Electrophysiological evidence for concurrent appetitive and defensive motivational system activation in cue- induced tobacco cravings

by

Andrew Faulkner

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Abstract

All current theories of environmental cue-induced drug craving (mainly incentive-sensitization, the affective motivational model, and elaborated-intrusion) involve activation of the brain's appetitive and defensive motivational systems, which modulate stimulus approach and avoidance, as well as emotion. However, these theories disagree on the extent each system is involved. We helped tease this apart by taking electroencephalographic recordings of smokers and non-smokers' brain activity as they viewed tobacco, food, and affective photos. On each image trial we had participants: 1)Form a mental image of the photo and rate it's 'vividness;' 2)Rate the photo's valence; and 3)Report cravings. Tobacco craving-inducing images had higher vividness, and produced valence scores and electroencephalographic event-related potential waveform patterns that aligned with concurrent appetitive and defensive system activation. These results best fit elaborated-intrusion. Thus, drug cravings are likely simultaneously pleasant and unpleasant, and arise from intrusions of vivid mental images resulting from withdrawal-associated negative affect and/or drug reward-associated environmental cues.

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Background

Addictive disorders and their secondary consequences are arguably the most expensive, widespread, and significant set of health problems facing society today. Most of this burden, however, isn't related to drugs normally associated with severe abuse such as heroin, but instead, from simple tobacco, which accounts for approximately 4 out of every 5 substance-related deaths. Smoking is currently the world's leading cause of preventable death, with about 6 million dying every year from related complications. Furthermore, the severity of the problems linked to smoking do not stem solely from its ubiquity and social acceptability: it is, in fact, also one of the most harmful on the level of an individual user. The per capita mortality associated with tobacco use is approximately 3 times that of heroin and alcohol, 30 times that of cocaine/crack, over 100 times that of ecstasy/MDMA, and over 10,000 times that of LSD and cannabis. More than half of all chronic smokers are eventually killed by their habit. Also, tobacco is also one of the greatest economic burdens on the healthcare system (and society in general) with hundreds of billions spent annually on treating smoking-related illness. Not only does its ubiquity and harmfulness result in a large number of smokers requiring treatment, but because many of the illnesses it can induce progress very slowly, smokers frequently end up requiring years of expensive medical care even if tobacco doesn't eventually kill them (President's Commission on Organized Crime, 1986; Surgeon General, 1989; Mackay, Erickson, & Shafay, 2006; World Health Organization, 2011).

Although smokers are generally aware of the serious impact of tobacco addiction, and despite the great desire most (approximately 69%) have to be free of their habit (Centers for Disease Control and Prevention, 2011), many are unable to permanently quit. The vast majority of all cessation attempts end in relapse, with about 93% reinstating their habit within 12 months. Even the use of smoking cessation therapies only increases the 1-year success rate to approximately 85% (Zhu et al, 2000; Piasecki, 2006). Thus, the difficulty of maintaining long-term abstinence is one of the most important challenges to overcome in the treatment of tobacco addiction, and in addictive disorders in general, most of which have similarly high rates of relapse.

Drug cues

A growing body of research literature suggests that drug-related cues (including smoking cues) in the environment may be one of the main precipitants of relapse, as well as one of the primary contributors to the maintenance of addictions. The powerful impact of environmental drug cues is exemplified by animal models of addiction. Animals are trained to self-administer a drug (e.g. via lever press) until they do so compulsively, escalate the quantity consumed, and persist even when drug administration is paired with aversive stimuli. At this point, the animal is considered to have an addiction to the drug (Markou et al, 1993; Heyne & Wolfgramm, 1998). If access to the drug is then removed for a very long period of time, the result is extinction of the self-administration response. However, regardless of how much time passes following extinction, presentation of an environmental cue previously associated with the drug will reinstate compulsive self-administration. This model demonstrates that drug cues operate at a level so basic that they can produce relapse and contribute to addiction even in animals, which appears to occur in a pattern mirroring that seen in humans. The construct validity and generalizability of this model is corroborated by the fact that it cannot be implemented using any drug that is not addictive to humans (See et al, 2003; Epstein et al, 2006), but can with all drugs that are, including alcohol (Wolfgramm & Heyne, 1991), amphetamine (Heyne & Wolffgramm, 1998), nicotine (Levin et al, 2007), and cocaine (Vanderschuren & Everitt, 2004).

Human research has also demonstrated the importance of drug cues in addiction. Firstly, attention is strongly captured by drug cues in those addicted to that particular drug, but not in healthy controls. This reflects an increase in mental resources assigned to these cues in addicts. Long-abstinent addicts also display this response, suggesting it can persist almost indefinitely (Lubman et al., 2000, 2008; Franken, 2003; Robbins & Ehrman, 2004). It is also backed up by self-report, as relapsed addicts – especially smokers – frequently cite exposure to environmental drug cues as a factor contributing to the failure of their attempts to quit (Shiffman et al, 2007; Heinz et al, 2008). Furthermore, when exposed to drug cues, addicts and ex-addicts often report experiencing cravings, which are powerful predictors – and likely causes – of drug use (Shiffman et al, 1996, 2002; Lubman et al, 2008; Field, Munafo, & Franken, 2009).

Cravings can be defined in the context of drug addiction as motivational states that intensely promote substance-seeking and ingestion (Baker et al, 1986; Sherman et al, 1986). They are one of the primary contributors to the continuation of drug use (Killen & Fortmann, 1997; Nestler et al, 2001; Breese et al,

2005), so the fact that drug cues so commonly induce cravings underscores how large a role these cues play in the maintenance of addictions (see Tiffany, 1990). Cravings are, in fact, one of the definitive features of addiction, as evidenced by their ubiquity in drug addicts (and controversially, in those with “behavioural addictions;” Holden, 2001). Indeed, they have been observed in the context of addictions to e.g. tobacco (Carpenter et al, 2009), alcohol (Tavares et al, 2005), caffeine (Kemps & Tiggemann, 2009), video games (Porter et al, 2010), cocaine (Franken et al, 2008), sex (Goodman, 1992), amphetamines (Lee et al, 2010), gambling (Tavares et al, 2005), chocolate (Steel et al, 2006), and heroin (Lubman et al, 2008). Furthermore, the aforementioned occurrence of drug cue-induced cravings in ex-addicts highlights their likely importance in the process of relapse, not just in addiction maintenance.

Appetitive and defensive motivational systems

Virtually all theories of drug craving argue that the existence and power of cue-induced cravings for drugs can be explained by motivational processes involving the appetitive motivational system and/or the defensive motivational system, which are sets of neural circuitry that (respectively) mediate approach- and aversion-related behaviours (Bradley, 2009; Lang & Bradley, 2010). They are dissociable from one another neuroanatomically, psychologically, and behaviourally. Furthermore, each is exclusively represented by a single system in the brain rather than several with similar functions (Seymour et al, 2007).

Appetitive motivational system (AMS)

More specifically, the appetitive motivational system (AMS) directs behaviour toward acquisition of survival and reproduction-promoting unconditioned reinforcers (URs) such as food and sex (Agmo et al, 1993; Kelley & Berridge, 2002; Hyman, 2005; Hyman, Malenka, & Nestler, 2006), and is responsible for positive reinforcement (Dayan & Balleine, 2002), positive affect, and pleasure (Lang & Bradley, 2010). It assigns motivational relevance to environmental cues present directly before activation of the dopaminergic projections from the ventral tegmental area (VTA) to the nucleus accumbens (NAcc), otherwise known as the reward pathway (Nestler, 2005). Besides the reward pathway, the AMS encompasses certain areas of the limbic system and globus pallidus (Lang et al, 1998), which are essential for emotion and execution/planning of movements, respectively (Schuenke et al, 2006). The AMS can thus be said to also initiate approach toward rewarding stimuli. Note that the AMS is also related to negative punishment, as organisms will perform behaviours to prevent removal of AMS-activating stimuli (Seymour et al, 2007).

Defensive motivational system (DMS)

The defensive motivational system (DMS), on the other hand, directs behaviour to respond to aversive stimuli (Lang & Bradley, 2010). These responses involve either self-defense, or active avoidance of the triggering stimulus (Metcalf & Mischel, 1999; Lang & Davis, 2005; Bradley, 2009). DMS-activating stimuli include such things as animals or people in attack positions (Lang et al, 1997), social rejection (Downey et al, 2004), and extremely novel stimuli (Bradley, 2009). The DMS is also the driver of positive punishment (Seymour et al, 2007), with motivational relevance assigned to any stimuli present directly before activation of the amygdala – a major aspect of the DMS, and the primary source of negative affect (NA). The DMS also includes certain regions that the amygdala projects into – mainly the periaqueductal central gray (PCG), nucleus reticularis pontis caudalis (NRPC), and hypothalamus – which produce the behavioural and physiological responses to different types of NA and aversive stimuli. More specifically, the PCG mediates coping behaviours (e.g. freezing, fighting), the NRPC produces startle responses, and the hypothalamus activates the autonomic nervous system (Lang et al, 1998). Negative reinforcement is also related to the DMS, as organisms will perform behaviours to avoid stimuli that activate it (Seymour et al, 2007).

Motivational system-based theories of craving

Although addiction and cue-induced drug craving almost invariably revolve around motivational processes, there is still no agreement about the role played by each system. Both the AMS and DMS individually have a great deal of evidence supporting their connection to craving, so teasing apart the importance of each is difficult, as any thorough explanation supporting the primacy of one system must also account for evidence supporting the other – some of which is indisputable. On the appetitive end, it has been repeatedly demonstrated (e.g. using positron emission tomography) that addictive drugs directly bind to receptors in the reward system, stimulating their firing by increasing dopamine transmission in the nucleus accumbens (Everitt, Dickinson & Robbins 2001; Hyman, 2005), resulting in activation that is indistinguishable from firing produced by a UR (Volkow & Wise, 2005). On the defensive side, discontinuation of addictive drugs after numerous successive uses results in an unpleasant withdrawal syndrome that includes negative affect (NA), and behaviour involving avoidance of the painful symptoms. These are definitive features of addictive drugs, and they clearly invoke appetitive and defensive processes.

The debate, however, surrounds which of these is the main driver of addiction, and which system is active during acute cravings (or if both play a primary role). There are currently three major theories positing different motivational system involvements: 1) incentive sensitization theory (IST); 2) the affective motivational model (AMM); and 3) elaborated-intrusion theory (EIT).

