12-2-2014

Executive Cognitive Functioning and Regulatory Deficits among Emerging Adult Nonmedical Prescription Opioid Users

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EXECUTIVE COGNITIVE FUNCTIONING AND REGULATORY DEFICITS AMONG EMERGING ADULT NONMEDICAL PRESCRIPTION OPIOID USERS

by

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A Thesis

Submitted in Partial Fulfillment of the

Requirements for the Degree of

Master of Science

Major: Psychology

The University of Memphis

December 2014

Abstract

Pickover, Alison Marisa. MS. The University of Memphis. December 2014. Executive cognitive functioning and regulatory deficits among emerging adult nonmedical prescription opioid users. Major Professor: James G. Murphy

Nonmedical prescription opioid (NMPO) use is elevated among emerging adults and may be related to deficits in executive cognitive functioning (ECF). This study examined relations between NMPO use, ECF deficits, and "downstream consequences" of poor self- and emotion regulation among emerging adults. Twenty-seven emerging adult NMPO users and 27 matched controls completed measures of ECF (working memory and interference control), self- and emotion regulation, and a clinical interview assessing substance use. NMPO users reported regulation deficits relative to controls, but groups did not differ on ECF measures. Among users, interference control was associated with NMPO use, working memory with alcohol use severity, and emotion regulation with NMPO use severity and marijuana use. Across groups, goal-directed and impulsive behavior when distressed was associated with interference control. Engagement in goal-directed behavior when distressed was additionally associated with working memory. These findings should be extended to inform research, prevention, and intervention.

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The widespread nonmedical use and abuse of prescription opioids has been widely recognized as a significant public health concern over the past decade (Zacny et al., 2003). Nonmedical prescription opioid (NMPO) use (defined here as the use of prescription opioids without a prescription or use in a manner that is different from as prescribed) is most common among 18-25 year olds (Substance Abuse and Mental Health Services Administration [SAMHSA], 2013c), and despite increasing awareness of this public health concern, rates of NMPO use have largely remained stable over the past decade (11.4% past year use among 18-25 year olds in 2002 versus 9.8% in 2011; SAMHSA, 2012b). Emerging adults between the ages of 18 and 25 are disproportionately represented among the population of NMPO users receiving treatment; in 2010, 18-24 year olds represented 28.4% of individuals admitted to publicly-funded substance abuse treatment programs for non-heroin opioid abuse, but only 9.9% of the United States population (SAMHSA, 2012a; U.S. Census Bureau, 2011). Little improvement was seen in 2011, with this percentile decreasing only to 27.3% (SAMHSA, 2013b). Similarly, 18-25 year olds represented 29.6% of specialty prescription opioid treatment recipients and approximately 33% of NMPO-dependent individuals in 2011(SAMSHA, 2012b). Beyond the risks and economic burden associated with severe patterns of NMPO use and its treatment, addiction to prescription opioids is also concerning given recent reports that individuals who become addicted transition to heroin use when prescription opioids become too expensive or are inaccessible (Cicero, Ellis, Surratt, & Kurtz, 2014; Kuehn, 2014).

NMPO use frequently co-occurs with other substance use, and particularly, the use of alcohol and marijuana. Catalano and colleagues (2011) assessed the substance use of 912 emerging adult nonusers, light users (less than 10 past-year instances of NMPO use) and heavy users (10 or more past-year instances of NMPO use) at grades 10, 11, and 12, and ages 19 and 20. They found that the majority of NMPO users (heavy or light) also endorsed alcohol and marijuana use at each time point, and nearly every single NMPO user endorsed alcohol and marijuana use at age 19, age 20, and ever (lifetime). Similarly, McCabe and colleagues (2005) found that among a sample of 10,904 college students nationwide, past-year NMPO users were over four times more likely to report multiple binge drinking episodes (i.e., having 4 or 5 drinks or more in one occasion for women and men) in the past two weeks, and over eight times more likely to report smoking marijuana in the past year, than their non-using college student counterparts. In line with these reports, an examination of data collected from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions by McCabe and colleagues (2006a) revealed higher rates of nonmedical prescription drug use among alcohol-disordered individuals and binge drinkers than among non-binge drinkers and alcohol abstainers. Further, rates of nonmedical prescription drug use among 18-24 year old alcohol-dependent individuals were elevated relative to their 25 and older alcohol-dependent counterparts. This research underscores the importance of developing a better understanding of NMPO use and its comorbidity with other substance use, particularly among emerging adults.

The current proposal was designed to examine one potentially important correlate of these phenomena among emerging adults, deficits in *executive cognitive functioning*.

First, executive cognitive functioning and its relation to substance use are introduced. Next, to understand the developmental context in which executive cognitive functioning and substance use interact, the neurodevelopmental and psychosocial characteristics of emerging adulthood are discussed. Then, the conceptual and empirical literature relating executive cognitive functioning deficits to opioid and other substance use is reviewed, with attention to downstream consequences like impaired self-regulation and emotion dysregulation (see Figure 1 for a model of this relationship).

Executive Cognitive Functioning

Executive cognitive functioning (ECF) is often invoked as an explanatory factor underlying the dysregulation of behaviors, emotions, and cognitions among substance users (Bechara, 2005; Clark, Thatcher, & Tapert, 2008; Giancola & Moss, 1998; Giancola & Tarter, 1999). ECF is conceptualized as a higher order construct that is integral to the planning, initiation, and self-regulation of goal-directed behavior (Royall et al., 2002) and also underlies the regulation of emotion (Zelazo & Cunningham, 2007). ECF is governed by the prefrontal cortex (PFC; Giancola & Tarter, 1999), with support from the limbic system, and in particular, the anterior cingulate cortex (ACC; Hunter, Hinkle, & Edidin, 2012).

Different domains of psychology offer converging explanations for the relation between ECF deficits and substance use in the form of dual process models. For example, Bechara's (2005) competing neural systems hypothesis posits the existence of two separate but interactive neural systems, including an impulsive system, critically influenced by the amygdala, and a reflective or executive system, critically influenced by the ventromedial PFC, with support from several other structures including the dorsolateral PFC and the ACC. The impulsive system is responsible for affective reactions elicited by aversive and appetitive stimuli, whereas the executive system controls affective states triggered by the memory of personal experiences or imagination of the hypothetical (e.g., post-use hangovers or visualizations of arrests on drug charges). When the executive system is functioning well, the decision to use drugs should elicit thoughts of negative consequences and an overall negative signal, resulting in a decision not to use a substance. Yet in regular drug users, this decision-making mechanism may be weakened or dysfunctional. In other words, a relatively weak executive system may result in patterns of behavior that are relatively more governed by hedonic impulses, resulting in myopic or “disadvantageous” decision making that prioritizes immediate rewards such as those associated with substance use (Bickel, Jarmolowicz, Mueller, Koffarnus, & Gatchalian, 2012). This hypothesis is supported by research showing that prefrontal cortical and ACC damage or dysfunction are associated with deficits in domains such as attention, working memory, decision making, and inhibitory control, as well as with emotional instability (Allman, Hakeem, Erwin, Nimchinsky, & Hof, 2001; Bush, Luu, & Posner, 2000; Giancola & Tarter, 1999; Hunter et al., 2012) and that these deficits, as discussed below, are conceptually and empirically related to substance use.

Emerging Adulthood

Emerging adulthood refers to the developmental period situated between adolescence and adulthood, approximately between the ages of 18 and 25 (Arnett, 2006; Tanner & Arnett, 2009). From a neurodevelopmental perspective, emerging adulthood is a period of significant brain development and maturation. The synaptic pruning and axon myelination that take place over these years allow for greater brain speed and efficiency, and they account for significant gray matter thinning and white matter growth during this period (Spear, 2013; Tanner & Arnett, 2009). Cognitive ability improves greatly during this time period, with verbal aptitude, numerical ability, and general intelligence peaking in emerging adulthood (Tanner & Arnett, 2009). There is significant maturation of the PFC and ACC during this time (Segalowitz & Davies, 2004), and frontostriatal regions of the brain show increased activation from adolescence to adulthood during ECF tasks that require cognitive control and behavioral inhibition (Rubia et al., 2006).

From a psychosocial perspective, this distinct developmental stage is characterized by five interrelated features (Arnett, 2006): identity exploration, instability, self-focus, feeling "in-between," and optimism for possibility. Emerging adulthood is a time both of exploration and instability in the domains of education, romantic relationships, occupations, ideologies and values. These individuals no longer view themselves as adolescents but also do not consider themselves to be adults. Often during this period individuals move out of their parents' homes, fostering increased autonomy and independent decision-making, concurrent with diminished obligations and social control. Perhaps having freed themselves from stressful and uncontrollable life circumstances, emerging adults often have high hopes for the future yet also often have periods of fluctuating mood and negative affect (Arnett, 2005, 2006; Tanner & Arnett, 2009).

