered as an independent variable into a LMM. A significant parameter for MAAS would reveal that it was associated with the outcome variable (Tempted Now or Drinking). To test MAAS as a moderator variable (Specific Aim 3), MAAS was entered in a LMM, along with the second independent variable

(Negative Affect, Stroop, IAT, or Tempted Now) and the interaction between MAAS and the second independent variable. A significant parameter for the interaction term would reveal that the MAAS significantly moderated the association between the second independent variable and the outcome variable (Tempted Now or Drinking).

For the analysis of MAAS as a predictor variable (Specific Aim 2) and moderator variable (Specific Aim 3), MAAS scores were coded both as a continuous variable and a binary variable. For the latter, MAAS scores < 4.33 (the median) were designated as "Low" MAAS scores and MAAS scores ≥ 4.33 were designated "High" MAAS scores. This was done to facilitate visualization of key findings. Using this procedure, four subjects were designated as low MAAS and seven as high MAAS (4 subjects had a MAAS score of 4.33, the median, and they were assigned to the high MAAS group).

The 11 participants completed a total of 491 assessments (444 RAs, 47 TAs). The analyses used all 491 assessments from all 11 participants. Inclusion of Assessment Type (TA vs. RA) as an independent variable did not change any of the reported findings.

POWER ANALYSIS

Power analyses were conducted using G*Power 3.1 (Faul, Erdfelder, Lang, & Buchner, 2007). All power analyses used alpha = .05 and a 2-tailed test. In the calculations described below, the power estimates account for the fact that repeated observations from the same person will be correlated, indexed by the intraclass correlation coefficient (ICC). For Specific Aim 2, assuming 11 participants, 500 assessments, and an intraclass correlation coefficient (ICC) = .5, the study would have power = .81 to detect a correlation, rho = .56 (i.e., a large effect size), between MAAS and outcome variables. If the ICC = .3 (i.e., the repeated measures EMA data were less

correlated), then power = .81 to detect a correlation, rho, = .46 (a medium-to-large effect size). For Specific Aim 3, power analyses are not provided because we know of no procedures that allow their estimation in this context. Given the small sample size, there will only be power to detect very large effect sizes for interactions.

CHAPTER 3: RESULTS

DESCRIPTIVE STATISTICS

The sample in the analysis included 11 subjects (5 females, 6 males) (Table 7). Two participants withdrew from the study prematurely (after two weeks of study participation); one due to the illness of spouse, and one due to a heavy relapse to alcohol. These two subjects provided data for the time they were in the study and their data were used in all analyses. The other 9 subjects participated for 4 weeks.

Data for compliance measures are presented in Table 7. On average, the participants carried the PDAs for 23.9 days (SD = 6.6). The average number of RAs completed was 40.4 per participant. The average number of TAs completed was 4.3.

FEASIBILITY OF 4-WEEK EMA PROTOCOL

The first Specific Aim was to examine the feasibility of a 4-Week EMA protocol with cognitive assessments in an alcohol relapse study.

To address Hypothesis 1.1, average compliance rate on RAs was computed. The average compliance rate was 70.2% (SD = 14.6).

To address Hypothesis 1.2, we plotted compliance by Day of study. The LMM indicated that there was no main effect of time-in-study on the participants' compliance rate, i.e., compliance rate did not decrease as time went on in the study, $F(1, 202) = 0.02$, $p = .90$ (Fig. 2).

ASSOCIATION BETWEEN MAAS AND TEMPTATION RATINGS/DRINKING

The second specific aim was to examine whether trait-mindfulness, as assessed by the MAAS, was associated with Tempted Now and Drinking

To address Hypothesis 2.1 LMMs tested whether MAAS scores were associated with Tempted Now. LMMs (Table 8) indicated that there was a significant effect of MAAS on Tempted Now, whether the MAAS was coded as a binary or continuous variable. Participants who scored "Low" on MAAS at baseline reported significantly higher Tempted Now ratings, compared to participants who scored "High" on MAAS at baseline (Fig. 3).

To address Hypothesis 2.2, LMMs tested whether MAAS scores were associated with Drinking. LMMs indicated that there was a significant main effect of MAAS on the reported numbers of drinks since the last assessment (Table 8). The "Low" MAAS group reported s significantly higher number of drinks compared to the "High" MAAS group (Fig. 4).