Incentive sensitization theory (IST): appetitive system primacy in craving

Robinson and Berridge's (1993, 2008) incentive sensitization theory (IST) argues that cue-induced drug cravings are primarily driven by the AMS, while the DMS has very little involvement. According to IST, exposure to the rewarding effects of an addictive drug produces alterations in the AMS that increase the incentive motivational relevance ('desirability') assigned to the drug and to cues associated with it. This results in a minor "wanting" for the drug. Each subsequent use of the drug produces further alterations of the AMS, which further increase the assigned motivational relevance. These changes cause the AMS to become hypersensitive to drug cues, eventually transforming the simple "wanting" of the rewarding effects of a drug into excessive, pathological drug craving. At this point, the AMS is activated to an enormous degree in the presence of drug cues, and especially during drug cravings. All of this is proposed to occur independently from the "liking" of a drug, and from systems involved in drug withdrawal, with sensitization in the AMS unrelated to changes in these other systems. IST argues that it is only these changes in the "wanting" of a drug that produce cravings, and furthermore, addiction. Later exposure to drug cues can then activate the AMS again, resulting in urges to use the drug (cravings) and to engage in behaviours required to obtain the drug (Cepeda-Benito et al, 2000). In other words, it is primarily the assignment of motivational relevance to drug-related cues via the mechanisms that assign motivational relevance to UR-related cues (occurring via the aforementioned 'hijacking' of the brain's reward system) that drive drug cravings, and ultimately, addictions (Robinson & Berridge, 2003; Versace et al, 2010). Only the appetitive system is truly involved in addiction in the framework of IST (Robinson & Berridge, 1993, 2008).

Evidence for Incentive Sensitization Theory (IST)

A large body of evidence supports IST, and thus that the AMS is the primary driver of cravings. Firstly, craving-inducing cues are generally rated by subjects as appetitive in nature, not aversive – that is, they induce feelings of excitement and interest, not deprivation. Mucha et al (1999) presented tobacco addicts with images of cigarettes being smoked, and had them rate both their desire to smoke a cigarette and their

emotional reaction to the image (in terms of valence and arousal) after each trial. Craving-inducing images were generally assigned positive emotional valence ratings, as were images of tobacco regardless of whether or not they produced cravings. This result has been replicated with multiple similar paradigms involving other drugs, different types of drug user (abstinent vs. casually using vs. currently dependent), and addiction-related stimuli with different characteristics – for example, cues presented through non-visual modalities (e.g. Zinser et al. 1999, Bushnell et al. 2000, Laar, Licht, Franken, & Hendriks, 2004; Wolfing, Flor, & Grusser, 2008). Also, drug addicts often report a continuous “want” for their drug of choice without tying that want to liking the drug or fearing withdrawal, sometimes even directly stating that it isn’t tied to liking or withdrawal (Evans et al, 2006; Robinson & Berridge, 2008).

IST can explain why addictive drugs (especially tobacco) have the potential to gain greater motivational relevance than URs, despite the fact that both activate the same neural pathways (Hyman, 2005; Holden, 2001). Firstly, drug reward can be experienced more frequently than reward associated with any individual UR, so reward-cue pairings can occur more frequently than pairings of a UR-cue pairings (Erickson, 2007). This is especially relevant to tobacco addiction, as each puff of a cigarette delivers a small reward, and the short half-life of nicotine requires typical chronic smokers to use tobacco very frequently, cumulatively resulting in 100s of nicotine rewards in a single day (Rose, 2006). Furthermore, these unusually numerous rewards in tobacco addiction can result in the occurrence of more secondary reinforcement, turning unrelated environmental cues into unconditioned stimuli (US) that can later induce drug cravings (Shiffman et al, 2002, 2007; Epstein et al, 2006; Rose, 2006; Erickson, 2007). Secondly, drug cues have less variety than UR-related cues. For example, in smokers, cigarettes can be extremely powerful USs due to their consistent association with nicotine reward. Thirdly, visual drug cues are often very simple (e.g. cigarettes are merely a white cylinder), which allows the brain’s motivational pathways to extract them from the perceptual stream very early in visual processing. This causes an addict’s attention to orient to a drug cues prior to conscious awareness of them – potentially as early as 100ms after exposure (Zhang & Luck, 2009; Versace et al, 2010). Fourthly, the reward system activation addictive drugs produce is unusually immediate – e.g., smoking delivers nicotine to the brain in seconds (Balster & Schuster, 1973; Samaha & Robinson, 2005). The temporal distance a reward has from the cue (or behaviour) that induced it directly reflects the likelihood of a cue-reward pairing, and its strength if it occurs (Henningfield & Keenan, 1993; Samaha &

Robinson, 2005; Schultz, 2010). Fifth, the amount of initial reward system activity certain highly addictive substances can produce can be larger than that produced by any UR. Thus, more AMS-related motivational salience is associated with the drug right away, as drug users can experience greater levels of reward than are naturally available (Di Chiara & Imperato, 1988; Di Chiara et al, 1998). Note that one could argue that at least some of these processes are DMS-based, but if that were the case, craving would likely be less powerful, as while the first few puffs (at most) of a single cigarette could assign motivational salience via negative reinforcement, once the subthreshold withdrawal has been removed, all proceeding puffs would relate mainly to positive, which would be dozens for each cigarette. Nonetheless, these factors do not provide evidence that the DMS is not present in cravings, they merely strongly suggest a large role for the AMS.

Another line of evidence comes from research using the startle reflex paradigm (SRP). When a highly startling stimulus (e.g. a sudden loud noise) is presented directly after a weaker stimulus, the result is a decreased startle response to the stronger stimulus. This phenomenon is known as prepulse inhibition (PPI). Many factors can alter PPI intensity and latency, most relating to emotion and attention, so numerous inferences can be made about the internal states of participants based on the level of PPI they present. SRP studies take advantage of this by semi-randomly inducing a startle reflex (e.g. using blasts of white noise) in participants that are concurrently being run through another experimental procedure (Vrana et al, 1988; Dempsey et al, 2007), often involving passive observation of various categories of visual images. These studies have demonstrated that activation of the AMS tends to attenuate PPI (Dempsey et al, 2007). This is evidenced both by the wide variety of appetitive stimuli that induce this attenuation (e.g. Baschnagel et al, 2009), and via neuroimaging studies showing PPI attenuation to occur in tandem with increases in activation of the mesolimbic dopaminergic system/reward pathway (Ott & Mandel, 1995; Swerdlow, et al, 1994; Bradley et al, 1999), which, as mentioned previously, is a major component of the AMS. A vast majority of SRP studies have found that addicts shown drug imagery (including smoking cues) tend to display the attenuated PPI characteristic of AMS activation (e.g. Rubio et al, in press, Dempsey et al, 2007, Geier et al, 2000).

The affective motivational model (AMM): defensive system primacy in craving

The defensive system is posited as the primary driver of addictions and relapse by the affective motivational model (AMM), proposed by Baker et al (2004). According to AMM, drug use is continued for

the sake of avoiding aversive states (associated with defensive system activation) – primarily withdrawal or environmental stressors – rather than out of an appetitive “want” for reward, as IST proposes. Once a person is addicted to a drug, it takes only until the drug has started to wear off for some withdrawal distress to start. All withdrawal syndromes are marked by NA, which is usually the first symptom. When this early-stage withdrawal syndrome appears, an addict will then use the drug to ameliorate it. However, because this continuously associates NA with withdrawal, and more importantly, reduction of NA with use of the drug, addicts will use the drug any time NA appears for any reason. This will often be effective, for 2 reasons: 1) the inherent ability of addictive drugs to temporarily alleviate certain types of NA quite effectively (e.g. opioids are anxiolytic; amphetamines relieve depression and fatigue); and 2) addicts are frequently in a state of very mild withdrawal, so using the drug will reduce withdrawal-related NA, lowered the net level of negative emotion they are experiencing. The success of this maladaptive method of emotional control will further increase the negatively reinforcing power of the drug (Baker et al., 2004).

Cravings are viewed in this framework as highly unpleasant experiences characterized by a strong desire to escape NA. Anything that induces NA (and thus defensive motivational system activity) will generate cravings due to the aforementioned association of NA with withdrawal distress. Since addicts are almost continuously in a state of mild withdrawal that is usually preconscious, drug cues also induce craving, by bringing this unconscious NA to the surface, and thus directly producing defensive system activation. Cravings can thus be viewed within AMM as being directly linked to defensive system activation (Baker et al, 1986, 1987, 2004; Muñoz et al, 2009).

Note that (for the sake of avoiding a straw man argument) AMM does concede that the appetitive system plays a role in addiction; but only during the very earliest stages of drug abuse. The appetitive system is what drives use of the drug beyond the initial experimentation with it, but this stops being a factor almost as soon as withdrawal symptoms begin to appear, which occurs after only a small handful of uses (Baker et al, 2004).

Evidence for the Affective Motivational Model (AMM)

AMM – and thus a primary role for the defensive system in craving – is supported by numerous lines of evidence. Firstly, the reason addicts most frequently report for using drugs - and for relapse - is a need to

eliminate NA (Goldman et al, 1987; Wetter et al, 1994; Shiffman et al, 2007). Smokers often describe cigarettes as “anxiety-reducing,” even though nicotine is a stimulant, and actually increases anxiety in non-smokers. This seemingly paradoxical effect is thus likely caused by reduction of the considerably greater anxiety generated by withdrawal, rather than any inherent anxiolytic properties of nicotine (Juliano & Brandon, 2002). Furthermore, craving intensity correlates with severity of withdrawal-induced NA, and relapse is most likely to occur when this peaks. For nicotine, this is 2 days after the last cigarette (Wikler, 1980; Baker et al, 1987; Hughes, 1992; Schuh & Stitzer, 1995; Jarvik, 2000). During withdrawal, NA reaches extremely high levels, especially at said peak (Shiffman et al, 1995; Baker et al, 2004; Sinha, 2008; Engelmann et al, 2011). Also, this NA can persist to some degree for months, or even years, after initial withdrawal in the form of post-acute withdrawal syndrome (PAWS). The symptoms of PAWS consist of the psychological - but generally not the physical - aspects of acute withdrawal: mainly mood disturbances, malaise, and cognitive impairment (Connors et al, 1996; Miller & Harris, 2000; Sinha, 2008), which explains how relapse can still occur long after drug use has ceased. These observations corroborate addicts’ claims that relapse is due to NA – even after a significant length of time as passed – as well as provide evidence that relapse and possibly craving altogether have their basis in negative reinforcement and are thus defensive in nature.

Some animal research also demonstrates a primary role for NA (and thus DMS-activation) in withdrawal and the continued use of a drug. Somatic aspects of withdrawal have been found to link poorly with the aversiveness of withdrawal in rats, as conditioned place aversions produced by opiate withdrawal still occur even if all physical symptoms of withdrawal are suppressed (Mucha, 1987; Hand et al, 1988; Baker et al, 2004). Amygdala activation (and thus DMS activation), however, has been shown to be essential for withdrawal-associated place aversion to occur, as amygdala lesions will eliminate this effect. Lesions of the nucleus accumbens (reward system), however, will not, which rules out negative punishment (and thus the AMS) as a driver of place aversion (Kelsey & Arnold, 1994; van Ree et al, 1999; Baker et al, 2004). These together provide evidence that the primary contributor to continued self-administration in animals is avoidance of NA-based withdrawal – and thus avoidance of DMS activation.