Although emerging adults are generally physically and psychologically fit (Tanner & Arnett, 2009), the independence, autonomy, and self-reliance that defines this stage of life may also foster experimentation and initiation of protracted substance use. Thus an important research goal has been to identify targetable factors that predispose or characterize the subset of emerging adults who engage in regular substance use. Recent efforts to identify personality and behavioral correlates of emerging adult substance use have identified sensation- or fun-seeking (Dennhardt & Murphy, 2013; Franken & Muris, 2006), impulsivity (Dennhardt & Murphy, 2013), preference for immediate versus delayed rewards (Kollins, 2003), risky decision-making (Goudriaan, Grekin, & Sher, 2011), and affective variables including negative affect, affect or emotion dysregulation (i.e., a breakdown of the ability to influence the nature, experience, and expression of emotions; Gross, 1998), and labile affect (Dennhardt & Murphy, 2013; Simons, Gaher, Correia, Hansen, & Christopher, 2005; Wong et al., 2013) as associated with, or predictive of, substance use and related problems. These efforts to characterize emerging adult substance users suggest that difficulty overriding prepotent responses or hedonic impulses in response to environmental and contextual stimuli in the service of planning, initiating, and achieving one's behavioral or emotional goals (e.g., attaining good grades or reducing stress) is a distinguishing feature of the subset of emerging adults who engage in substance use. Deficient ECF, which is central to these precise difficulties, therefore provides a unifying perspective for the findings of the recent literature.

ECF and Substance Use

Unity and diversity of executive cognitive functions. Below, the specific relations between ECF, regulatory deficits, and substance use will be reviewed. However, before their discussion, it is useful to understand the latent structure of ECF. A confirmatory factor analysis of ECF by Miyake and colleagues (2000) among emerging adults uncovered three distinct, yet interrelated ECF domains: *working memory* or information updating, *inhibition*, and *cognitive flexibility* or shifting. This conceptualization of ECF as both unitary and diverse has been supported across development (Best & Miller, 2010), and the three-factor model has been replicated among other age groups (e.g., children ages 8 to 13; Lehto, Juujärvi, Kooistra, & Pulkkinen, 2003). Because use of the three-factor model provides clarity and avoids redundancy in understanding and measuring ECF, working memory, inhibition, and cognitive flexibility will be discussed separately below.

Working memory. Working memory refers to the concurrent storage and manipulation of information (Baddeley, 1992). Diminished working memory may contribute to risk for drug use and diminished regulatory control by affecting decision-making, attentional shifting, and inhibitory control[1] (Bechara & Martin, 2004; Bickel et al., 2011; Garavan & Stout, 2005). For example, when working memory is busy managing drug-related rumination or craving, behavioral or emotional control can be difficult to implement. Salient (e.g., drug-related) information is more likely to be rehearsed in working memory, and when such information is encountered (e.g., exposure to environmental drug cues), it is difficult to control one's attentional resources (Hester & Garavan, 2005). Hester and Garavan (2005) demonstrated this phenomenon across a series of studies, showing that when undergraduate students were asked to maintain a set of items in working memory, the ability to shift and to inhibit a prepotent response in subsequent tasks was diminished. Further support for this perspective has come from studies across users of different drug types which ask those users, and controls, to perform inhibitory control tasks that simultaneously require maintaining a set of items in working memory (Garavan & Stout, 2005). These studies show increased ACC

[1] Though working memory and inhibition are conceptually related and influence one another, a principle component analysis by St Clair-Thompson and Gathercole (2006) indicated that scores from working memory and inhibition tasks load onto two separate factors.

activation with increased memory load in controls. However, in drug users, the outcome is much different; instead, there is diminished activation of the ACC, which is involved in attention and emotion regulation (Hunter et al., 2011) accompanied by reduced activation of the right PFC, which is responsible for inhibition (Garavan & Stout, 2005). Taken together, this research supports the hypothesis that diminished working memory capacity decreases the ability to effectively regulate responses.

Among emerging adults, binge drinkers evidence greater working memory deficits than nonbinge drinkers (Parada et al., 2012), and working memory shows direct and indirect effects (through impulsivity) on alcohol problems (Gunn & Finn, 2013). Working memory also interacts with implicit alcohol cognitions to longitudinally predict alcohol use. For example, Thush and colleagues (2008) found that among adolescents and emerging adults with low working memory capacity, alcohol-related positive arousal cognitions (as measured by an Implicit Association Test) predicted greater alcohol use one month later.

Marijuana has also been studied in relation to working memory. Although emerging adult marijuana users typically do not show behaviorally measurable deficits on working memory tasks (Ehrenreich et al., 1999; Smith, Longo, Fried, Hogan, & Cameron, 2010), imaging studies suggest greater brain activity when performing those tasks relative to nonuser controls, suggesting a compensatory recruitment of greater neural resources (Smith et al., 2010).

Working memory and other ECF deficits have not been studied among emerging adult NMPO users. However, on a working memory task from the Cambridge Neuropsychological Test Automated Battery (CANTAB; Cambridge Cognition Ltd), adult male heroin users showed deficits relative to amphetamine users and healthy controls (Ornstein et al., 2000). Similarly, deficits have been found across a variety of memory tasks among methadone maintenance patients relative to non-user controls (Darke et al., 2000).

Inhibition. Inhibition refers to the stopping of a prepotent motor response or mental process (MacLeod, 2007; Nigg, 2000). Inhibition is an integral part of self-regulation, the action of one altering her or his own responses or inner states (Baumeister et al., 2007). For example, the self-regulatory abilities of delaying gratification and overriding a prepotent response (Baumeister et al., 2007; Baumeister & Heatherton, 1996) by definition necessitate successful inhibitory control. Delay of gratification requires one to override or inhibit preference for immediate gratification in order to attain a distal goal or larger future reward (Baumesiter et al., 2007; Bickel et al., 2012). Suppressing a programmed, learned, or habitual response when cued requires the inhibition of acting on one's impulse (Baumeister & Heatherton, 1996). Substance use is often depicted as a prototypic example of a self-regulatory failure because it involves the relative devaluation of long-term benefits (e.g., health and academic or career achievement), or costs (poor future health, relationship, or vocational outcomes), compared to the short-term reward of getting high or reducing an aversive state such as stress or boredom, and because the act of engaging in substance use itself is a response to internal or environmental cues (e.g., stress or the presence of alcohol cues) that one has failed to suppressed.

Because self-regulatory ability can function as a limited resource (Baumesiter & Heatherton, 1996; Muraven & Baumeister, 2000), breakdowns in self-regulation or self-control such as engagement in substance use may be more likely when a previous task, event, or state (e.g., fatigue) has taxed one's capacity for inhibitory control and depleted one's reserve. For example, a study by Muraven and colleagues (2002) asked a sample of male social drinkers to complete either a high inhibition (suppress the thought of a white bear) or low inhibition (simple arithmetic) task. In a subsequent task in which they were provided with and consumed alcohol, those men in the high inhibition condition consumed greater quantities of alcohol than those who were in the low inhibition condition. Building on this finding that effortful inhibitory control impairs subsequent self-regulatory ability, other studies have found that individuals who chronically seek to inhibit a certain behavior (e.g., dieters and chronic alcohol users) are more susceptible to self-regulatory failures (having dessert and drinking) when they encounter salient environmental cues (a dessert or drink menu; Baumeister et al., 2007). Taken together, this line of research suggests that when inhibitory control is low or poorly managed, individuals may be more likely to engage in substance use, especially in the presence of valenced cues.

If substance use is a self-regulatory failure due to low or poorly managed inhibitory control, it would be expected that substance users would show self-regulatory deficits in other life domains as well. In fact, many studies have demonstrated that substance users broadly evidence low self-regulatory capacity. For example, across a number of studies, substance users broadly (Bickel et al., 2012) and opioid users in particular (see Bickel & Marsch, 2001 for a review) have been shown to devalue delayed monetary rewards relative to controls. Similarly, heavy drinking undergraduate students devalue such rewards relative to light drinkers (Vuchinich & Simpson, 1998). Emerging adults who use substances attain lower grades, show less involvement in academic activities, and are at greater risk for discontinuous college enrollment (Arria et al., 2013; Mustane & Tewksbury, 2005; Roebuck, French, & Dennis, 2004; Singleton, 2007), suggesting poor academic-related self-regulation. In terms of health-related self-regulatory failures, undergraduate binge drinking is associated with unhealthy eating patterns and weight management behaviors, consumption of fast food, and desire to weigh less, even after adjusting for socioeconomic status (Nelson, Lust, Story, & Ehlinger, 2009). Overall, self-regulation is broadly impaired in substance users, suggesting that impaired inhibitory control both directly and indirectly (through the depletion of resources when self-regulation is exerted in other life domains) creates risk for substance use.

From a "coping as inhibition" perspective, inhibitory control plays a central role in the monitoring of threatening stimuli and management of arousal. Inhibition is used to maintain attention by suppressing distracting stimuli, and it is used to override, block, or modulate affective responses in order to regulate emotion (Muraven & Baumeister, 2000). For example, in a sample of clinically depressed individuals, individuals in remission, and healthy controls with no history of clinical depression, greater ability to inhibit negative material was shown to be related to increased use of adaptive emotion regulation strategies such as reflection and reappraisal, and decreased use of maladaptive strategies such as suppression (Joormann & Gotlib, 2010). In the context of the substance user then, it may be that poor inhibitory control impedes the implementation of effective emotion regulation strategies, and the individual must resort to other less adaptive coping modalities (i.e., substance use). In other words, to the extent that substance use is motivated by stress or depressed mood (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Khantzian, 1997, 1985; Rhodes & Jason, 1990; Wand, 2008; Wills & Filer, 1996), a breakdown in the management of attention and arousal and subsequent emotion dysregulation may explain why individuals with diminished inhibitory capacity may be at risk for engaging in substance use to alleviate negative affect.