MAAS AS A MODERATOR VARIABLE

LMMs testing moderation are reported in Table 8, which reports the parameter estimates and significance of interaction terms.

To address Hypothesis 3.1 LMMs tested whether higher mindfulness weakened the relationship between NA and Tempted Now ratings. There was no evidence for an interaction between MAAS group and NA (Table 8). The non-significant interaction is illustrated in Figure 5. LMMs indicated that, for the Low MAAS group, there was a significant association between NA and Tempted Now, PE = 0.58, SE = 0.28, p = .04 (not shown in Table 8). For the High MAAS group, there was also a significant association between NA and Tempted Now, PE = 0.55, SE = 0.23, p = .02 (not shown in Table 8).

Hypothesis 3.2 examined whether higher mindfulness weakened the relationship between cognitive biases and Tempted Now. For the Stroop (attentional bias), there was evidence for an interaction between MAAS group and Stroop when MAAS was coded as a binary variable, but not when entered as a continuous variable (Table 8). The interaction is illustrated in Figure 6. There was no association between the Stroop and Tempted Now for the Low MAAS, PE = -0.002, SE = 0.001, p = .20 (not shown in Table 8), or High MAAS group, PE = 0.002, SE = 0.001, p = .10 (not shown in Table 8). For the IAT (approach bias), there was no evidence for an interaction between MAAS group and IAT (Table 8). The non-significant interaction is illustrated in Figure 7. There was no association between the IAT and Tempted Now for the Low MAAS, p = .17, or High MAAS group, p = .99.

Hypothesis 3.3 examined whether mindfulness weakened the relationship between Tempted Now and Drinking. There was evidence for a significant interaction between MAAS and Tempted Now (Table 8; Fig. 8). There was a significant association between Tempted Now and Drinking for the Low MAAS, PE = 0.16, SE = 0.05, p = .002 (not shown in Table 8), but not the High 004DAAS group, PE = -0.01, SE = 0.01, p = .50 (not shown in Table 8).

CHAPTER 4: DISCUSSION

The current study examined the feasibility of conducting a 4-week EMA study to examine relapse processes in 11 Dutch outpatients with alcohol dependence in the Netherlands. The study also examined trait mindfulness as both as predictor and moderator variable. Specifically, the study examined whether MAAS scores predicted tempted now ratings and drinking. In addition, the study also examined whether MAAS score moderated the associations between negative affect and tempted now ratings, between cognitive biases and tempted now ratings, and between tempted now ratings and drinking.

FEASIBILITY OF 4-WEEK EMA PROTOCOL

The study found that 9 of the 11 subjects completed the 4-week protocol, with two subjects terminating the study after two weeks. All participants provided at least two weeks of EMA data. In addition the compliance rate of 70% is consistent with most addiction studies using EMA methods (Hypothesis 1). Importantly, the compliance rate did not drop over time, suggesting that a 4-week study is feasible in this population. This result is encouraging, because the current study required the participants to carry the PDAs for a longer duration than other alcohol studies using EMA.

ASSOCIATION BETWEEN MAAS AND TEMPTATION RATINGS/DRINKING

Consistent with hypotheses, the study provided evidence that trait mindfulness was negatively associated with tempted now ratings and drinking. Participants who scored high on the MAAS scale at baseline reported lower tempted now ratings (Hypothesis 2.1) compared to those who scored lower on the scale. Participants with high

mindfulness also reported lower numbers of drinks consumed (Hypothesis 2.2) when compared to those with low mindfulness.

The main findings of the study support the general consensus in the literature that mindfulness exerts a protective role against alcohol use (see also Adams et al., 2015). For example, in persons recovering from alcohol dependence, those with high trait mindfulness reported less craving than those with low trait-mindfulness (Garland, 2011).

An investigation of the psychological processes linking mindfulness and craving or use was beyond the scope of the current study. Indeed, the mechanisms linking mindfulness and addiction have not been widely examined. Nonetheless, a number of candidate mechanisms can be posited. For example, mindfulness may decrease craving or use by promoting a decentered perspective. Decentering is considered a component of mindfulness (Shapiro et al., 2006) and can be defined as "watching one's thoughts and emotions in a non-judgmental way, or non-attachment to one's thoughts, feelings, and emotions" (Fresco, Moore, et al., 2007; Fresco, Segal, Buis, & Kennedy, 2007).