More corroborating evidence comes from Morgan et al (2010), who found a significantly weaker correlation between a drug’s rewarding and psychologically addictive properties, $r = 0.34, p = 0.50$; than

between a drug's psychologically and physically addictive potential, $r = 0.97, p < 0.0001$. The latter correlation is so high that it suggests these constructs are essentially synonymous, which suggests that escape from withdrawal distress (and thus DMS activation) plays a larger role in drug addiction than anything relating to the AMS.

Research on chippers also supports AMM: people who use tobacco frequently and for long periods of time without developing addictions. Chippers never crave tobacco, rarely smoke more than 5 cigarettes per day, and don't experience nicotine withdrawal regardless of how often or for how long they smoke daily. In other words, they are essentially immune to the dependence-inducing effects of nicotine, but still experience the reward associated with smoking. This again suggests that negative reinforcement (not positive) is primarily responsible for addiction (at least in the case of tobacco) since positive reinforcement is present in chippers, but is not enough to induce addiction (Shiffman et al, 1994, 1995; Baker et al, 2004).

Finally, withdrawal appears very early in the course of an addiction. Mild, slightly uncomfortable withdrawal syndromes have been reported after a very small number of consequent uses of an addictive drug (Heishman et al, 1989; Hesselbrock et al, 2000). These are consistently reported by addicts and drug users to have NA as a symptom (e.g. Kosman & Unna, 1968; Mansky, 1978; Gold, Washton, & Dackis, 1985). This is corroborated by the finding that even within the first few uses of a drug, falling drug levels tend to induce both NA and craving (Fendt & Mucha, 2001), which increases in effect with more uses of the drug (Baker et al, 1987; Wikler, 1980). Also, mild withdrawal symptoms have been observed in rats after only a single injection of morphine (Grilly & Gowans, 1986). Thus, discontinuation of the use of an addictive drug under almost any circumstance seems to produce at least slight activation of the DMS (Baker et al, 2004).

Elaborated intrusion theory (EIT) and motivational system co-activation in craving

Kavanagh, May, and Andrade (2005) proposed a cognitive theory involving both AMS and DMS activation during a craving, known as Elaborated-intrusion (EIT). EIT states that cravings begin with the intrusive appearance of a mental image of an appetitive target – in this case an addictive drug. These intrusive images can be induced both by: 1) internal states, mainly NA associated with withdrawal distress or physical feelings indicative of physiological deficit; and 2) external cues such as the sight of someone using a drug, or a picture of drug paraphernalia. Since the images are primarily of the attractive features of the drug,

they are appetitive in nature, but because they immediately generate a sense of being deprived, they are also defensive. Kavanagh et al describe these two aspects as “imaginary relish” and “exquisite torture,” respectively. If the image has affective properties (enough associated desire and deprivation) that are of a certain level of intensity, it will – barring an intervening external distraction – automatically initiate the second stage of craving: elaboration. In this phase, other information about the desired object (drug) is involuntarily retrieved via associative processes – that is, via neural connections linking to areas connected to the brain regions responsible for the initial image. Memories and verbal thoughts associated with the drug quickly appear, the intruding image becomes more vivid and complex, and other sensory impressions of the drug begin to intrude – even outside the visual modality (e.g. smell, taste). All of this intensifies the initial affective reaction, which in turn produces further elaboration. This cyclically increasing activation can eventually completely override the ability to attend to anything but the desired object, resulting in consummation of the craving (e.g. by smoking), which ends it (Kavanagh et al, 2005).

Note that EIT does not suggest that both DMS and AMS activation will always both be involved in cravings to an equal degree, only that both are usually present, and that which has primacy depends on the amount of background DMS activation and physiological deficit. When very little of either is present, the cravings are less intense and more appetitive in nature, as there is less unpleasantness for the mental image to draw attention to. However, note that even when no withdrawal or NA is present, a sense of being deprived of the pleasurable effects of the drug (AMS-activation) could potentially result in DMS activation, albeit to a considerably lesser degree.

Evidence for activation of both pathways in craving

Although many studies primarily support the role of only one of the two motivational systems in addiction and craving, they generally do not rule out a role for the other. Furthermore, there are lines of evidence that directly suggest an involvement for both.

Firstly, there are numerous drugs that are solely positively reinforcing or solely negatively reinforcing that do not induce cravings and are not addictive. Drugs that produce reward but not withdrawal (and are thus only appetitive in nature) do not induce compulsive self-administration in humans or animals (Robinson & Berridge, 1993; Hyman & Malenka, 2001). These include LSD (“acid”), mescaline (“peyote”), and

psilocybin (“magic mushrooms”) (Goldstein & Kalant, 1990; Obrien, 2001; Nichols, 2004; Lüscher & Ungless, 2006). Cocaine, amphetamine, and ketamine are often presented as counterexamples to this point, but the notion that these drugs do not produce physical dependence is in fact a misconception based on the lack of somatic symptoms involved in their withdrawal syndromes. Both amphetamine and cocaine cause extremely severe depression and fatigue upon discontinuation, which animal research suggests are due to actual changes in the brain induced by the drugs (Cryan et al, 2003). Ketamine has also recently also been found to produce withdrawal symptoms upon discontinuation, consistently mainly of anxiety (Morgan & Curran, 2012). There are thus no known drugs that solely activate the reward-system that are addictive. On the flipside, drugs that can produce physical dependence but not reward, and furthermore, do not *block* reward (as antipsychotics do) are not craved, and do not produce the compulsive self-administration that marks addiction (e.g. anticonvulsants, psychopharmacologically inactive painkillers such as the NSAIDs). A particularly good example can be found in antidepressants, because they by definition eliminate states analogous to drug withdrawal (depression and anxiety – the most problematic symptoms of most drug withdrawals) that are naturally present in an individual without ever having previously used an addictive drug. They are thus *immediately* negatively reinforcing. Furthermore, stopping them frequently causes withdrawal syndromes that include extreme NA and serious somatic symptoms (van Geffen et al, 2005; Warner et al, 2006; Baldwin et al, 2007; Haddad & Anderson, 2007; McHugh & Krishnidas, 2011). Essentially, antidepressants have every negatively reinforcing property a drug can possess, with none that are appetitive. Thus, if only the DMS and negative reinforcement was involved, they should be extremely addictive – but all patterns of use associated with antidepressants consistently do not meet any diagnostic criteria for an addictive disorder (Haddad & Anderson, 2007; APA, 2000). This consistent observation of the presence of both systems in every widely studied addictive drug – along with counterexamples of drugs activate only one but are not addictive – suggests that both systems are required for a drug addiction to result.

Although it is extremely well-evidenced that craving is a significant part of withdrawal (e.g. Jarvik et al, 1995; Jorenby et al., 1996; Nader et al., 1997), the complete elimination of withdrawal syndromes only reduces cravings – it does not altogether eliminate them. For example, though nicotine patches ameliorate all of the somatic and affective symptoms of nicotine withdrawal and reduce spontaneous cravings triggered by the presence of these symptoms, abstinent smokers still experience cravings when viewing tobacco imagery

(Tiffany, Sanderson-Cox, & Elash, 2000). These cue-reactive cravings then intensify when withdrawal-related negative affect (NA) appears, and additively increase as the NA increases in severity (Coney et al, 1997; Robbins et al, 2000). Thus, it seems the AMS alone can produce cravings, but that the DMS strengthens them. These findings point to dual involvement of the AMS and DMS in craving, which is in line with EIT's major predictions relating to the intrusion stage of craving.

There is evidence suggesting that cues associated with escape from aversive circumstances may be appetitive in nature. In other words, the emotional state of relief may itself be positively reinforcing as well as bound to the negative reinforcement related to the elimination of an aversive state. Seymour et al (2005) found numerous neural substrates common to both relief of pain and administration of reward – including activity in the VTA to NAcc reward pathway. This is corroborated by psychological/behavioural paradigms (Solomon et al, 1980a; Daw et al, 2002). Also, virtually all CNS-activating drugs with nonspecific pain relief properties (in other words, not targeting a specific type of pain linked to a physical mechanism – e.g. triptans for treating migraine; NSAIDS like Advil for inflammation) also have rewarding effects that can promote compulsive self-administration – for example, cannabis, opioids, and certain dissociative anaesthetics such as PCP (Fields, 2004). These observations suggest (but do not prove) that the pursuit of safety when in danger may be at least partially analogous to the pursuit of food when hungry (Seymour et al, 2005) or the pursuit of drugs when in withdrawal. If this is the case, even when imagery-induced cravings are highly unpleasant due to the state of deprivation, and are thus tied to the DMS, the craved stimulus should still be an activator of the appetitive motivational system due to the positively reinforcing feelings of relief the drug-related stimulus can bring – even if it was that specific stimulus that induced the (acute) craving to begin with (Kelley & Berridge, 2002; Seymour et al, 2005). On the flipside, denial of expected pleasure is actively aversive in nature, which has long been known through research on negative punishment ([citation needed]). This denial does, in fact, activate regions of the brain associated with the DMS (Seymour et al, 2005), providing evidence that even if no withdrawal or direct state of deprivation is present, the DMS is activated to some degree merely by the negative punishment of being denied reward system activation. This again points to co-activation of both systems during cravings.

Inconsistency in Psychophysiological and Self-rating Measures

Much of the disagreement between the three theories likely comes from heavy reliance on psychophysiological techniques (e.g. SRP) and self-report in prior research on craving. Although studies utilizing only these types of measures can provide some evidence and a starting point for determining which motivational system is primarily involved in tobacco craving (and likely all drug craving), there is great inconsistency in the results obtained by these methods. This is often even observed between studies using the same paradigms.

The reasons behind the inconsistency with self-report measure-based studies on craving are fairly clear: they have long been known to lack reliability when used without more direct measures to back up participant claims and ratings. This is caused by the introspection illusion: a cognitive bias that produces strong feelings of direct insight into mental states, which results in confident but extremely inaccurate explanations for one's thoughts and behaviours when asked to introspect in any way. It still occurs when using better controlled introspective methods like rating scales (Nisbett & Wilson, 1977).

The inconsistency among psychophysical measures used to measure aspects of craving is almost as great as that seen with self-report. Even psychophysical studies using the same methods often contradict one another, which occurs frequently enough to prevent consensus. For example, some SRP studies report no modulation of PPI in addicts in response to drug cues, implying neither system is involved (Orain-Pelissolo et al, 2004; Franken et al, 2004); and certain others show enhancement of PPI, implying defensive activation (Engelmann et al, 2011); both of which are in contrast to the slight majority of PPI studies mentioned earlier that provide evidence for AMS activation.