The notion that individuals use substances to alleviate negative affect has been supported by studies across substance classes and severity level. Latent profiles based on coping and emotion regulation strategies predict adolescent and emerging adult prescription drug use and severity of problems (Wong et al., 2013). Negative mood regulation expectancies (i.e., the belief that one's action will alleviate negative affect) are associated with college student substance use and problems (Kassel, Jackson, & Unrod, 2000; Simons et al., 2005). Emotional differentiation, which is related to the management of negative emotional states and implementation of regulatory strategies, interacts with negative affect to predict alcohol outcomes among emerging adults (Kashdan, Ferssizidis, Collins, & Muraven, 2010). Further, affective lability (i.e., fluctuation in affective states) is associated with alcohol problems among college students (Simons & Carey, 2006). Fox and colleagues (2007, 2008) have found emotion regulation deficits in alcohol disordered individuals relative to social drinkers and in treatment-seeking adult cocaine users relative to healthy controls. Finally, improvements in emotion regulation are associated with reductions in substance use (Axelrod, Perepletchikova, Holtzman, & Sinha, 2011). From a "coping as inhibition" perspective then, the strong relationship between emotion dysregulation and substance use supports the role of deficient inhibition in substance use.

Types of inhibition. In the substance use literature, inhibition is usually distinguished as either behavioral inhibition, the stopping of a prepotent motor response (Nigg, 2000), or as cognitive inhibition, "the stopping or overriding of a mental process, in whole or in part, with or without intention" (MacLeod, 2007, p.5). Though the behavioral-cognitive inhibition distinction may be questionable from a psychometric standpoint (Friedman & Miyake, 2004) and coarse compared to other inhibition taxonomies (MacLeod, 2007; Nigg, 2000), research has shown that opioid users perform poorly on what have largely been considered prototypic measures of cognitive inhibition (i.e., the Stroop Test; Stroop, 1935), but do not show behaviorally-measurable deficits on prototypic measures of behavioral inhibition (e.g., Stop Signal and Go/No-go tasks; Ersche, 2011; Ersche & Sahakian, 2007). Thus, the focus here is on cognitive disinhibition.

Interference control. In opioid users, cognitive disinhibition has almost exclusively been studied in terms of interference control (Ersche & Sahakian, 2007), defined as the suppression of competing or irrelevant stimuli in order to perform a primary response (MacLeod, 2007; Nigg, 2000) and measured by the Stroop Test. In the Stoop Test, a series of single word stimuli are presented, including words that are color names. The challenge then is to identify the color of the text that the word is presented in, ignoring the word's semantic content. Research suggests that both primarily heroin-using (Fishbein et al., 2007) as well as polysubstance-using (Verdejo-Garcia et al., 2007) heroin-dependent individuals evidence difficulty completing this task relative to controls. Additionally, methadone-maintained patients (Mintzer & Stitzer, 2002; Prosser et al.,

2006) and former methadone-treated patients within a period of protracted abstinence (Prosser et al., 2006) show deficits in interference control relative to healthy controls.

Emerging adult substance use research has also examined interference control deficits. Randall and colleagues (2004) found that female university students who drank moderately evidenced lower interference control on a modified version of the Stroop Test than low drinking females. Gruber and colleagues (2011) found that among emerging and young adults, Stroop task performance was impaired among early onset marijuana smokers relative to non-user controls. Cousijn and colleagues (2013) did not find interference control differences between emerging adult heavy marijuana users and controls that had not used in the past month, nor did they find differences between marijuana disordered and marijuana non-disordered emerging adults. Nevertheless, some research suggests a pattern similar to that found in marijuana users during working memory tasks, such that atypical brain activation may occur among marijuana users when completing the Stroop task, even in the absence of behaviorally measurable deficits (Solowij & Pesa, 2011).

Cognitive flexibility. Cognitive flexibility refers to the ability to select, implement, and switch between task sets or actions in response to stimuli (Eslinger & Grattan, 1993), and it has been proposed to be central to resisting temptations and achieving ones' goals (Monsell, 2003).[2] Because resisting the urge to use drugs would seem to necessitate this ability to shift from one avenue of thought or action (substance

[2]Although Monsell (2003) mentions the Stroop Test as a measure of shifting, this notion has not been supported elsewhere in the literature; that is, in Miyake and colleagues (2000) confirmatory factor analysis of executive function, Stroop Test scores distinctly loaded onto a factor of inhibition, and not cognitive flexibility (or working memory). Stroop Test scores were significantly correlated with scores on other inhibition tasks (i.e., Antisaccade, Stop-Signal), but not with scores on cognitive flexibility tasks, including the WCST.

use) to another (aversive affects such as hangovers or alternatives such as studying or exercising), it might be assumed that cognitive flexibility is impaired in substance users. However, there is little evidence to suggest that this ability is impaired in primarily opioid users (Davis, Liddiard, & McMillan, 2002; Ersche, 2011; Ersche & Sahakian, 2007). Evidence of cognitive flexibility deficits among emerging adult substance users is limited and inconsistent (Ehrenreich et al., 1999; Gruber, Sagar, Dahlgren, Racine, & Lukas, 2011), and it does not appear that emerging adult drinkers are prone to these impairments (Parada et al., 2012; Randall, Elsabagh, Hartley, & File, 2004).

There are also methodological limitations to measuring cognitive flexibility. Although the Wisconsin Card Sort Task (WCST; Berg, 1948), in which cards are sorted according to an unknown and changing rule, is typically used as a measure of one's ability to shift between sets (Ersche, 20011; Nyhus & Barceló, 2009), an examination and comparison of the psychometric properties of the WCST in adult substance users and undergraduate students revealed significant measurement error and unsatisfactory alternate-form reliability of the WCST (Bowden et al., 1998). These findings led the authors to caution against the task's use among clinical populations in its current form. Elsewhere, the validity of the WCST as a measure of prefrontal executive functioning has been seriously undermined (Nyhus & Barceló, 2009). Therefore, due to the dearth of literature suggesting cognitive flexibility deficits in opioid users, and in light of the measurement limitations of this construct, cognitive flexibility was not measured in the current proposal.

Research limitations. One major limitation of the current ECF and substance use literature is that research on opioid use and ECF has relied on mostly adult heroin and methadone-dependent or methadone-maintained samples. Given the possibility that ECF deficits may predispose individuals to engaging in substance use, it would be useful to extend the findings on ECF, heroin and methadone use to other NMPO use, especially in emerging adults without a history of chronic misuse, in order to determine whether working memory and interference control deficits are causal mechanisms underlying initiation of use, as well as whether they may be targetable risk factors for future NMPO prevention and early intervention efforts. Additionally, it may be particularly important to understand associations between other commonly used opioids and ECF as some research suggests that, despite the pharmacologically similar mechanisms of action and similar subjective effects of heroin and other NMPOs (National Institute on Drug Abuse [NIDA], 2011, 2013), the deficits associated with different classes of opioids may not be uniform (Davis & Templer, 1988; Ersche & Sahakian, 2007; Rapeli, Fabritius, Kalska, & Alho, 2011). Given this relatively underdeveloped domain of research, an important first step is to determine whether ECF deficits are correlates of NMPO use in vulnerable populations (e.g., OxyContin and Vicodin use among emerging adults; Johnston, O'Malley, Bachman, & Schulenberg, 2013).

Present Research

The goal of the present study was to examine the relations between NMPO use and ECF and regulatory deficits in an emerging adult population. Specifically, 18–25 year old NMPO users and age- and gender-matched controls were compared on a battery of ECF and self- and emotion regulation measures. Due to the prominence of other substance use among emerging adults and NMPO users, deficits associated with alcohol and marijuana were also explored. A secondary aim was to assess two downstream consequences of diminished ECF, poor self-regulation and emotion dysregulation. Associations between working memory deficits, interference control deficits, impaired self-regulation, and emotion dysregulation were examined. The hypotheses were as follows: (a) NMPO-users would show deficits across the four domains of investigation relative to nonuser controls, (b) NMPO, alcohol, and marijuana use would be associated with deficits, and (c) all four ECF domains would be significantly associated with one another and with regulatory ability.

Method

Participants

Participants were 54 undergraduate students from the University of Memphis (*n* = 27 per group), ages 18-25, recruited as part of a larger study on college student NMPO use. Participants were recruited using the University of Memphis Sona System (an online psychology research sign-up system), through in-class screenings, and by flyers posted on the university's campus. Eligibility criteria for each group was as follows: *Nonmedical prescription opioid users*: nonmedical use of prescription opioids one or more times in the past year; *Non-user control:* no past year drug use, consumption of alcohol on one or less days in a typical week in the past 30 days, and one or less past month binge episodes. Exclusion criteria for all groups included reported history of bipolar disorder diagnosis, reported history of psychotic symptoms or psychotic disorder, reported history of a significant head injury (e.g., that included loss of consciousness or a concussion diagnosis with lasting effects), and current, medically-appropriate routine use of psychiatric medication other than antidepressants. Because participants were asked to abstain from using substances on the day of their study appointment, individuals who were maintained on methadone or who received another opioid replacement therapy and individuals who reported current (past month) alcohol or opioid withdrawal symptoms were also excluded from the study. To further diminish the likelihood of recruiting individuals with past month withdrawal symptoms, those who reported use of opioids on 25 days or more out of the past 30, and those who report daily binge episodes, were excluded. Eligible participants were matched on age and gender.

Measures

All self-report measures are included in Appendices A – C.