Ruscio (2012) conducted a multiple mediation analysis to examine the variables that mediated the association between trait mindfulness, assessed using the MAAS, and nicotine dependence. In addition to perceived stress, and negative and positive affect, she assessed a decentered perspective using a depression IAT task (see A.C. Ruscio, 2012 for details). The association between MAAS scores and dependence was found to be partially mediated by both positive affect and by decentering (A.C. Ruscio, 2012). Relatedly, recent neurobiological investigations of dispositional mindfulness have shown that more mindful individuals exhibit greater prefrontal activation and reduced amygdala

activation during affect labeling tasks (Way, Creswell, Eisenberger, & Lieberman, 2010). The pattern of brain activity may be a brain mechanism of a decentered perspective.

Mindfulness may also decrease craving or use by reducing negative affect or stress. In alcohol use, Adams et al. (2015) recently reported that the association between mindfulness (assessed using the MAAS) and likelihood of an alcohol use disorder was mediated by perceived stress. That is, higher levels of mindfulness were associated with lower perceived stress which in turn was associated with a lower likelihood of an alcohol use disorder. Pertinent to the current manuscript, Adams et al. (2015) also tested mindfulness as a moderator. They reported that mindfulness moderated the association between perceived stress and alcohol use such that stress increased alcohol use in participants with low levels of mindfulness but not in participants with high levels of mindfulness. These findings underscore the utility of examining mindfulness as both a predictor and moderator variable.

Finally, Garland et al. (2011) examined the association between mindfulness and attentional bias in alcohol dependent participants. They reported that individuals with higher levels of mindfulness (assessed by the MAAS) exhibited less attentional bias to alcohol cues. That is, more mindful individuals may be better able to disengage attention from alcohol cues. In addition, the heart rate (HR) and high-frequency heart rate variability (HFHRV) of participants was assessed using a stress paradigm. The study found that those with higher mindfulness exhibited greater HR and HFHRV recovery and that attentional bias partially mediated this association.

As well as addressing the mechanisms above, future studies can address some of the complex issues surrounding the psychological processes underlying mindfulness.

First, decentering is more than "not taking it personal;" it requires active, non-evaluative, and open acceptance of the experiences (D. B. Brown, Bravo, Roos, & Pearson, 2015; Fresco, Moore, et al., 2007; Fresco, Segal, et al., 2007). These processes need to be unpackaged. Second, the re-framing or re-processing of the experience as a mental event that is not necessarily real *or* true should be further explored. For instance, for someone with 20 years of alcohol dependence the process of reframing a debilitating craving to drink may require a very specific kind of cognitive process to succeed in differentiating the experience ("I am having the sensation of craving") from its meaning ("I *am* craving." "I *need* to drink to feel less bad, or great"). Third, the mechanisms of mindfulness may be intertwined with psychophysiological processes (Garland et al., 2011), and future studies would benefit from assessment of psychophysiological variables.

MAAS AS A MODERATOR VARIABLE

The current study generated mixed findings regarding the role of mindfulness as a moderator variable. First, there was no evidence that MAAS moderated the association between negative affect and tempted now ratings. There was a positive association of similar magnitude between negative affect and tempted now ratings for both low and high MAAS participants. Therefore, trait mindfulness did not significantly weaken the relationship between negative affect and tempted now ratings (Hypothesis 3.1).

This absence of a moderation effect may be due to methodological limitation, such as the limited sample size. However, it is also possible that participants low in mindfulness adopt alternative strategies to mitigate the impact of negative affect. For instance, Rogojanski et al. (2011) found that thought suppression training—and not

mindfulness training—increased self-efficacy in cigarette smokers with higher anxiety sensitivity in a cue-exposure paradigm. Perhaps some persons in the low trait-mindfulness group engaged in similar cognitive strategies such that the impact of negative affect was no greater in these participants than in the high mindfulness participants.