Some of the reasons for the unreliability of psychophysiological studies of craving are elucidated by Field, Munafo, & Franken (2009), who conducted a meta-analysis that found psychophysiological studies to produce very small overall correlations between subjective cravings and indexes of attentional bias in response to drug cues (Modified Stroop: $r = 0.15$; Visual probe: $r = 0.19$; all other physiological measures: $r = 0.20$). This is the essential link required to analyze the relationship between craving and motivational system activation, since attentional bias is the core effect produced by the brain's motivational systems during perception. These paradigms were also determined to only act as very indirect measures of

attention, which means that they can at best also only be very indirect measures of motivational bias. Their analyses unsurprisingly found that none of the tasks were able to differentiate between appetitive and defensive motivational system activation with any degree of reliability, with inconsistency even existing within individual studies (which was sometimes overlooked by the original researchers). They concluded that these issues make psychophysiological paradigm-based craving studies highly sensitive to minor changes in experiment design, with slight differences able to produce entirely different results. This was especially the case in studies attempting to make inferences about activation in specific motivational pathways, rather than just attentional bias. (It should be noted that these were a minority: most simply examined attentional bias)

ERP

Issues present with psychophysiological and self-report measures can be greatly mitigated by indexing motivation and attention using event-related potentials (ERPs) taken from electroencephalographic (EEG) recordings. In Field, Munafo, & Franken's (2009) aforementioned meta-analysis, ERP-based paradigms were found to compare self-rated subjective cravings and attentional biases toward drug cues more directly and with greater sensitivity than any other technique. They also determined that these ERP-based findings were also likely more accurate, for 3 major reasons. Firstly, and perhaps most importantly, the results were highly consistent between ERP studies. Secondly, ERP is based on a neuroimaging technique – EEG, which measures spikes in electrical activity generated by the firing of pools of millions of neurons throughout the brain – and thus examines data that can very roughly correspond to active neural regions (in the order of magnitude of few centimeters). It is thus closely linked to the neural circuitry responsible for attention and motivation (Bressler & Ding, 2006). Finally, ERP has extremely high temporal sensitivity, as EEG can record as many as 2000 data points per second (McClernon & Gilbert, 2004). This allows for a more accurate examination of processes that appear at very specific time periods following presentation of a stimulus, as is the case with our measures of interest. Given these reasons, it is unsurprisingly that Field, Munafo, & Franken (2009) observed a larger average correlation between attentional bias and subjective craving found in the literature using ERP-based, rather than psychophysiological measures: $r = 0.37$ across all ERP studies; and $r = 0.48$ for studies that included a particularly sensitive and robust component of the ERP waveform referred to as the p300, which seems to closely align with attention-orienting and affective aspects of stimuli (e.g. Patel & Azzam, 2005; Polich, 2009)

ERP components of interest: p300 & LPP

An ERP component can be defined as a section of EEG data that is time-locked to a stimulus, appears at approximately the same spatial location on the skull, has a recognizable pattern that is mostly conserved across studies, and tends to appear in response to the same types of stimuli and/or mental states and reactions. Although ERP studies have received some criticism for the use of components due to their potential to be assigned arbitrarily to sections of a waveform, the consistency observed between results using more robust, well-evidenced, and clearly visible components (as well as with studies using other neuroimaging techniques such as fMRI) - suggest that ERP analysis is an appropriate technique when conservative components are used (e.g. Carlson et al, 2011). Furthermore, all reported ERP studies in Field, Munafo, & Franken (2009) were component-based, but again, kept within the boundaries of more conservative components.

The first component we selected was a positive amplitude posterior waveform time-locked to 300ms after the presentation of a stimulus known as the p300. It was selected due to its robust connection to attention/affect/motivation, long history of use, high visibility, and ubiquity across studies (Yeung & Sanfey, 2004; Nieuwenhuis et al, 2005). As a general rule, more motivationally relevant stimuli produce larger amplitude p300s by utilizing more of the brain's attentional resources. Also, appetitive motivation usually generates a significant p300 response on the left side of the head, but not the right (Sutton & Davidson, 2000; Nijs et al, 2009). These features make the p300 an excellent measure for determining the amount each motivational pathway is involved in reactions to various stimuli. The amount and type of motivational relevance a stimulus possesses is also indexed by the size of a relatively long-lasting positive-amplitude (primarily) centroparietal component known as the late positive potential, or LPP – our second component of interest (Schupp et al., 2000; Low et al. 2008; Bradley, 2009; Lang & Bradley, 2010). The LPP appears between approximately 300 (at the very earliest) and 600ms after a stimulus, and continues for another 300-900ms, at which point the wave usually drops back to baseline (Schupp et al, 2000; Stockburger et al, 2009; Lang & Bradley, 2010). Similar to the p300, AMS activity tends to be more left-hemispheric for the LPP. However, the LPP seems to have a stronger connection to specific motivational system activation (Davidson et al, 1990; Sutton & Davidson, 2000; Sutton & Davidson, 2000; Nijs et al, 2009).

Both the LPP and p300 have been successfully employed in numerous prior studies on craving in response to drug cues. The vast majority of these studies found that addicts – but not healthy controls –

attend more strongly to drug cues than to most other stimuli, and assign drug cues levels of motivational relevance greater than those normally assigned to URs. These results have been observed across numerous disparate participant categories (depressed, addicted to different drugs, etc.), appetitive objects (primarily drugs and drug-like stimuli such as sugar), sensory modalities of cue presentation (e.g. visual imagery, auditory, gustatory, word presentation), and cue-reactivity paradigm variations (Begleiter et al., 1983; Warren & McDonough, 1999; Schupp et al, 2000, 2006; Rozenkrants et al, 2008; Nijs et al, 2009; Lubman et al, 2010; Vollstädt-klein et al, 2010; Versace et al, 2010; Franken et al, 2004, 2011; Engelmann, 2011). The connection between these components and motivational relevance have been further evidenced by studies that examined the amplitude of p300 and LPP responses to cues while concurrently performing non-electrophysiological motivational system activation/attention orientation tests, such as the SRP, Stroop tests, and participant ratings of craving, image valence, and image arousal (e.g. Herrmann et al, 2000, 2001; Laar et al, 2004; Franken et al, 2004; Lubman et al, 2008; Field, Munafo, & Franken, 2009; Versace et al, 2010).

Cravings and ERP

Although there is a fairly extensive body of ERP literature examining cravings in response to drug cues, ERPs have been used very little to compare drug cravings and affective states, or drug cravings and cravings for URs (e.g. food). Furthermore, even less research has attempted to use ERP to tease apart the amount the AMS and DMS play a role in drug cravings. Nonetheless, a few existing studies do touch on these areas.

Lubman et al. (2008) found opiate addicts to display larger p300s in response to drug stimuli than to affectively positive UR-related images (erotic photos), and affectively neutral images. His results suggest that drug cravings activate the appetitive pathway, as drug cues in addicts and appetitive/UR-linked erotic cues in controls both produced significantly larger p300s than the neutral images, and both produced the same general activation pattern (in terms of waveform shape). However, no negative condition was included, so the defensive system could not be examined.

Versace et al (2010) found enhancement of the LPP in response to tobacco images in smokers, an effect that mirrored increases in LPP amplitudes occurring in response to positive valenced stimuli – a result that provides more evidence for the primacy of the appetitive system in craving. That said, UR-related stimuli

(such as erotic and food photos) were not used in the positive valence condition, so it cannot be confirmed that these images actually activated the appetitive system. The study can thus only be said to have compared tobacco cues to neutral and defensive system activating images. Furthermore, a non-smoker control group was not included.

Engelmann et al (2011) conducted a startle-probe ERP study on never-smokers, current-smokers, and 48-hour abstinent smokers (who were thus in nicotine withdrawal), during presentation of tobacco, and positive, neutral, and negative valence photos. His paradigm allowed for determination of both the valence and intensity of participant reactions. Tobacco images produced significantly more intense reactions in 48-hr abstinent smokers in withdrawal that were experiencing craving than any reaction observed in any other subject-condition pairing. However, the researchers did not examine the direction of activity for this condition, so it was impossible to determine if the response was appetitive or defensive. Also, greater emotional reactivity to negative stimuli was observed in the 48-hr abstinent smokers, which suggests that the experience of withdrawal likely includes continuous background defensive system activity, which may cause hyper-reactivity to affectively negative cues. Furthermore, a key analysis required to dissociate specific motivational pathway activation from other aspects of emotion and motivation was not conducted, which – in combination with the preceding issues – means no real conclusions can be drawn about what extent the DMS and AMS were involved in these results. Note, however, that the study was focused on differences in emotional reactivity induced by tobacco withdrawal, not cue-reactivity and the affective aspects of craving, so controlling for these the results would not have been relevant to the conclusions they drew. This limits the inferences that can be made using the study's results in regards to the motivational aspects of craving.

Finally, Dunning et al (2011) compared abstinent and currently using cocaine addicts to healthy controls on their ERP responses to cocaine-related, affectively neutral, affectively negative and affectively positive photos. Significantly greater early LPP amplitudes were observed in cocaine users upon observation of cocaine cues than in the controls. The researchers controlled for numerous participant characteristics that may have biased the results due to inherent differences between cocaine-users and other members of the population (e.g. depression and cigarette-smoking), which mitigated many confounds inherent in research on addict populations. However, the positive valence condition again did not use specifically UR-related stimuli, so activation of the appetitive system again cannot be confirmed. On top of this, ERP differences were

examined between photo categories rather than between reported cravings and valence reactions to specific stimuli (determined by ratings of each individual stimulus directly following observation). While it did examine participant craving for cocaine, their measure was based on ratings done before and after the image presentation. Thus, their paradigm did not have a self-report measure that could capture changes in craving status produced by exposure to the cocaine images. Also, the study did not examine the highly-sensitive p300 component separately from the LPP, which lowers the strength of their ERP-related findings. Finally, decreased LPP amplitudes were found in cocaine addicts in response to positive and negative-valence images, so the equal response to cocaine and emotional cues may have been due to this decreased emotional reactivity occurring concurrently with an increase in the relevance of cocaine cues. Thus, there was not necessarily a link to defensive and/or appetitive motivation in response to the cocaine cues, as simple decrease in overall motivation to everything but cocaine could also explain the results, which was, in fact, the tentative conclusion of the researchers in regards to this particular result.

Purpose

To help elucidate the extent to which each motivational pathway is linked to cue-induced tobacco cravings and differentiate between IST, AMM, and EIT, we designed a study that deals with each of the aforementioned issues simultaneously in a single experimental paradigm. To recap, no prior study comparing ERP responses to drug cues and affective stimuli in the context of determining activation of motivational pathways had all of the following features concurrently: 1) a condition intended to activate the appetitive pathway by the display of cues relating to URs (as in Lubman et al, 2008): most simply used high valence images regardless of content; 2) Self-reported craving and emotional valence ratings in response to each individual stimulus (as in Engelmann et al, 2011); 3) A non-addict control group; 4) A negatively-valenced image condition; 5) An examination of both the LPP and p300; 6) An experimental paradigm specifically focused on reactivity to affective and drug-related visual stimuli – e.g. Engelmann et al (2011) used a startle-cue paradigm primarily intended to examine alterations in reactivity brought on by withdrawal; and 7) A specific focus on tobacco.