Substance use. Past-month alcohol use was assessed using a self-report, computerized version of the Daily Drinking Questionnaire (DDQ; Collins, Parks, & Marlatt, 1985). This measure provides an estimate of typical drinks per week in the past month. The DDQ has been widely used with college students and is highly correlated with self-monitoring and other self-report measures of drinking (Kivlahan et al., 1990). Participants also reported their number of binge episodes in the past month.

Past-month and past-year substance use, age of initiation of NMPO use, and *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM–5*; American Psychiatric Association, 2013) substance use disorder (SUD) and alcohol use disorder (AUD) symptoms were assessed as part of a longer clinical interview. Specifically, participants reported on days of use of marijuana, cocaine, designer drugs, hallucinogens, methamphetamine, and synthetic drugs (e.g., K2, spice), as well as on days of nonmedical prescription opioid, anxiolytic, stimulant, and sleep medication use in the past month and past year. To assess *DSM–5* SUD and AUD symptoms, questions were drawn from the Structured Clinical Interview for DSM-IV Axis I Disorders substance use modules and were adapted to fit the updated criteria for *DSM–5*.

Clinical interviews were conducted by trained graduate-level clinical psychology students. Self-reported substance use by college students is generally accurate (Hagman, Clifford, Noel, Davis, & Cramond, 2007), and accuracy is improved when, as in the current proposal, participants are assured of confidentiality and no negative consequences, and when intoxication has been ruled out objectively (Tucker, Vuchinich, & Murphy, 2002).

Working memory. Working memory (WM) was assessed using a computerized auditory digit span task (DS) from the PEBL battery. Participants first heard a series of three single digits were asked to type the series as it was spoken. After two successive series of digits (one "trial"), the number of digits presented increased by one. The task ended when two consecutive series were misidentified or after 10 trials were completed. Participants were then asked to repeat the task; however, this time, they were asked to type the series of digits in the reversed order. Stimuli were presented 1000 ms apart, with 1500 ms inter-trial intervals. DS is a reliable estimate of WM (Blackburn & Benton, 1957), and the forward and backward recall tasks are functionally identical to the sequenced recall (and sequenced recall reversed) of digits-auditory training elements used by Bickel and colleagues (2011) that resulted in decreased devaluation of delayed rewards post-training in a sample of stimulant users. Recall tasks of this nature are significantly correlated with each other as well as with other measures of WM (St Clair-Thompson & Gathercole, 2006).

Cognitive disinhibition. Cognitive disinhibition was assessed using the Color–Word Stroop Test (Stroop, 1935) from the PEBL battery. As mentioned earlier, in the Stroop Test, participants are presented with a single color word or non-color word, one at a time, and are asked to identify the color of the text that each word appears in. Stimuli are either congruent (the color word and the text color are the same; e.g., "green" in green text), incongruent (the color word and the text color are different; e.g., "blue" in green text), or control stimuli (a non-color word; e.g., "and" in green text). Participants were instructed to respond using keys 1 through 4 on the keyboard, corresponding to red, blue, green, and yellow. They were allowed time to acclimate to the keyboard and corresponding colors and were then presented with instructions to determine the color that written words appear in. Following a set of practice trials which included all three types of stimuli, participants were presented with 168 non-blocked stimuli (56 congruent, 56 incongruent, and 56 control). A short break was allowed midway through the test trials. During both practice and test trials, participants were reminded on screen to respond as quickly and accurately as possible. If a participant did not respond to a given stimulus within 2000 ms, the words "too slow" were presented on the screen and subsequently the next stimulus was presented. Performance on the Stroop Test was quantified as (a) the difference in reaction times (RT) between incongruent and control trials (interference score; IS) and (b) mean response time across incongruent trials. The Stroop Test is a widely used measure of cognitive inhibitory control and in a confirmatory factor analysis of ECF conducted by Miyake and colleagues (2000), the Stroop Test was shown to load on the same factor as other prototypic measures of inhibitory control (see also, St Clair-Thompson & Gathercole, 2006). Prior studies indicate acceptable test–retest reliability of the Stroop Test (Siegrist, 1997; Strauss, Allen, Jorgensen, & Cramer, 2005; Wöstmann et al., 2013). As mentioned earlier, behaviorally measurable deficits on the Stroop Test are commonly found among adult opioid users (Fishbein et al., 2007; Mintzer & Stitzer, 2002; Prosser et al., 2006; Verdejo-Garcia et al., 2007) and emerging adult substance users (Gruber et al., 2011; Randall et al., 2004).

Self-regulation. The Self-Regulation Questionnaire – Short (SSRQ; Carey, Neal, & Collins, 2004) is a 31-item measure of one's ability to engage in goal-directed behavior and to withstand immediate temptation in service of achieving temporally distal but desired outcomes. Participants are asked to indicate how well each item describes them, with response options ranging from 1 (*strongly disagree*) to 5 (*strongly agree*). Items are summed to compute a single total score. Items include "I usually keep track of my progress toward my goals" and "I usually think before I act." The SSRQ is highly positively correlated with its longer parent measure (Carey et al., 2004). It is positively correlated with future time perspective and it is negatively correlated with present-hedonistic time perspective (Carey et al., 2007) and substance-related self-regulatory failures (Carey et al., 2004) among emerging adults. Additionally, in a study of undergraduate student binge drinkers, self-regulation as measured by the SSRQ predicted reductions in drinks per drinking day and in peak BAC and interacted with treatment condition to predict reductions in drinks per week, 1-month post intervention (Carey et al., 2007). The internal consistency of the SSRQ in this sample was excellent ($\alpha = .81$).

Emotion dysregulation. The Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004) is a 36-item multidimensional self-report assessment of deficits in the following domains: awareness, understanding, and acceptance of one's emotions; engagement in goal-directed activity and impulse control in the context of negative emotions; and access to strategies perceived as instrumental to regulating one's emotions. Participants are asked to indicate how often frequently each item describes them, with response options ranging from of 1 (*almost never*) to 5 (*almost always*). The DERS yields a total score as well as scores on six subscales: nonacceptance of emotional responses; difficulties engaging in goal-directed behavior; impulse control difficulties; lack of emotional awareness; limited access to emotion regulation strategies; and lack of emotional clarity. Higher DERS scores (indicating greater emotion dysregulation) have been found among various clinical populations with disorders characterized by emotion dysregulation (Fox, Axelrod, Paliwal, Sleeper, & Sinha, 2007; Neumann, van Lier, Gratz, & Koot, 2010; Williams, Grisham, Erskine, & Cassedy, 2012). The internal consistency of the DERS in this sample was excellent (α = .93), and the internal consistency of the DERS subscales in this study ranged from good to excellent (αs = .81 - .92).

Procedure

Students who met inclusion criteria as per the screener completed by all students using the University of Memphis Sona System, or those who meet inclusion criteria as indicated on those screeners distributed in class, were contacted to further determine eligibility status. Other interested university students were instructed via flyers to contact the lab by phone or email and similarly contacted to determine eligibility status. Determination of eligibility status included a short questionnaire regarding inclusion and exclusion criteria. Eligible and interested individuals were scheduled for an appointment and were asked to abstain from using substances on the day of their study appointment.

Upon arrival for the appointment, participants were provided with a written consent form and were verbally informed of the study's purpose, risks, benefits, compensation, and all other pertinent study details prior to beginning the assessment battery. Participants were breathalyzed prior to starting the assessment battery to rule out acute alcohol intoxication at the time of their appointment. (Participants were informed of this procedure during the recruitment phone call and were reminded during the consent process.) No participant evidenced a blood alcohol content above zero. The measures included in the present study took approximately 20 min to complete, and the entire session lasted approximately 1.5 hours. All measures were completed in private rooms on lab computers. ECF tasks were administered first, using the Psychology Experiment Building Language (PEBL) test battery (version 0.8; http://pebl.sourceforge.net), a resource which provides free computer-administered tests available for download online. Administration of the ECF tasks was counterbalanced. Self-report measures were administered subsequently, followed by a brief clinical assessment. Upon completion, students were awarded 2 hours of credit for participation or a payment of $20 for participation.

Analytic Plan

Power

For the present study, a power analysis based on earlier literature in this domain was challenging due to the wide range of ECF deficits that can be measured, the heterogeneity in tasks and versions of these tasks that can be administered to measure any specific deficit, and the multiple outcome measures any one task can yield. Acknowledging these challenges, the present power analysis was based on the effect sizes obtained by Fishbein and colleagues (2007). In examining working memory and interference control among primarily heroin users and demographically-matched controls, Fishbein and colleagues found small (Cohen's $d = 0.26$) to medium ($d = 0.65$) effect sizes across multiple outcome measures (M_{ES}=.39). Therefore the present power analysis was based on an estimated effect size of .39 for all contrasts between NMPO users and controls. Ideally, this study would have had an *n* of 63 per group for a power of .70 (one-tailed $\alpha = .05$). Acknowledging that with an *n* of only 27 per group this study may have been underpowered to detect small ($d = 0.20$) to medium ($d = 0.50$) effects, it should be noted that the findings of the present study will provide effect size estimates that can be used to design future, more adequately-powered studies.