With respect to the cognitive biases, there was only limited evidence that trait mindfulness weakened the association between cognitive biases and tempted now ratings (Hypothesis 3.2). For attentional bias, the pertinent interaction was significant when MAAS was scored as a binary variable, and nonsignificant when MAAS was treated as a continuous variable. Specifically, attentional bias and tempted now ratings were significantly associated in the low MAAS group, but not in the high MAAS group. For approach bias, the pertinent interaction was not significant. Therefore, trait mindfulness did not weaken the relationship between approach bias and tempted now ratings.

In contrast, there was clearer evidence that trait mindfulness weakened the relationship between tempted now ratings and number of drinks consumed (Hypothesis 3.3). When reporting a tempted now rating of 2 or more (vs. 1), participants with low mindfulness reported a significant increase in the number of drinks consumed since the last assessment, whereas those with high mindfulness did not. That is, participants with low trait-mindfulness reported drinking more when they were tempted, but the same was not true for participants of high trait mindfulness.

This finding is in line with other studies that found mindfulness to attenuate the influence of predictors of substance use. For example, Ostafin et al. (2008) found that a high level of trait-acceptance weakened the association between approach-bias and

alcohol consumed. A high level of trait mindfulness and executive control was also found to weaken the association between attentional bias and preoccupation with alcohol (Ostafin et al., 2013). As noted earlier, Adams et al. (2015) reported that mindfulness moderated the association between perceived stress and alcohol use such that stress increased alcohol use in participants with low levels of mindfulness but not in participants with high levels of mindfulness. Finally, Witkiewitz et al. (2012) found that Mindfulness-based Relapse Prevention (MBRP) attenuated depressive symptoms' effects on craving for alcohol and other drugs at 2-month after MBRP.

In sum, while the findings were mixed, trait mindfulness may play a protective role in maintaining abstinence, as it may break the link between desire for alcohol and actual drinking behaviors. Further research is required to explore the precise mechanisms by which mindfulness attenuates the association between tempted now ratings and drinking. For example, mindfulness may promote tolerance of urges, and urges may be stress-inducing (Snelleman et al., 2016). Mindfulness may also enhance self-efficacy to deal with urges as well as reduce expectations that drinking will reduce distress or urges (Adams et al., 2015). Moreover, the fact that dispositional mindfulness may attenuate the relationship between tempted now ratings and use may explain why the association between craving/urge and use in addiction is not always robust (Wray, Merrill, & Monti, 2014).

LIMITATIONS

As a report of preliminary analyses, the study had a number of limitations. First, the number of participants (n = 11) was small. Given the small sample size, the analyses should be considered preliminary. A complete analysis involving all 43 participants will

be reported when the data analysis has been completed. Second, due to the sample size, the study would have had low power to detect interaction effects. Third, when examining the association between trait mindfulness and study outcomes the current study did not examine the influence of control variables, such as socioeconomic status, gender, and age. Thus, the independent contribution of trait mindfulness over other control variables is not known. This should be examined in future studies. Fourth, tempted now ratings were assessed at each assessment, and self-reported drinking was assessed as the amount of drinking since the previous assessment. Therefore, drinking occurred before the tempted now ratings. Thus, the current data may reflect the moderating influence of mindfulness between drinking and tempted ratings in addition to, or instead of, the moderating influence between tempted ratings and drinking. Additional analyses would be required to determine whether trait mindfulness weakens the association between tempted ratings and subsequent drinking. Future research could also examine whether trait mindfulness weakens the between- and/or within-subject associations between tempted ratings and drinking. Fifth, the data are correlational. Therefore, it is now know whether trait mindfulness causes lower tempted now ratings or drinking behavior. Sixth, parameter estimates from mixed models may be biased if missing data are not missing at random. Future analyses can compare the results when including and excluding participants who dropped out of the study early (and who therefore contributed, data only early in the study).