Our method used a passive-viewing paradigm that had smokers and healthy participants passively view 6 categories of photos: tobacco, food (appetitive), neutral valence, non-appetitive positive valence, and threat-based negative valence. Following the presentation of each photo, we asked participants to form a

mental image of the stimulus and rate its vividness (mental image clarity), which causes participants to more deeply process the stimulus (if they follow instructions). Several preceding studies strongly suggest that this should increase the likelihood that a craving will result (e.g. Kemps & Tiggemann, 2007, 2009, 2010), as does EIT. Participants also rated whether or not they experienced a craving in response to the photo and the image's emotional valence, with valence included because it is virtually always modulated by the AMS and DMS (though not all changes in valence are entirely produced by motivational systems) (Weike & Alfons, 2004; Smith et al, 2006; Munoz et al, 2009). These ratings were then used to break the trials down into conditions for comparison of ERP activity - primarily tobacco craving (drug-cue), food craving (appetitive system activation), no craving plus negative valence rating (defensive system activation), and no craving plus neutral valence rating (no motivational system activated) (see Figure 5). This paradigm will not only allow us to examine whether cravings for tobacco activate the defensive or appetitive system, but can also provide us with a rough measure of the extent of this activation based on certain characteristics of the ERP response, as well as test for possible concurrent activation of both systems.

Hypotheses

If visual cue-induced cravings for tobacco do indeed operate via the hijacking of motivational pathways, there are 3 possible (rough) patterns of activation that may be responsible. Our paradigm was designed to dissociate between them. These are, as mentioned before, primarily AMS-associated tobacco craving (IST), primarily DMS-associated tobacco craving (AMM), and tobacco craving associated with both the AMS and DMS (EIT). (Each theory's predictions summarized in Table 6)

Note that given all of the evidence supporting the both the defensive and the appetitive models of craving individually, along with the specific evidence for EIT, we personally hypothesize that our results will best support the concurrent AMS and DMS activation model (see Table 6).

IST predictions

The IST-based appetitive model predicts greater LPP and p300 amplitude in the left hemisphere (but not the right) for both tobacco and food craving than any other condition. There should also either be no difference between tobacco and food craving, or a difference solely in the left hemisphere. The left hemisphere is linked to AMS activity, so if only the AMS is involved, it should primarily be the left

hemisphere displaying changes (Davidson et al, 1990; Sutton & Davidson, 2000). Note, however, that if the left-hemisphere amplitude increase produced by AMS were so great that the increased voltage could propagate to the right-hemisphere enough to produce significant results, we could alternatively observe bilaterally increased amplitudes for cravings vs. no cravings, but with a greater increase in the left hemisphere. This would support IST under the condition that there is either 1) no significant difference in amplitude between tobacco and food cravings; or 2) asymmetrically greater activation for one of the two systems, skewed towards the left hemisphere (in other words, the difference in amplitude between food and tobacco craving would be significantly larger in the left hemisphere than the difference between them in the right).

Emotional valence ratings of both tobacco and food craving-inducing images should be higher than ratings of neutral and negative images (Munoz et al, 2009). No predictions regarding vividness can be made with IST.

AMM predictions

An AMM-based defensive model predicts significantly greater p300/LPP amplitudes for both tobacco craving-inducing and negative-valence-rated images over neutral images – with no significant differences between the tobacco and negative conditions. These differences should be observed bilaterally, or in only the right hemisphere (Kayser et al, 1997), with no significantly greater activation in the left than right hemisphere. However, bilateral activation is a more likely result, as although spectral analyses of EEG data show greater right-hemisphere activation in response to negative images/ defensive pathway-activating cues, ERP-based analyses demonstrate such differences much less consistently. Bilateral activation would nonetheless still provide evidence for this second mechanism, simply because the aforementioned appetitive system-linked left-hemispheric p300/LPP amplitude enhancement is more robust; thus, equally bilateral activation would suggest that appetitive system activation is not present (Davidson et al, 1990; Sutton & Davidson, 2000).

Since this model argues that drug cues would act almost as threat-related cues by inducing fear of withdrawal distress, we should see lower valence ratings of tobacco-craving inducing images than either

food-craving inducing or neutral images (Baker et al, 2004). AMM cannot make any specific predictions about vividness

EIT predictions

If both motivational systems are concurrently active during tobacco cravings (EIT), we should see bilaterally increased p300 and LPP amplitudes in response both to photos that induce tobacco cravings, and negative valence-rated photos, with further increased amplitude in the left hemisphere for all tobacco craving-inducing, but not negative valence-rated photos (based on information in: Davidson et al, 1990; Sutton & Davidson, 2000; Baker et al, 2004; Lang & Bradley, 2010). Said left hemisphere amplitude increase should, in this case, be similar between tobacco and food – but not the activation in the right hemisphere. Alternatively, we could see increases in amplitude in both hemispheres that are larger in the left for all cravings, but with a significantly larger– yet hemispherically symmetrical – effect for tobacco cravings. This would only occur if observed food cravings were actually producing a small amount of DMS activation – in other words, if there was at least a bit of hunger present in some participants, and/or if left hemisphere activation were propagating to the right (as discussed previously). The LPP is more likely to display this result, as if a craving results from a photo, “elaboration” could begin very shortly after attention orients – potentially immediately after the p300. Elaboration is more likely than intrusion to produce unpleasant emotions, so if our observed food cravings did indeed have a tiny amount of associated hunger, the very small amount of NA/valence that could result from the minor deprivation would be more likely to appear at this slightly later phase. It is, however, essential that this increase be symmetrical, as this would imply that the difference between tobacco and food craving was primarily (if not entirely) DMS-related.

Also, participants should give tobacco-craving inducing images valence ratings that are higher than negative images, but lower than food craving-inducing images. We might also see no significant differences in valence rating between the neutral-rated images, and tobacco craving-inducing images. The positive and negative valences robustly induced by activation of each system could effectively cancel each out, resulting in a net valence closer to neutral. Analogues of this effect have been observed in previous studies, with simultaneous activation of both systems (induced using methods that did not involve craving) producing no modulation of the startle reflex (Lang, 1995) or alterations in the perception of pain (Meagher et al, 2001), as would result from activation of either system individually. In other words, concurrent DMS and AMS

activity predicts that cravings produce “mixed feelings” that average out to neutral, or closer to neutral than would be seen if only one of the two were activated. Finally, vividness is strongly predicted by EIT to be increased in the presence of drug cravings, as if EIT is correct, “elaboration” would kick in if the initial photo produced a craving (by acting as an ‘intrusive image’), which would result in rapid increases in the mental image’s vividness via the associative processes involved in elaboration. These processes should almost immediately activate neural pathways linked to other sensory traces associated with the drug, resulting in an influx of information that can be rapidly added to the initial mental image. This extra information would produce an increase in the clarity, detail, and realism (in other words, vividness) of the intrusive image, which would be, in this case, the mental image of the photo.

Methods

Participants

60 subjects were recruited via the Carleton University subject pool (SONA system). Thus, all participants were university students, and thus of adequate cognitive ability to understand and properly perform the study. Smokers not currently undergoing smoking cessation treatment were especially encouraged to participate, but this was not a requirement. After screening, 53 met the basic inclusion criteria: no presence of suicidality, sight in both eyes, at least moderate English fluency, perfect vision after correction, and no previous participation in a study involving visual imagery. We discarded 5 participants' data due to the presence of excessive noise and/or severe technical errors, leaving 48 in the dataset (25 male, 24 female; 15 smokers, 33 non-smokers). The mean participant age was 22, with all but 1 within a range of 18-29 years of age (this participant was 46).

Participants were instructed to eat 90 minutes before the study, but to avoid smoking tobacco in this period. Thus, there would be an average of approximately 2 ½ hours between the last meal or cigarette and the first displayed image in either respective category. In the case of food, this was intended to ensure participants were experiencing minimal – if any – hunger, thus helping ensure any food cravings present would be almost purely appetitive in nature, without the influence of potentially DMS-activating deprivation. This interval was selected somewhat roughly, but nonetheless with a basis in earlier research. Studies of appetite and meal frequency have shown significant differences in overall amount of hunger experienced in a day between the consumption of 1 and 2, and 2 and 3 meals per day, but not between 3, 4, 5, and 6 meals per day (reviewed in Leidy & Campbell, 2010). We then made the assumption that an average length day is about 16 hours, and that there would be approximately equal distances between meals 1 and 2, meals 2 and 3, and meal 3 and sleep onset. Therefore, an average participant should be eating about every ~2 hours thus seemed to be a safe distance to place between eating and the experiment to ensure that participants were neither hungry nor influenced by any potential effects stemming from satiety - e.g. an aversion to certain foods (Barkeling et al, 1990). With tobacco, we wanted to ensure that participants would experience tobacco cravings without the complicating presence of full physical withdrawal from nicotine, but with enough time between their last cigarette and the first smoking image to ensure they were at least somewhat deprived. 2

hours is the point at which nicotine withdrawal is able to start, with full onset of symptoms generally rising between 2 and 12 hours (Hughes et al, 1994). Most smokers in our study would thus be in the earliest stage of nicotine withdrawal, and therefore be feeling certain affective symptoms of nicotine withdrawal, but would not be experiencing any somatic symptoms. Daily smokers have a cigarette at a mean rate of one every 57 minutes (16.8 cigarettes and 16 hours awake each day on average), making a typical smoker in our study an average of 1.5 hours overdue upon observing the first tobacco image (Maurice et al, 2005). There should thus at least be psychological deprivation present, even if the mild affective aspects of nicotine withdrawal had not yet appeared upon viewing the first tobacco photo.

Questionnaire data

Subjects first completed the Shorter PROMIS Questionnaire (SPQ) for simultaneous assessment of multiple addictive behaviours, which tested for the presence (and severity) of addictions to tobacco, compulsive helping, alcohol, prescription drugs, recreational drugs, caffeine, shopping, sex, gambling, work, addictive relationship styles, food (in the form of “food bingeing”), food starving, and exercise (Christo et al, 2003). The Beck Depression Inventory (BDI; Beck et al., 1961), State-Trait Anxiety Inventory (STAI; Spielberger, 1983), and a general food craving questionnaire (Cepeda-Benito et al, 2000) were then administered to test for the presence and severity of depressive and anxious symptoms, and to assess the participant’s baseline level of hunger, respectively. This was followed by a miscellaneous data questionnaire consisting of questions about demographics, socioeconomic status, the presence of mental and physical disorders, visual acuity, sleep quantity, smoking status, psychoactive drug use (including tobacco), handedness, English fluency, educational attainment, political orientation, physical characteristics (IE height, weight), and opinion of smoking (See appendix for list of specific questions).