Data Analysis

All data analysis was performed using SPSS v.19.0 (IBM Corp., Armonk, NY, USA). Prior to analyses, data was checked for outliers, skewness, and kurtosis. Three participants' data from the ECF tasks were omitted from the ECF analyses due to a computer malfunction during the administration of these tasks. Stroop Test trials in which participants failed to respond within 2000ms or responded incorrectly were also excluded from analyses. Nonparametric tests (i.e., Spearman's rho correlation coefficients) were used to evaluate the magnitude and direction of the relations between ECF, regulatory, and substance use measures due to observation of a large number of outliers and non-normal distributions. However, to satisfy statistical assumptions appropriate to the NMPO user and matched control group analyses (i.e., independent samples *t*-tests for measures of self- and emotion regulation and mixed model ANOVAs for ECF measures), outliers were corrected for DS backward and the DERS impulse subscale, and the DERS nonacceptance, impulse, and clarity subscales and IS were log-transformed prior to those tests, as per the recommendations outlined by Tabachnick and Fidell (2012). Preliminary analyses revealed no statistically significant group differences on gender, age, ethnicity or WRAT score. There was also no significant group difference on number of Stroop Test errors made; thus these variables were not included as covariates in the group analyses.

Results

Descriptive Statistics

Descriptive statistics for demographic information and dependent measures are presented in Table 1, and descriptive statistics for substance use variables are presented in Table 2. Past-month NMPO use was endorsed by 63.0% of the NMPO-using group, but this use was infrequent (*Mdn* = 1.00, *IQR* = 0.00 – 2.00). Annual days of NMPO use were higher (*Mdn* = 15.00, *IQR* = 3.00 – 40.00), but endorsement of opioid SUD symptoms was low (*Mdn* = 1.00, *IQR* = 0.00 – 2.50). Age of initiation of NMPO use was typically 17 years (*Mdn* = 17.00, *IQR* = 16.00 – 18.00). Among this group, drinking was common (typical drinks per week: *Mdn* = 6.00, *IQR* = 3.00 – 12.50). Binge drinking was endorsed by 63.0% of users but was relatively infrequent (past-month binge episodes: *Mdn* = 2.00, *IQR* = 0.00 – 4.75), and endorsement of AUD symptoms was low as well (*Mdn* = 1.50, *IQR* = 1.00 – 3.75). Age of initiation of alcohol use was typically 16 years (*Mdn* = 16.00, *IQR* = 14.00 – 17.00).

Other past-month drug use was common among NMPO users. Marijuana use was most prevalent, with 77.8% of NMPO users reporting past-month use. Additionally, 37.0% used prescription sedatives, 25.9% used prescription stimulants, 14.8% used cocaine, 11.1 % used hallucinogens, and 7.4% used designer drugs in the past month. No NMPO users reported past-month heroin, methamphetamine, or prescription sleep drug use. Age of drug use initiation (NMPO or other) was typically 16 years (*Mdn* = 16.00, *IQR* = 16.00 – 18.00), and 74.1% of the sample reported marijuana as the first drug they used.

Group Differences on ECF and Measures of Self- and Emotion Regulation

A series of mixed-model ANOVAs, with group as the between subjects factor and order as the within subjects factor, were conducted to compare NMPO users and controls on the ECF tasks. These analyses revealed no main effect of group, order, or group by order interaction on DS forward, DS backward, incongruent RT, or IS. However, independent samples *t*-tests revealed that NMPO users reported inferior regulatory control on the SSRQ total score (t [52] = 4.16, $p < .001$; M_{users} = 113.70, SD_{users} = 10.53; $M_{controls}$ = 128.30, $SD_{controls}$ = 14.87), DERS total score (t [52] = -2.50, $p = .016$; M_{users} = 78.78, SD_{users} = 17.38; $M_{controls}$ = 65.96, $SD_{controls}$ = 20.24), and DERS clarity subscale (t [52] = -3.90, $p < .001$; M_{users} = 13.11, SD_{users} = 4.89; $M_{controls}$ = 8.93, $SD_{controls}$ = 3.17). Group differences on the DERS impulse subscale approached significance in the same direction (t [52] = -1.92, $p = .060$; M_{users} 12.22, SD_{users} 5.47; $M_{controls}$ = 9.78, $SD_{controls}$ = 4.02). Significant and nonsignificant trend-level group differences are depicted in Figures 2, 3, 4, and 5.

Associations among NMPO, Alcohol, and Marijuana Use Variables among NMPO Users

Greater past-month NMPO use was moderately associated with younger age of NMPO use initiation ($r_{s\,=}$ -.397, $p = .041$) and greater past-year marijuana use ($r_{s\,=}$ .454, *p*

= .017), and greater past-year NMPO use was moderately associated with younger age of (any) drug use initiation (r_s = -.430, p = .025) and more opioid SUD symptoms (r_s = .662, p < .001). Opioid SUD symptoms also evidenced a non-significant trend level association with age of drug use initiation in the expected direction (r_s = -.345, p = .091). Younger age of NMPO use initiation evidenced a moderate association with past-year marijuana use (r_s = -.442, p = .021) and a moderate nonsignificant trend-level association with past-month marijuana use (r_s = -.331, p = .092).

Associations among ECF and Self- and Emotion Regulation among the Full Sample

Significant correlations in the expected directions were observed for several of the performance scores on the ECF tasks. These correlations are presented in table 3. DS forward evidenced moderate associations with DS backward (p = .025) and incongruent RT (p = .017), and incongruent RT evidenced a large association with IS (p < .001). ECF was also associated with outcomes on the self-report measures of regulatory function; greater emotion dysregulation on the DERS goals subscale evidenced a small association with poorer performance on the DS backward (p = .045) and a moderate association with slower incongruent RT on the Stroop Test (p = .013). The association between DERS goals and IS also approached significance in the expected direction (p = .057). Greater dysregulation on the DERS impulse scale evidenced a moderate association with slower incongruent RTs (p = .018). A small non-significant trend-level association was observed among the DERS strategy subscale and IS in the expected direction (p = .053). Correlations between the SSRQ total score and DERS total score and subscale scores were in the expected direction and moderate in magnitude (p's ≤ .013) with two exceptions; SSRQ total score evidenced a small association with the

DERS nonacceptance subscale (*p* = .031) and a small non-significant trend level association with the DERS goals subscale (*p* = .054).

Associations among ECF and Self- and Emotion Regulation and Substance Use Variables among NMPO Users

Significant correlations in the expected directions were also observed for several of the substance use variables and ECF and self- and emotion regulation. These correlations are presented in tables 4 and 5. A moderate non-significant trend-level association was observed for past-month NMPO use and IS, such that with greater NMPO use, interference control was poorer (*p* = .083). A moderate non-significant trend-level association was also observed in the expected direction for opioid SUD symptoms and the DERS impulse subscale (*p* = .089). AUD symptoms evidenced a non-significant trend-level association with DS backwards, such that greater severity was related to poorer working memory (*p* = .086). Unexpectedly, typical drinks per week was *negatively* correlated with IS (*p* = .031). ECF was not significantly related to marijuana use or severity, but higher scores on the DERS awareness subscale were moderately associated with greater past-year marijuana use as expected (*p* = .045). Surprisingly, greater past-year marijuana use was moderately associated with *lower* scores on the DERS goals subscale (i.e., poorer ability to engage in goal-directed behavior when upset; *p* = .037).

Discussion

Overall Findings and Group Differences

The present study examined the association between ECF and self- and emotion regulation deficits and NMPO use in emerging adults. NMPO users in this sample used an average of 15 times in the past year and endorsed regular alcohol use and substantial marijuana use; in fact, frequency and severity of marijuana use well exceeded that of NMPO use despite selection criteria based on NMPO use. As indicated by their SSRQ and DERS scores, NMPO users reported poorer self-regulation ability and greater emotion dysregulation compared with gender- and age-matched controls. Further, DERS subscale elevations indicated that NMPO users have deficits in engaging in goal-directed activity and controlling impulses in the face of distress relative to their non-using peers. The findings of relative regulatory deficits among NMPO users is consistent with a large literature supporting the relation between substance use and impaired self-regulation (Baumeister et al., 2007; Bickel et al., 2012; Bickel & Marsch, 2001; Muraven et al., 2000; Vuchinich & Simpson, 1998) and emotion dysregulation (Fox et al., 2007, 2008; Kassel et al., 2000; Simons et al., 2005; Simons & Carey, 2006; Wong et al., 2013), and they extend this literature to emerging adult NMPO users, an important but understudied group.

NMPO users and matched controls did not differ on two measures of ECF, the auditory digit span task, which measures working memory, and the Color-Word Stroop Test, which measures interference control, a widely-studied type of cognitive inhibitory control. These results were surprising given that adult opioid users typically perform poorly relative to controls on working memory tasks (Darke, Sims, McDonald, & Wickes, 2000; Fishbein et al., 2007; Ornstein et al., 2000) and show "profound impairment" (Ersche & Sahakian, 2007, p. 322) on the Stroop Test irrespective of the type of opioid abused. In considering the lack of these hypothesized finings, it is important to note that the study was underpowered. Other potential explanations include the possibility that the behavioral tasks administered were not sensitive enough to detect relative deficits, or that ECF deficits exist in different domains (e.g., behavioral inhibition, visuospatial working memory) that were not assessed by the auditory digit span and Stroop Test. Potentially, ECF is impaired in NMPO users, but deficits are hard or impossible to detect at the behavioral level and may only be seen at the level of fMRI (i.e., at a neural level of analysis). Indeed, authors elsewhere have reported differences in the neural activity of marijuana users during ECF tasks, even in the absence of behavioral deficits (Smith et al., 2010; Solowij & Pesa, 2011). Alternatively, NMPO use may not be associated with ECF deficits at all; however this explanation represents a significant departure from the extensive literature reviewed earlier. It may be the case that ECF deficits are not predisposing risk factors for NMPO use in emerging adulthood, but rather they are consequences of long-term, heavy use. If ECF deficits are more consequence than cause, then the lack of deficits observed here may be because this sample did not consist of severe or experienced enough users. A final possibility is that ECF deficits do have an etiological role in NMPO use but are more relevant in differentiating nonusers or infrequent users from severe users. In this study, NMPO users were assessed early in their use trajectories (NMPO users were 20 years old on average and typically reported initiating NMPO use at age 17) and endorsed use at fairly low levels; thus this group may have consisted of individuals whose long-term outcomes will ultimately vary greatly in terms of severity. Nonetheless, without longitudinal data available, it is impossible to determine their future severity levels, or to know how heterogeneous or homogenous the NMPO group was. Future, longitudinal studies will be crucial to elucidating these possibilities.