Last, trait mindfulness was measured with a unidimensional scale. MAAS was chosen because it is one of the earliest, most validated, and frequently used mindfulness assessments; it is also the only one with a psychometrically validated adaptation in

Dutch. However, recent clinical studies involving trait mindfulness have increasingly recognized its multidimensional nature. Specifically, the Five-Facet Mindfulness Scale (FFMQ) (Baer et al., 2008) has generated consistent data to support that different factors of mindfulness may have different predictive and treatment utilities in clinical conditions. Recently, three Dutch studies have validated the translation of FFMQ into Dutch in clinical and non-clinical populations (Bohlmeijer, ten Klooster, Fledderus, Veehof, & Baer, 2011; de Bruin, Zijlstra, van de Weijer-Bergsma, & Bögels, 2011; Veehof, Oskam, Schreurs, & Bohlmeijer, 2011).

STRENGTHS

The study had several strengths. First, to the author's knowledge, this is the first study to examine feasibility in conducting four-weeks of EMA with patients who recently succeeded in completing alcohol dependence treatment. It is also one of the few EMA studies to be conducted in the Netherlands and the first to report compliance data. Second, the study tracked the participants during a "high risk" period for relapse. Third, the study's conceptualization of trait mindfulness, negative affect, cognitive biases, and tempted now contributed knowledge of "who" may be at risk of drinking (e.g., those with low trait-mindfulness), and "when" one may be at risk (e.g., when temptation ratings are elevated). Last, the choice to measure mindfulness from a trait perspective may contribute to the field's on-going effort to differentiate the role of state- vs. trait-mindfulness in clinical interventions.

FUTURE DIRECTIONS

Although beyond the scope of this study, analysis of EMA data could result in the development of algorithms that could be used to determine when to intervene via mobile

devices, “just in time.” If a unique constellation of changes in psychological processes, identified through EMA, tended to precede relapses, an intervention (mindfulness-based or otherwise) could be administered via mobile devices to target those processes. In this way, interventions could be delivered when the participant is most in need of the intervention, minimizing participant burden and perhaps reducing the risk of relapse.

Future studies could also examine the effect of MBCT treatment on study variables. For example it would be interesting to observe whether MBCT treatment (manipulated as an independent variable) moderates the association between tempted now ratings and drinking. Recently, Dimidjian et al. (2015) have provided recommendations on how to conduct mindfulness-based translational and intervention studies.

Another direction is to explore in greater depth the prospective association between tempted now ratings and drinking, and its moderation by mindfulness. One specific way is to examine the reasons why individuals are tempted to drink. For instance, a measure of “momentary reasons to drink,” may provide a more detailed assessment of temptation, by identifying motivations, desire, reasons, and behavioral intentions. Such an assessment will help us understand how different contexts lead to different decision-making mechanisms across temptation episodes and persons.

As well as examining the prospective association between tempted ratings and drinking, future studies could also examine the prospective association between drinking and tempted ratings, and its moderation by mindfulness. Drinking could potentially increase or decrease tempted ratings. Studies have investigated the idiom “one drink often leads to another” in various populations. The studies suggested that the type of

motivation or craving as a main determinant for when and where such dynamic occur, For instance, a drinker's susceptibility to reward vs. relief craving may influence craving type and intensity across positive and negative settings (Glockner-Rist, Lemenager, Mann, & Group, 2013), motivation to enhance experiences vs. coping with negativity showed distinct activation following mood induction (Birch et al., 2008), and situational and social contexts explained the inconsistencies in the self-medicating literature (Mohr, Arpin, & McCabe, 2015; Monk & Heim, 2013). EMA data is well-suited to hone-in on the unique contribution and interaction of these factors in drinking trajectories.

Future mindfulness research could benefit from a comprehensive assessment of related constructs such as coping behaviors, problem solving strategies and spirituality. For instance, mindfulness is more beneficial for individuals who rely on avoidant coping (Bowen et al., 2014; Eisenlohr-Moul et al., 2012). In addition, trait and state mindfulness help one solve insight but not non-insight problems (Ostafin & Kassman, 2012). Trait mindfulness appears to function similarly to spirituality but is distinct (Crescentini, Matiz, & Fabbro, 2015; Shorey et al., 2015).

CONCLUSIONS

In sum, this pilot EMA study provided evidence that alcohol-dependent participants with higher trait mindfulness reported lower tempted ratings and less drinking. There was also evidence that trait mindfulness also moderated the association between tempted now ratings and drinking. Future research should examine these preliminary findings using larger sample sizes and more comprehensive assessment of relevant constructs