EEG and EOG data acquisition

EEG recordings were taken with a Compumedics Neuroscan 32-channel Quik-cap EEG headset with embedded Ag/Ag/Cl-sintered electrodes, amplified with a SynAmps RT high input impedance (10 G Ω) direct current amplifier, and referenced to the nasal supratip. Electrodes were arranged according to the international 10-20 system (Figure 1). Scalp impedance was kept below 2 K Ω for all electrodes, using a conductive electrolyte solution. Vertical electrooculography (EOG) readings were taken by 2 electrodes –

one 2mm above and the other 2mm below the bottom of the eye (Figure 4). The sampling rate was 1000Hz for both EEG and EOG. The E-Prime 2.0 experimental stimulus presentation software package (Psychology Software Tools, 2007) was used to present visual stimuli and in-study instructions to participants, while EEG data and events were simultaneously recorded to disk using Scan 4.4 (Compumedics Neuroscan, Charlotte, NC, USA). Events consisted of participant responses, presentation of photos (with markers specific to image type), the beginning and end of each block, and the display of specific questions (see Figure 4).

Environment setup

Past research has found that, regardless of duration, sounds have the potential to generate spikes in ERP data (Kushnerenko et al, 2001) – which does not exclude random background noises (e.g. experimenter coughing, hallway footsteps, etc.). Furthermore, minor sounds generated by the general experimental setup could correspond to stimuli - e.g. the small tapping sound from the key when participants respond, or perhaps an electrical hum. To control for these, 4 speakers, arranged to be approximately 3 feet from the front-left, front-right, back-left, and back-right of the participant were set up to play pink noise continuously throughout the experiment at 65db (see Figure 2). Also, the stimuli were displayed in the top-right corner of the room, with a sound blocking divider placed approximately 1.5ft to the participant's left, to prevent sound from seeping in from the side of the room containing the experiment controls (IE stimulus generating computer) (Figure 3).

A response box for rating vividness, emotional valence, and cravings was created via modification of a standard desktop computer keyboard, and fastened to the edge of a desk surface, precisely 1 foot from front of the chair upon which participants were seated (which was bolted to the ground). A standard plasma display was used for presentation of the stimuli, situated approximately 2.5 feet in front of the participants (bolted down), and 0.4 feet from the end of the response box. The EEG wire box was situated at the far left corner of the surface, out of direct line of site of the participant - if he/she is viewing the stimulus presentation screen (Figure 3).

Some research has found occipital EEG activity synchronization with the flicker frequency of fluorescent lighting (Kuller et al, 1998; Johansson & Sanstroem, 2003), as well as other inconsistent effects (Kuller et al, 1998; Kuller & Wetterberg, 1993). Furthermore, the more extensive steady state visually

evoked potential literature – involving induced EEG responses to flicker rate manipulations - has shown now well-established neural activity effects to 1-100Hz range flickers, which overlaps with the 50-120Hz (although usually 100-120) flicker of fluorescent lights (IE Muller et al, 1998; Herrmann, 2001). Since said effects were seen with light sources *aimed* at the eye, to avoid potential noise from flicker phenomena, the room was lit with a single upward facing standing lamp positioned to have no direct line-of-sight between the bulb and participant eyes. External light (via doorway cracks) was also blocked.

Room odour was controlled using a continuous release air-freshener, to minimize smell differences induced by IE temperature changes, previous participants, etc. It has long been well-established that odour affects EEG responses (IE Lorig, 1989; Klemm et al, 1992), and the use of a consistent odour eliminated variation from subject-to-subject, providing a moderate means of control over such effects.

The strong impact of electromagnetic fields on EEG (e.g. Kramarenko & Tan, 2003) was lessened by shutting off all proximal wireless networks. Subjects were also asked to turn off all electronic devices, especially cellular phones. Furthermore, the testing chamber was situated in an isolated area of the containing building away from major known sources of electromagnetic interference.

Selection of post-stimulus temporal regions of interest

Our time windows were determined by extracting intervals from studies examining components of interest, averaging these intervals, then rounding to the nearest ten (Eq. 1):

Equation 1

$$I_{ERP} = \frac{\text{round} \left(\left(\frac{\sum \frac{t_1 + t_2}{2}}{n_{studies}} - \frac{\sum \frac{t_1 - t_2}{2}}{2} \right) * 10 \right)}{10} \text{ to } \frac{\text{round} \left(\left(\frac{\sum \frac{t_1 + t_2}{2}}{n_{studies}} + \frac{\sum \frac{t_1 - t_2}{2}}{2} \right) * 10 \right)}{10}$$

Our ERP time windows were: p300:200ms-500ms; LPP = 450-900ms. All were calculated from 11 or more sources (Appendix H contains full list). After generating a grand average file combining all ERP files (of 0 to 1300ms post-stimulus) into a single waveform, we used visual inspection to select smaller regions of interest these calculated ranges. With the p300, we narrowed the peak down to a specific point using peak-picking software included in BESA 5.2. Since the LPP is a range, the entire component was chosen by visual inspection.

Stimuli

Two hundred photos were selected from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2005) based on image content and associated normative emotional valence ratings. 100 of our selected photos were affectively neutral, 30 were affectively negative, 10 were affectively positive, and 30 were of appetizing food. These pictures were matched such that each group had approximately equal mean arousal scores, as well as to have around the same number of pictures with arousal scores sitting in the upper and lower 20% range. Because the IAPS contains very few tobacco-related pictures, we used 30 photos of actions and objects pertaining to tobacco use that were created specifically for this experiment, or taken from various free image archives on the internet. This is a minor limitation of this study, as these photos had no associated norm valence and arousal scores, as are present for IAPS photos. However, the valence rating issue was mostly controlled for by the self-rated measures gathered from our participants directly after the viewing of each image, leaving only the arousal scores uncontrolled. Nonetheless, these photos possessed no properties suggestive of excessively high or low arousal. All photos in all categories were selected to exclude faces and erotica, and to minimize the presence of hands, as all three have unique effects on human EEG signals (McCarthy, Puce, & Belger, 1999). On the 1-9 IAPS normative rating scale for emotional valence (Lang, Bradley, & Cuthbert, 2005), all selected affectively negative images sat in the bottom 25% of all ratings and were below a score of 3.25 (mean = 2.3), all were neutral in the middle 25% and between 4.4 and 6.25, and all positive were in the top 25% and above 6.9 ($\bar{X} = 7.7$). (See Appendix A, Appendix B).

The stimuli were arranged into 5 blocks. 3 experimental blocks were shown in total, each consisting of 60 images: 30 from the specific category and 30 taken at random (across subjects) from the 100 neutral images present in the study. All images were used for all subjects across all trials, but which neutral images appeared in which block - and which trial - was random. To minimize expectation and habituation effects, whether a category-specific or neutral image was shown at any given stimulus was also kept random - although all 60 were always shown by the end of each block. A positive valence block was also present, which always contained the 11 positive images selected from the IAPS. Also, there was always a neutral block consisting of 10 images randomly selected from the experiment's 100 neutral images. All subjects were always exposed to all 201 stimuli by the end of the experiment.

Self-rating measures

Vividness

Vividness can be defined as the clarity, amount of detail, and richness of an internal mental image (D'Angiulli & Reeves, 2007). It is usually examined using the Vividness of Visual Imagery Questionnaire 2 (VVIQ2) (Marks, 1973, 1995; Pearson, 1995), which measures the tendency for a participant's images to be vivid – that is, it rates vividness as a participant characteristic. This was not, however, appropriate for our experiment, as our interest was in the relationship between the vividness ratings of individual images, and their link to the presence of acute cravings. We thus instead placed a vividness condition into each trial following display of the stimulus, within which vividness scores were taken by having participants fixate their gaze on a crosshair at the center of the screen, imagine the photo they just observed as sitting on top of the crosshair. Participants then rated the image using the response box on a 1-to-7 self-report Likert scale, with 1 for "no image formed", 2 for "very vague/dim", 3 for "somewhat vague/dim", all the way up to 7, for "perfectly vivid, as if actually viewing an image." Each stimulus thus had an associated vividness rating, which could then be compared to the 2 other characteristics of the stimulus that participants were asked to rate: emotional reaction (valence), and whether or not a craving was induced. This procedure has been successfully employed in numerous previous studies with similar image-rating based paradigms (e.g. Hertzog & Dunlosky, 2006; D'Angiulli, 2009; Alter & Balcetis, 2010).

This measure is important for several reasons. Firstly, cravings can be directly induced in a lab setting by having subjects imagine desirable items and rate the vividness of the mental image they generate (Green, Rogers, & Elliman, 2000). Thus, the presence of a vividness condition will facilitate the induction of cravings in our participants, as is intended by our experimental paradigm. This is especially important for the testing of EIT, since one of its central points is that cravings are greatly intensified by ruminating on the initial image of a desired object, and that *mental* images are what make the craving. Secondly, drug -related images are usually rated as more vivid in the presence of an addiction (Cepeda-Benito & Tiffany, 1996). We can thus use self-rated vividness as another indirect measure of craving. Higher vividness ratings are also usually assigned to food-related images, an effect that is enhanced when participants are experiencing cravings for food (Harvey et al, 2005). As these cravings intensify, the mental images of food can become intrusively vivid, to the point of being highly distracting (Steel, Kemps, & Tiggemann, 2006). This suggests

that vividness may be linked to appetitive system activity, which means that self-reported vividness may provide us with a rough measure of activation of this pathway as well.

Valence

Following the vividness condition, participants rated the emotional valence (meaning pleasantness or unpleasantness) of the preceding image using an adaptation of the Self-Assessment Manikin scale (SAM), which was the measure initially used to gather the normative IAPS scores (Lang et al. 1997; Lang et al, 2005). The original instrument consisted of nine small drawings representing people in various affective states, with each representing a different valence rating. However, we replaced these drawings with an analogous 9-point Likert scale that defined specific ratings using words, in order to keep the modality of the trial-rating conditions consistent. It was presented in the form of a screen instructing participants to “Rate the emotion the preceding image elicited on a scale of 1 to 9, where 1 means extremely unhappy and 9 means extremely happy.” Although participants received an in-depth explanation of the SAM when the study began, the preceding screen was displayed in each experimental trial as a reminder, and to prompt participants to record their valence rating via the response box.