Associations among ECF and Self- and Emotion Regulation and Substance Use Variables

Although ECF deficits did not differentiate NMPO users from matched controls, among NMPO users, the association between NMPO use and IS approached significance. Specifically, individuals with higher levels of past-month NMPO use showed poorer interference control on the Stroop Test. These results are consistent with research indicating deficits of this nature in heroin users (Fishbein et al., 2007) and methadone maintenance patients (Mintzer & Stitzer, 2002; Prosser et al., 2006), and they suggest that even among relatively low frequency-low severity opioid users, impaired interference control is associated with greater NMPO use. The association between AUD symptoms and performance on the backwards portion of the digit span also approached significance, indicating a relationship between greater alcohol use severity and poorer working memory. Parada and colleagues (2012) observed similar impairment on the backward digit span among young adult binge drinkers relative to nonbinge drinkers; however it is notable that severity of alcohol use was much greater among the binge drinkers in that study compared to the substance users in the present one.

Substance use was associated with emotion dysregulation in this study as well. For instance, the association between greater *DSM*–5 opioid SUD symptoms and greater difficulty controlling impulses in the face of distress approached significance. Similarly, this subscale has been shown to differentiate more severe drinkers (alcohol-dependent) from social drinkers (Fox et al., 2008). Another finding was that greater past-month marijuana use was significantly associated with greater difficulty engaging in goal-directed activity when distressed; thus NMPO users who engage in comorbid use of marijuana, especially at a high frequency, may represent a subgroup at elevated risk.

Alcohol use was not associated with ECF. The lack of a relation between alcohol variables and ECF may be due to low rates of binge drinking in this sample; the most robust relations between alcohol use and ECF are related to drinking patterns characterized by binge and withdrawal cycles (Stephens & Duka, 2006), and in this sample, the average number of past-month binge episodes was only (approximately) three. Alcohol use was also not associated with regulatory deficits. A large literature suggests that emerging adult alcohol use (quantity and frequency of drinking) is heavily influenced by demographic and social-contextual variables such as gender, ethnicity, and peer influence (Borsari & Carey, 2001; Borsari, Murphy, & Barnett, 2007). Greater severity of use (alcohol problems) is associated with impulsivity, affect lability, low mood and stress (Ham & Hope, 2003); thus it was expected in this study that *DSM* 5–AUD symptoms would be related to regulatory deficits. However, symptom rates were fairly low (approximately two symptoms were endorsed on average), and restricted variability may have undermined this author's ability to detect an association. Similarly, marijuana use was not associated with ECF. The lack of a relationship between marijuana use and ECF is consistent with a number of other studies of emerging adults that suggest that ECF deficits are not observable at a behavioral level of analysis (Cousijn et al., 2013; Ehrenreich et al., 1999; Smith et al., 2010). Instead, as mentioned earlier, differences are often observed at the neural level when measured with fMRI (Smith et al., 2010; Solowij & Pesa, 2011).

Associations among ECF and Self- and Emotion Regulation among the Full Sample

A number of significant associations were found for the ECF and self- and emotion regulation measures in the full sample. Moderate associations were observed for outcome scores on the digit span and Stroop Test, and these findings provide support for the unity and diversity of executive cognitive functions consistent with the latent structure proposed by Miyake and colleagues (2000). Moderate associations were also found for the SSRQ and the DERS and the majority of its subscales; better ability to self-regulate one's behavior and resist temptation was associated with better emotion regulation as expected. However, self-reported self-regulatory ability was not associated with performance any of the ECF measures. Although it is unusual that ECF would not demonstrate associations with self-regulatory ability, one possibility is that contextual factors (e.g., deprivation or distress) may moderate this relationship, and because the SSRQ assesses overarching rather than context-specific self-regulation, associations were not detected. That impulse control and engagement in goal-directed behavior *when upset* were associated with ECF may provide support for this hypothesis.

Greater difficulty engaging in goal-directed behavior in the face of distress was associated with poorer performance on the backward digit span and slower incongruent reaction times on the Stroop Test. A similar pattern was observed for goal-directed behavior and interference score and approached significance. These results suggest that ECF is implicated particularly in the ability to regulate goal-directed activities when upset, and that several different facets of ECF are employed in service of this type of emotion regulation. The ability to control one's impulses during periods of poor affect demonstrated relations uniquely with interference control, as deficits of this type of emotion regulation were associated with slower incongruent reaction times on the Stroop Test but not with measures of working memory. Interestingly, the goals and impulsivity subscales of the DERS are the only two that concern behavior subsequent to emotional experiences rather than reactions to one's emotional experiences (Gratz & Roemer, 2004). These findings suggest that interference control may be particularly relevant to regulating behavior when distressed rather than making appraisals of emotion. Differentiating the goals and impulsivity subscales is the unique relationship between goals and working memory; intact working memory may then be crucial to the ability to shift to and initiate purposeful action after disengaging from an emotional experience.

Limitations

Several limitations of this study should be noted. As mentioned earlier, the small sample size of this study may have prevented the detection of significant associations. Although studies with severe opioid users suggest moderate magnitude ECF deficits, any deficits in low frequency-low severity or early-trajectory users may be small and require large samples to detect. Future research is needed to replicate these findings in larger samples of low severity users. The extension of this work to other, larger samples with low severity of use is particularly important given that much of the research on ECF is conducted among severe users, likely due to the fact that they more readily present for treatment (e.g., at methadone maintenance clinics). Given preliminary findings that even low-severity users evidence deficits, it is important that this population does not remain overlooked. A second limitation of our sample was the considerable amount of polysubstance use among NMPO users. The use of multiple substances makes it difficult to draw clear conclusions about the uniqueness of these deficits to NMPO use in particular rather than to substance use more broadly. However, it is notable that the overwhelming majority of NMPO users (and even light users) use alcohol, marijuana, and other drugs in addition to opioids (Catalano et al., 2011); thus recruiting a group of individuals who used no substances other than opioids would likely have significantly limited the generalizability of the results of this study and would inaccurately reflect the reality of the majority of NMPO users. Another limitation is the use of self-report measures of self-regulation and emotion dysregulation. Although self-report is commonly used to assess these constructs, especially emotion dysregulation, real-time psychological assessment approaches such as experience sampling methods (ESM) or ecological momentary assessment (EMA) might provide nuanced insights into the relations between regulatory failures and substance use (e.g., Gottfredson & Hussong, 2013). Another methodological limitation is the limited assessment of ECF. Only two domains of ECF were assessed, working memory and cognitive inhibition (particularly, interference control). Further, these domains were assessed by only two tasks, the auditory digit span and the Color-Word Stroop Test. Future research might extend the present findings by utilizing a more extensive battery. The use of other measures might also illuminate whether other ECF domains are related to specific emotion regulation difficulties beyond the relations identified here. Finally, the present study was cross-sectional; thus cause, consequence, and mere association of ECF, regulatory deficits, and substance use cannot be disentangled. Some studies have found ECF deficits to precede substance use (Giancola & Tarter, 1999), others find that ECF deficits result from substance use (Stephens & Duka, 2008), and still others suggest that some deficits may be due to withdrawal or overdose history rather than substance use itself (Ersche &

Sahakian, 2007). Prospective studies are needed to clarify the nature of the relationship among NMPO users.

Conclusion

Despite these limitations, the results of the present study provide preliminary support for the association between NMPO use and ECF and regulatory deficits among emerging adults. Specifically, self- and emotion regulation appear to be diminished in NMPO users relative to healthy controls. Among NMPO users, interference control deficits appear to vary with frequency of NMPO use, whereas working memory capacity appears to vary with alcohol use severity, and emotion dysregulation is associated with NMPO use severity and marijuana use. Across substance users and controls, difficulties in the ability to regulate behavior in the face of distress was found to be associated with interference control deficits, whereas responding to one's emotional responses was independent of ECF. Additionally, engaging in goal-directed behavior when upset appears to entail working memory, whereas impulse control when upset does not. These findings represent an initial step toward identifying targets for future NMPO prevention and early intervention efforts. Future research should attempt to further illuminate the role of these deficits in nonmedical prescription opioid use in emerging adult populations.