Craving

In the instructions given prior to the experiment, cravings were described to participants as “extremely intense desires – especially for food or tobacco.” Several scenarios and examples were then provided for clarification – as one example, we told smokers to remember how they felt when in a situation when they had not smoked in many hours, were at the time unable, and had just thought about having a cigarette - such as on a long train or plane ride. Participants were also encouraged to ask questions about this measure. In each trial, craving was rated on a simple categorical scale that was presented via the following screen: “Press 1 if you experienced no cravings upon viewing the preceding image or upon generating the mental image, 2 if you experienced a food craving, 3 if you experienced a tobacco craving, 4 if you experienced a craving for both food and tobacco simultaneously, and 5 if you experienced any other craving.” This was displayed in every trial immediately after the valence condition. Although this scale can only gather dichotomous data on each type of craving, and is thus not as sensitive as a Likert scale, the already numerous conditions present in each trial - along with the large number of displayed photos - made brevity and the simplicity of each condition an important concern. Having participants rate food, tobacco, and ‘other’ cravings on Likert scales would

require greatly lengthening or complexifying each trial. Were we to add a screen asking participants to rate craving intensity that only appears if they report a craving on the first (categorical) measure, it would add confusion and discourage participants from reporting cravings, as doing so would lengthen the experiment. If we instead replaced the conditional measure with 3 separate measures, the number of ratings present in each trial would increase by 2. Both solutions could produce fatigue effects and result in participants rushing through the procedure, which would generate noisy and erroneous ratings that do not accurately reflect the participant's mental state. Also, the use of highly simplistic single-response scales reduces potential ruminations on craving, which can increase self-rated craving strength in a way not actually associated with the stimulus, but instead with the rating of craving itself. Furthermore, when many ratings are required and/or the amount of available time to assess craving is constrained (both of which were issues in the present study), simpler scales produce better results (Sayette et al, 2000). Indeed, previous studies have successfully employed dichotomous rating scales similar to ours in such circumstances (e.g. Shiffman et al, 1995). Furthermore, studies that utilize single-item dichotomous rating scales of craving still consistently find the construct to have diagnostic utility – that is, they are predictive of certain medically relevant outcomes (Foroud et al, 2007; Tiffany & Wray, 2012). Even some previous studies that used non-dichotomous single-item scales to assess momentary drug cravings found that converting the resulting ratings to a binary variable was more useful than trying to analyze based on level, as this produced a highly skewed distribution (e.g. Mol et al, 2005).

Procedure

On arrival, participants received and filled out Carleton Ethics Review Board-approved informed consent forms, which they were explicitly instructed to carefully read. They were then familiarized with the laboratory and experiment. Participants completed the questionnaires (BDI, STAI, etc.) - which were presented via a locked spreadsheet in Microsoft Excel - while the EEG and EOG electrodes were attached and calibrated. The pink noise was started upon completion of the questionnaires. Extensive initial instructions on our operational definitions of vividness, emotional valence in reaction to imagery, and craving were given via onscreen information presented with E-Prime 2.1. Baseline information was then taken: initially a 20s recording in which participants were instructed to stare at a crosshair at the center of the screen, followed by a self-rating of their *acute* mood on a 1-9 scale - 1 being extremely unhappy, 9 being

extremely elated. This scale has been validated and successfully employed in earlier research (IE Lee et al, 2011).

5 photo blocks were presented to subjects: practice, negative, neutral, tobacco, and positive. Practice and positive were always presented first and last, respectively: the former for participants to learn how to do the experiment before starting, and the latter to restore positive mood after the potentially distressing images in the negative block. Negative, neutral, and tobacco were presented in between the practice and positive blocks, in an order randomized across subjects. Each trial began with a photo displayed for 1.3 seconds, then the vividness, emotional valence, and craving tasks. All stimuli were followed by a blank screen shown for 1 second to prevent afterimages from influencing mental images (e.g. participants rating said afterimages instead of self-generated mental images of the photo), then a crosshair at the center of the screen. This cued participants to form a mental image of the preceding photo (as was instructed prior to each trial in the practice block) sitting on top of said crosshair, and rate their generated image's "vividness" via the response box. The vividness, emotional valence, and craving tasks were each followed by a 350ms blank screen (see Figure 5). At the end of each block, a break was taken for us to rehydrate the electrodes to keep impedance below 2Ω , as well as for participants to drink water if thirsty, which we encouraged to prevent interaction effects between hunger and thirst from occurring (Bolles, 1961). Mood ratings and 20s baseline recordings were conducted following each break, then again at the end of the experiment.

The practice block followed the same procedure as the experimental blocks. However, participants were encouraged to ask questions throughout, and responses from this block were discarded. Also, on-screen instructions were displayed prior to each image, as well as before each vividness task, image valence rating, and craving self-report condition. The positive block at the end of the experiment was also similar to the experimental blocks, except that it only contained IAPS-rated positively valenced photos. Following the positive block, a short debriefing/instruction screen was displayed to prevent participants from removing the EEG cap themselves, which could result in electrical shocks or damage to the equipment. The headsets were then carefully removed, and the participants given a full debriefing (see Figure 5).

EEG artifact correction

All artifact corrections were conducted using procedures and algorithms built into BESA 5.2 (Brain Electrical Source Analysis, MEGIS Software GmbH, Munich, Germany). 3-dimensional Laplacian spline interpolation (method outlined in Srinivasan et al, 1996) was used to correct contaminated single electrodes, which was required for approximately 4% of all channels. Eyeblink artifacts were removed using a blind-source separation-based independent component analysis (outlined in Jung et al, 2000). Large movement artifacts were identified using visual inspection, and all trial blocks containing one were not included in the analyses. The EEG data was then broken into 1300ms epochs beginning at stimulus presentation, and transformed to a baseline consisting of the 200ms prior to each epoch.

Analyses

The psychophysical, self-report, and participant characteristic data was analyzed using SPSS 20.1. Participants were divided into smoker and non-smoker categories based on self-report. Questionnaire data were evaluated with one-way ANOVAs, for comparison of smokers to non-smokers on sex, age, hours of sleep the preceding night, craving for food, state and trait anxiety, depression, number of addictions, and severity of addiction to tobacco.

To compare self-ratings of images that induced tobacco cravings against categories intended to link to appetitive and defensive motivational system activity, a “craving vs. image type” factor (henceforth referred to as “rating condition factor” with levels described as “rating condition”) was defined that divided trial ratings into 4 levels: 1) neutral image type with no craving (no motivational system activation); 2) food craving (appetitive system); 3) tobacco craving; and 4) negative image type with no craving (defensive system). Craving was based on self-report, while image types were based on each image’s original assigned category. Images that induced “other” cravings, or simultaneous food and tobacco cravings were excluded to avoid the confusion and confounds these conditions would introduce. Also, conditions where tobacco cravings were experienced by non-smokers were excluded, since our interest is in tobacco cravings in the context of addiction. The rating condition factor was used as a grouping variable in a one-way ANOVA, in which it was compared against emotional valence. Chi-square analyses, one-way ANOVA, Spearman’s r correlation analyses, and independent sample t-tests were conducted on participant ratings of the presented

photos, which were reported craving, generated mental image vividness, and emotional valence. These analyses included comparisons of these ratings between photo categories, mood ratings given for each the trial block, and participant characteristics (with participants divided into categories and compared).

Neuroscan SCAN 4.4, the MATLAB EEGLab plugin, BESA 5.2, and SPSS 20 were used for all analyses performed on the EEG data. Based on earlier research, our electrodes of interest for the p300 were primarily C3, C4, CP3, CP4, P3, P4, P7, P8, Pz, and Cz; and C3, C4, CP3, CP4, P3, P4, P7, P8, Pz, Cz, O1, O2, Oz, F3, F4, F7, F8, Fz, FC3, and FC4 for the LPP. These encompass all of the 10-20 system 36-channel EEG electrodes that displayed significant results in at least one of the aforementioned craving studies. For peak analysis of the p300, we examined the peak voltage, as is the standard procedure for this component (Carmel & Bentin, 2002; Donchin et al, 1983). The area under the curve (AUC) was used for the LPP, since it is a waveform component rather than a spike - peak analysis would thus be inappropriate. Furthermore, although they are more conservative overall, area measurements are less sensitive to noise (van Boxtel, 1998).

A 2-way condition x electrode Greenhouse-Geisser-corrected repeated-measures analysis of variance (ANOVA) was conducted on both ERP measures (p300 and LPP) to determine whether our main conditions of interest had an overall effect on peak amplitude. Three levels were defined for condition based on participant-reported trial responses: tobacco craving, food craving, and no craving; with each electrode defined as a variate. A Sidak pairwise-comparison test was conducted across all electrodes. We next conducted repeated measures multivariate analysis of variance (MANOVA) with condition and electrode location as independent variables, for both the p300 and LPP. Each electrode's average outputted peak voltage (and AUC, for the LPP) was treated as an individual dependent variable (henceforth called 'amplitude') that varied by participant.

Results

Participant characteristics

There were no differences between the included smoking and non-smoking participants (*smokers*: $n = 15$; *nonsmokers*: $n = 33$) - assessed via one-way ANOVA - in sex ($F_{1,47} = 2.123, p = 0.152$), total number of addictions as rated by the SPQ ($F_{1,47} = 18.722, p = 0.337$) or level of depression as measured by the BDI score ($F_{1,47} = 0.572; p = 0.453$). Despite nicotine's appetite suppressing (Jessen et al, 2005) and anxiogenic properties (Kenny, Cheeta, & File, 2000), no differences (via LPP) were found between participant groups in scores on the General State Food Craving Questionnaire ($F_{1,47} = 1.745, p = 0.193$), or STAI ($F_{1,47} = 0.927, p = 0.341$). Due to a questionnaire error (a poorly placed question) and missed responses by participants, two self-report categories did not have scores for all subjects, but regardless, no significant differences were seen between smoking and non-smoking groups on these measures: hours of sleep the preceding night ($n_{smokers} = 7; n_{controls} = 21; F_{1,26} = 0.876, p = 0.358$), and age ($n_{smokers} = 14; n_{controls} = 32; F_{1,44} = 0.084; p = 0.773$). Altogether, this demonstrated that, after eliminating problematic subjects that did not fit certain criteria, there was likely no difference between smokers and non-smokers on most potentially confounding participant characteristics (supports hypothesis 1 in Table 6).

Significant differences were observed between smokers and non-smokers on SPQ scores under the tobacco addiction category ($F_{1,47} = 66.531, p < 0.0001$), as well as severity of tobacco addiction ($F_{1,47} = 22.324, p < 0.0001$). This confirms that our division of participants into smoking and non-smoking categories based on self-reported smoking status matched ratings of level of addiction to tobacco (supports Table 6 hypothesis 2).

Subjective ratings of photos

As expected, tobacco and food photos produced more tobacco and food cravings, respectively, than any other photo category ($\chi = 4062.94, df = 16, p < 0.001$; supports Table 6 hypothesis 3). Also, smokers reported cravings in response to tobacco photos significantly more often than non-smokers ($F_{1,44} = 24.165; p < 0.0001$), while cravings for food were observed equally between smokers and non-smokers in response to food photos ($F_{1,44} = 0.112; p = 0.739$) (supports Table 6 hypothesis 4). Out of 1658 observed

cravings, only 487 were observed in response to any image not relating to food or tobacco. These results essentially confirm that the tobacco images had the intended effect of producing tobacco cravings specifically in smokers, and that the food images were equally appetizing to participants in both categories.

No significant differences in number of cravings induced per image were observed between any individual images in the tobacco condition ($\chi = 29.249, df = 29, p = 0.432$) or any individual food images in the food condition ($\chi = 40.904; df = 29; p = 0.07$). Furthermore, average valence ratings for each tobacco image that did not induce a craving sat above the negative and below the positive ranges with which the images were arranged into categories (3.72 to 5.39), as well as with food (5.61 to 6.61).