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Appendix A

Table 1

Means, Standard Deviations, and Percentages on Demographic and Dependent Measures

	Full Sample	NMPO Users	Controls
Gender (% Female)	57.4	59.3	55.6
Age	20.00 (1.60)	20.04 (1.61)	19.96 (1.62)
Ethnicity (% Caucasian)	48.1	51.9	44.4
DS forward	6.92 (1.32)	7.22 (1.28)	6.64 (1.32)
DS backward	5.73 (1.44)	5.83 (1.30)	5.64 (1.58)
Incongruent RT	857.65 (161.45)	841.68 (159.91)	872.97 (164.70)
IS	80.19 (63.46)	82.68 (67.25)	77.90 (61.10)
SSRQ total*	121.00 (14.73)	113.70 (10.53)	128.30 (14.87)
DERS total**	72.37 (19.77)	78.78 (17.38)	65.96 (20.24)

Note. Due to partial missing, *N*'s vary; $N_{\text{full sample}} = 48 – 54$; $N_{\text{NMPO users}} = 23 – 27$; $N_{\text{controls}} = 25-27$. NMPO = nonmedical prescription opioid. DS = digit span. RT = reaction time. IS = Interference Score. SSRQ = Self-Regulation Questionnaire – Short; higher scores reflect greater self-regulation. DERS = Difficulties in Emotion Regulation Scale; higher scores reflect greater difficulties with emotion regulation.

* Denotes significant group difference, $p < .01$

** Denotes significant group difference, $p < .001$

Table 2

Descriptive Statistics for Substance Use Variables for NMPO Users

	Mdn (*IQR*)
Past-month NMPO use	1.00 (.00 – 2.00)
Past-year NMPO use	15.00 (3.00 – 40.00)
DSM–5 SUD symptoms – opioid	1.00 (.00 – 2.50)
Age of NMPO use initiation	17.00 (16.00 – 18.00)
Typical drinks per week	6.00 (3.00 – 12.50)
Past-month binge episodes	2.00 (0.00 – 4.75)
DSM–5 AUD symptoms	1.50 (1.00 – 3.75)
Age of alcohol use initiation	16.00 (14.00 – 17.00)
Past-month marijuana use	4.00 (1.00 – 20.00)
Past-year marijuana use	100.00 (9.00 – 230.00)
DSM–5 SUD symptoms – cannabis	3.50 (1.00 – 6.00)
Age of drug use initiation	16.00 (16.00 – 18.00)

Note. *DSM–5* SUD symptoms – cannabis were only assessed among past year marijuana users. NMPO = nonmedical prescription opioid. SUD = substance use disorder. AUD = alcohol use disorder. Due to partial missing data, *N*'s vary; *N* = 18 – 27.

Table 3

Associations among ECF and Self-and Emotion Regulation among Full Sample

Variable	1	2	3	4	5	6
1. DS – forward	--					
2. DS – backward	.324*	--				
3. Incongruent RT	-.342*	-.123	--			
4. IS	-.188	.128	.513	--		
5. SSRQ total score	.214	.238	-.181	-.189	--	
6. DERS total score	-.125	.030	.195	.226	-.494**	--

Note. N = 48 – 54. Spearman's rho correlation coefficients are presented. DS = Digit Span. RT = reaction time. IS = Interference Score. SSRQ = Self-Regulation Questionnaire – Short; higher scores reflect greater self-regulation. DERS = Difficulties in Emotion Regulation Scale; higher scores reflect greater difficulties with emotion regulation.

* $p < .05$. ** $p < .001$.

Table 4

Associations among ECF Measures and Substance Use Variables among NMPO Users

	DS – forward	DS – backward	Incongruent RT	Interference score
Past-month NMPO use	.079	.051	-.091	.369†
Past-year NMPO use	.033	.092	.049	.344
DSM–5 SUD symptoms – opioid	.167	-.117	.004	.100
Typical drinks per week	.083	-.140	-.163	-.451*
DSM–5 AUD symptoms	.064	-.394†	.085	.157
Past-month marijuana use	.111	-.057	-.168	-.046
Past-year marijuana use	.204	-.102	-.129	.128
DSM–5 SUD symptoms – cannabis	.318	.107	.126	-.042

Note. Spearman's rho correlation coefficients are presented. NMPO = nonmedical prescription opioid. SUD = substance use disorder. AUD = alcohol use disorder. DS = Digit Span. RT = reaction time.

† $p < .10$. * $p < .05$. ** $p < .01$.

Table 5

Associations among Self- and Emotion Regulation and Substance Use Variables among NMPO Users

	SSRQ	DERS	Imp	Aware	Goals	Non	Strat	Clar
Past-month NMPO use	.127	-.075	-.060	.212	-.173	-.130	-.171	-.056
Past-year NMPO use	.153	.103	.011	.016	.180	.058	-.008	-.008
DSM–5 SUD symptoms – opioid	.201	-.351	.347†	-.025	.141	.185	.028	-.073
Typical drinks per week	-.140	.158	.238	-.019	-.087	.104	.190	.067
DSM–5 AUD symptoms	-.249	.161	.209	.197	-.106	.177	.047	-.056
Past-month marijuana use	-.048	-.042	-.289	.285	-.373†	-.103	.109	.120
Past-year marijuana usE	-.090	-.106	-.322	.389*	-.404*	-.204	-.073	.038
DSM–5 SUD symptoms – cannabis	-.274	-.340	-.333	.159	-.356	-.211	-.137	-.195

Note. Spearman's rho correlation coefficients are presented. NMPO = nonmedical prescription opioid. SUD = substance use disorder. AUD = alcohol use. SSRQ = Self-Regulation Questionnaire – Short; higher scores reflect greater self-regulation. DERS = Difficulties in Emotion Regulation Scale; Imp = DERS impulse subscale; Aware = DERS awareness subscale; Goals = DERS goals subscale; Non = DERS nonacceptance subscale; Strat = DERS strategies subscale; Clar = DERS clarity subscale; higher scores reflect greater difficulties with emotion regulation.

† $p < .10$. * $p < .05$.

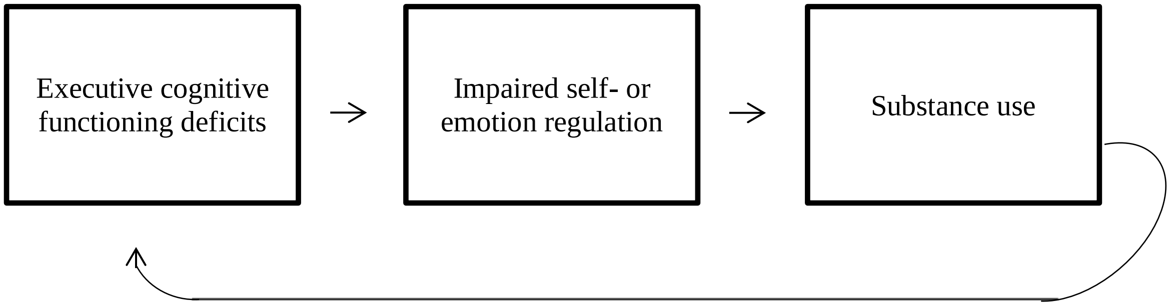

Figure 1. Relations between executive cognitive functioning deficits, impaired self-regulation and emotion dysregulation, and substance use

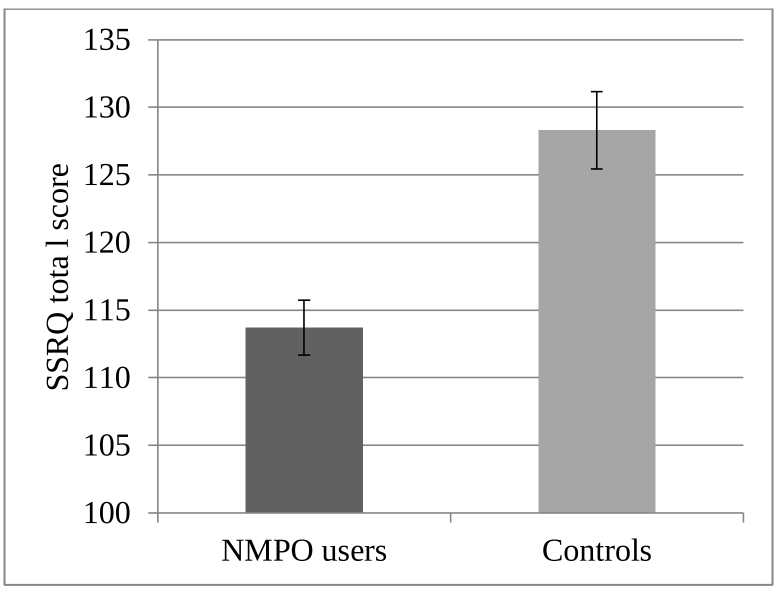

Figure 2. Mean Self-Regulation Questionnaire – Short total score values for nonmedical prescription opioid users and controls; higher scores reflect greater self-regulation. Error bars represent ± 1 standard error of the mean. $N = 27$ per group. Groups significantly differ, $t(52) = 4.16$, $p < .001$.

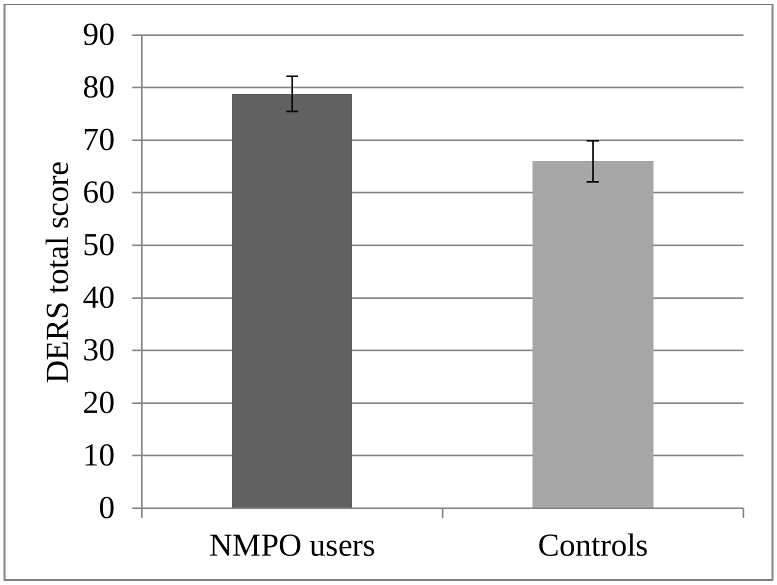

Figure 3. Mean Difficulties in Emotion Regulation Scale total score values for nonmedical prescription opioid users and controls; higher scores reflect greater difficulties with emotion regulation. Error bars represent ± 1 standard error of the mean. N = 27 per group. Groups significantly differ, t (52) = -2.50, p = .016.

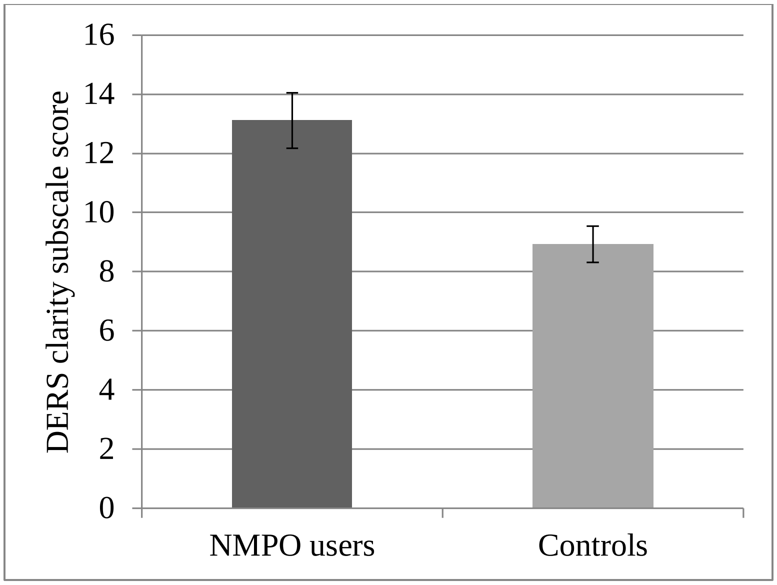

Figure 4. Mean Difficulties in Emotion Regulation clarity subscale score values for nonmedical prescription opioid users and controls; higher scores reflect greater difficulties with emotion regulation. Error bars represent ± 1 standard error of the mean. N = 27 per group. Groups significantly differ, t (52) = -3.90, p < .001.

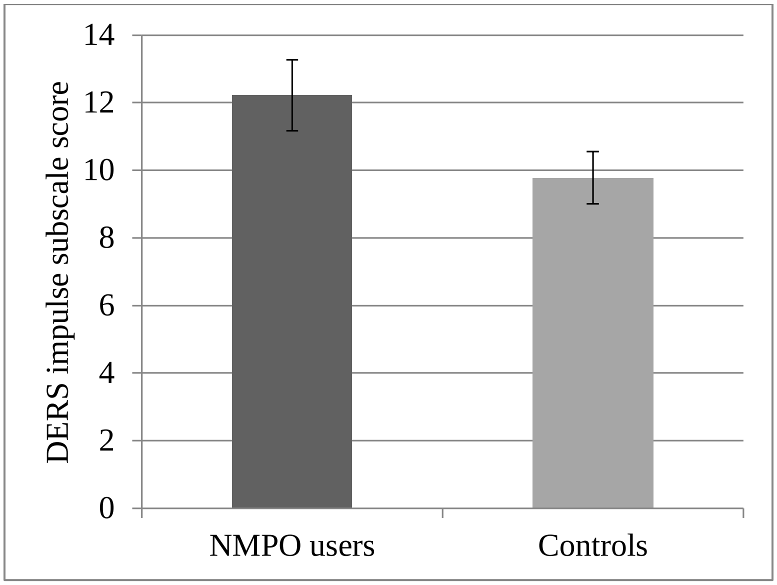

Figure 5. Mean Difficulties in Emotion Regulation impulse subscale score values for nonmedical prescription opioid users and controls; higher scores reflect greater difficulties with emotion regulation. Error bars represent ± 1 standard error of the mean. N = 27 per group. Groups differences approach significance; t (52) = -1.92, p = .060.

Appendix B

Daily Drinking Questionnaire

The questions below ask about your alcohol consumption.

For the **past month,** fill in for each calendar day the number of standard drinks you **usually drink** on that day **during a typical week**, and the number of hours over which you consume this amount (i.e., the time from 1st sip to last sip). When we say one drink, we mean 12 oz. of beer, 5 oz. of wine, or 1.5 oz. of hard liquor (see picture on the left). Malt liquor is stronger than regular beer, so one 40 oz. Malt Liquor beverage such as Colt 45 counts as 5 standard drinks. Fill in an amount for each of the 7 days. If you do not typically drink on a given day, fill in 0 for that day.

Day	Sun	Mon	Tues	Wed	Thurs	Fri	Sat
# of drinks usually consumed							
# of hours							

QUESTIONS FOR MALES ONLY

IN THE PAST MONTH how many times have you had 5 or more drinks (in one occasion)? ____ ____ times

QUESTIONS FOR FEMALES ONLY

IN THE PAST MONTH how many times have you had 4 or more drinks (in one occasion)? ____ ____ times

Appendix C

Self-Regulation Questionnaire – Short

Please respond to the following questions by circling the response that best describes how you are. There are no right or wrong answers. Work quickly and don't think too long about your answers.

Response categories:

1	2	3	4	5
Strongly Disagree	Disagree	Uncertain or Unsure	Agree	Strongly Agree

01 I usually keep track of my progress toward my goals.
02 I have trouble making up my mind about things.
03 I get easily distracted from my plans.
04 I don't notice the effects of my actions until it's too late.
05 I am able to accomplish goals I set for myself.
06 I put off making decisions.
07 It's hard for me to notice when I've "had enough" (alcohol, food, sweets).
08 If I wanted to change, I am confident that I could do it.
09 When it comes to deciding about a change, I feel overwhelmed by the choices.
10 I have trouble following through with things once I've made up my mind to do something.
11 I don't seem to learn from my mistakes.
12 I can stick to a plan that's working well.
13 I usually only have to make a mistake one time in order to learn from it.
14 I have personal standards, and try to live up to them.
15 As soon as I see a problem or challenge, I start looking for possible solutions.
16 I have a hard time setting goals for myself.
17 I have a lot of willpower.
18 When I'm trying to change something, I pay a lot of attention to how I'm doing.
19 I have trouble making plans to help me reach my goals.
20 I am able to resist temptation.
21 I set goals for myself and keep track of my progress.
22 Most of the time I don't pay attention to what I'm doing.
23 I tend to keep doing the same thing, even when it doesn't work.
24 I can usually find several different possibilities when I want to change something.
25 Once I have a goal, I can usually plan how to reach it.
26 If I make a resolution to change something, I pay a lot of attention to how I'm doing.
27 Often I don't notice what I'm doing until someone calls it to my attention.
28 I usually think before I act.
29 I learn from my mistakes.
30 I know how I want to be.
31 I give up quickly.

Appendix D

Difficulties in Emotion Regulation Scale

Please indicate how often the following 36 statements apply to you by writing the appropriate number from the scale above (1 – 5) in the box alongside each item.

Response categories:

1 Almost never (0-10%)
2 Sometimes (11-35%)
3 About half the time (36-65%)
4 Most of the time (66 – 90%)
5 Almost always (91-100%)

1. I am clear about my feelings.
2. I pay attention to how I feel.
3. I experience my emotions as overwhelming and out of control.
4. I have no idea how I am feeling.
5. I have difficulty making sense out of my feelings.
6. I am attentive to my feelings.
7. I know exactly how I am feeling.
8. I care about what I am feeling.
9. I am confused about how I feel.
10. When I'm upset, I acknowledge my emotions.
11. When I'm upset, I become angry with myself for feeling that way.
12. When I'm upset, I become embarrassed for feeling that way.
13. When I'm upset, I have difficulty getting work done.
14. When I'm upset, I become out of control.
15. When I'm upset, I believe that I will remain that way for a long time.
16. When I'm upset, I believe that I'll end up feeling very depressed.
17. When I'm upset, I believe that my feelings are valid and important.
18. When I'm upset, I have difficulty focusing on other things.
19. When I'm upset, I feel out of control.
20. When I'm upset, I can still get things done.
21. When I'm upset, I feel ashamed with myself for feeling that way.
22. When I'm upset, I know that I can find a way to eventually feel better.
23. When I'm upset, I feel like I am weak.
24. When I'm upset, I feel like I can remain in control of my behaviors.
25. When I'm upset, I feel guilty for feeling that way.
26. When I'm upset, I have difficulty concentrating.

27. When I'm upset, I have difficulty controlling my behaviors.
28. When I'm upset, I believe there is nothing I can do to make myself feel better.
29. When I'm upset, I become irritated with myself for feeling that way.
30. When I'm upset, I start to feel very bad about myself.
31. When I'm upset, I believe that wallowing in it is all I can do.
32. When I'm upset, I lose control over my behaviors.
33. When I'm upset, I have difficulty thinking about anything else.
34. When I'm upset, I take time to figure out what I'm really feeling.
35. When I'm upset, it takes me a long time to feel better.
36. When I'm upset, my emotions feel overwhelming.