A significant main effect of rating condition was found on emotion ($F_{3,6871} = 1024.5, p < 0.001$) via one-way ANOVA. Sidak-corrected post-hoc tests found tobacco-craving inducing images to have significantly lower valence ratings ($\bar{X} = 5.79$) than those that induced food cravings ($\bar{X} = 6.38$), but significantly higher valence than the neutral ($\bar{X} = 4.71$) and negative ($\bar{X} = 2.38$) images (all $p < 0.01$) (Figure 6) (supports Table 6 hypotheses 5, 16, and 17; counters 6 and 11).

A one-way ANOVA - with all trials in the negative photo block again excluded - was conducted between the self-reported craving and vividness of participant mental images (with craving as the grouping variable). This displayed a significant main effect of craving ($F_3 = 13.313, p < 0.0001$). Post-hoc Sidak tests found significantly greater vividness ratings for photos participants rated as producing cravings for food ($p < 0.01$) and tobacco ($p < 0.05$) than those that produced no cravings. A significant positive correlation was observed between vividness and emotional valence ($r = 0.11; p < 0.01$), which had no visible bimodality. The same analysis was conducted with vividness grouped using an emotion/craving variable with 5 levels: 1) No craving and self-rated neutral valence; 2) No craving and negative; 3) No craving and positive; 4) Food craving; and 5) Tobacco craving. This displayed a significant main effect on vividness ($F = 74.151, df = 5, p < 0.0001$). Sidak-corrected post-hoc tests showed that vividness of positive valence was greater than that of all other conditions ($\bar{X}_{pos} = 5.70; all p < 0.001$), food significantly greater than all the rest of the conditions ($\bar{X}_{food} = 5.49; p < 0.001 for all$), except for tobacco where the difference was nonsignificant ($\bar{X}_{tob} = 5.30; p = 0.220$), and tobacco only nonsignificantly greater than negative ($X_{neg} =$

5.20; $p = 0.26$). Neutral-rated images were rated as significantly less than all other categories ($\bar{X}_{neu} = 4.8$; all $p < 0.0001$) (see Figure 8).

A one-way ANOVA of craving vs. background mood (rating before the block), with craving as the grouping variable, found a significant effect of mood on craving ($F = 20.123, df = 4, p < 0.0001$). Sidak-corrected post-hoc tests found significantly higher mood for food than no craving ($p < 0.0001$); and for food than tobacco craving ($p < 0.05$). There were no significant differences between tobacco craving and no craving ($p = 0.882$). (Supports Table 6 hypothesis 18; counters 7, 12, and 19)

ERP

p300

The repeated-measures ANOVA demonstrated that the p300 varied as a function of both condition ($F_{5,25} = 4.933, p < 0.01, \varepsilon = 0.417$) and electrode ($F_{17,13} = 2.939, p < 0.05, \varepsilon = 0.191$), justifying univariate analyses. Post-hoc tests found significantly larger p300 amplitudes for both food cravings than tobacco cravings ($p < 0.05$), and for both types of craving than for non-craving-inducing neutral images (see Table 1 for full results).

A significant main effect of condition on amplitude across all scalp locations was observed via MANOVA (*Pillai's* $F_{100,650} = 1.428, p < 0.05$), consistent with the preceding ANOVA. Pairwise comparisons found multiple electrode-specific differences in p300 amplitude between conditions (full results reported in Table 2). Significantly larger amplitudes were observed for food and/or tobacco craving versus no craving at electrodes C3 (food, $p < 0.001$; tobacco, $p < 0.05$), CP3 (food, $p < 0.001$; tobacco, $p < 0.01$), P3 (food, $p < 0.05$, tobacco, $p < 0.0001$), P8 (food, $p < 0.05$), and Pz (food approaches significance, $p = 0.07$; tobacco, $p < 0.05$).

The greater number of significant left-hemisphere electrodes suggests a greater increase in activation in this hemisphere in response to tobacco craving. To test this, we used paired-samples t-tests to compare the left vs. right hemisphere difference between the p300 amplitude of the tobacco and no craving conditions. Electrodes found significant in the preceding MANOVA were compared against their counterpart in the opposite hemisphere: P3 vs P4, C3 vs C4, CP3 vs CP4, and P7 vs P8. We found significantly greater p300 amplitude for tobacco craving vs. no craving trials in smokers in electrode P3 than its right hemisphere

counterpart P4 ($t = 2.291$, $df = 13$, $p < 0.05$). While the other 3 electrode-pairs did not display significance, the left hemisphere electrode consistently displayed higher p300 amplitude ($\bar{X}_{C3} - \bar{X}_{C4} = 0.36441$; $\bar{X}_{CP3} - \bar{X}_{CP4} = 0.034$; $\bar{X}_{P7} - \bar{X}_{P8} = 1.12594$). This is likely attributable to a low observed power (Pillai's trace: 0.102). (Supports Table 6 hypothesis 8; counters 13; mixed result for hypothesis 20).

Overall, the craving conditions are significantly different from the other 2 (no craving and negative valence), suggesting that these electrodes are sensitive to the detection of craving. A Sidak-corrected post-hoc test found no significant differences in p300 amplitude between food and tobacco craving on any electrode except P3, where tobacco craving was greater than food craving ($p = 0.46$). Significantly larger p300 amplitudes were observed between both craving (food and tobacco) conditions and no craving, solely on left-hemisphere electrodes: C3, P3 & CP3 ($p < 0.05$ for both all food vs. no craving; and tobacco vs. no craving). Virtually no activity was seen on the right hemisphere, excepting an aberrant drop in p300 amplitude in response to food images in comparison to neutral in P8 ($p < 0.05$), which was not present in any other condition at any other electrode. This same result with food approached significance in TP8 ($p = 0.08$), but was not mirrored by the tobacco craving condition in either P8 or TP8 – in fact, the tobacco craving spike went (non-significantly) in the opposite direction in both cases.

LPP

The LPP was analyzed with all 20 electrodes of interest (rather than 18) due to the tendency for the LPP to display a slightly more frontal scalp distribution. Repeated-measures ANOVA showed that the LPP also varied as a function of condition ($F_{5,25} = 11.113$, $p < 0.001$, $\varepsilon = 0.345$) and electrode ($F_{17,13} = 4.252$, $p < 0.01$, $\varepsilon = 0.407$). Post-hoc tests (with Bonferroni corrections) demonstrated larger areas under the curve for tobacco cravings than food cravings; and for tobacco and food cravings than non-craving inducing neutral images (all $p < 0.01$).

A significant main effect of condition on area under the curve across all scalp locations was also observed via MANOVA (Pillai's $F_{100,650} = 1.341$, $p < 0.05$). Bonferroni-corrected pairwise comparisons found multiple electrode-specific differences in LPP amplitude between conditions, with significantly larger areas under the curve observed for food and tobacco craving versus no craving conditions at left hemisphere electrodes, and most electrodes at the midline and in the right hemisphere. Tobacco craving had a larger area

under the curve than food craving at most electrodes as well, in both hemispheres and at the midline (see Table 3, Table 4, Table 5 for all results). Also, there was a greater area under the curve for images rated to have positive valence than neutral or negative valence, with negative valence also showing a significantly larger LPP than neutral valence for half of the electrodes of interest – specifically F3, Fz, Cz, Pz, Oz, C3, C4, CP3, and CP4 ($p < 0.05$). When the value of these electrodes for negative valence was added to their value for food craving, minus the amount observed for neutral valence with no craving, their areas under the curve became essentially the same as those in the tobacco craving condition, with no significant differences whatsoever between the conditions – with the exception of Cz ($t = -2.418, df = 11, p < 0.05$). Furthermore, Pz, C4, CP3, and CP4 significantly correlated in this condition, which was unexpected given the small sample size left in this analysis after removal of non-smokers from the tobacco craving condition, and the smaller number of subjects that reported negative valence ($n = 12$ for all electrodes. Pz: $r = 0.683, p < 0.01$; C4: $r = 0.774, p < 0.005$; CP3: $r = 0.635, p < 0.05$; CP4: $r = 0.633, p < 0.05$). All other electrodes displayed nonsignificant moderate positive correlations in the correct direction (F3: $r = 0.301$; Cz: $r = 0.426$; Oz: $r = 0.401$; C3: $r = 0.258$), excepting Fz, which displayed a tiny correlation in the opposite direction (Fz: $r = -0.090$).

Although the same number of electrodes showing greater area under the curve for tobacco craving than neutral imagery were observed across both hemispheres, a paired-samples t-test found greater area under the curve in electrode P7 than its right hemisphere counterpart P8 ($p < 0.05$), with the same result approaching significance for electrode CP3 vs. CP4 ($p = 0.07$). There was a significant correlation between all 8 left-hemisphere electrodes and their right-hemisphere counterparts (for all electrodes: $r > 0.6, p < 0.05$). Note that the pairs were selected based on which electrodes were significant in the preceding MANOVA. Thus, the results point towards increased bilateral LPP activation linked to tobacco cravings that occurred in nearly the same pattern in both sides of the brain, with activation in the left-hemisphere increased slightly further than that in the right . (Supports Table 6 hypotheses 21 and 23; counters 9, 10, 14, and 15)

Discussion

Our findings strongly support the hypothesis that tobacco cravings are linked to activation in both the AMS and DMS, although AMS activation appeared to have a slightly larger role. This may have been due to the relatively small amount of deprivation participants were experiencing from nicotine (though it should have been enough to produce some DMS activation, which we did indeed observe). The results supported certain aspects of elaborated-intrusion theory (EIT) – primarily those relating to intrusion, as the elaboration phase is less relevant to cue-reactivity and thus could not be examined as deeply (although elaboration was touched on in our paradigm by having participants generate mental images of each photo and rate their vividness). Our data produced several lines of converging evidence for these tentative conclusions.

Valence

EIT was supported by analyses of our participants' subjective ratings of individual trials. Trials with cravings produced higher valence ratings than those without (Figure 6). This held even when images in all conditions but tobacco and food were removed. Since no images in the tobacco and food conditions had any large differences between others in the same condition on either valence or ability to induce cravings (measured by number of cravings the image produced), it is very likely that this result came from craving itself, and not from image properties. Given that greater self-rated emotional valence is linked to higher appetitive motivational system activation (Gable & Harmon-Jones, 2008a, 2008b, 2010), this demonstrates that both food and tobacco cravings likely link to the AMS. Also, tobacco cravings displayed lower valence than food cravings, but still higher than those that did not induce cravings. This suggests that DMS activity may have been present specifically for this condition, since the result was closer to that seen with negative valence. The fact that tobacco craving-inducing images still also produced higher valence than neutral images, however, suggests that the AMS may be more involved than the DMS. We would expect equal valence for neutral and craving if both systems were involved to the same degree, as each system would in that case push the valence up or down equally. However, it must be noted that it is possible that DMS activation may “pull down” emotional valence to a smaller degree than the AMS pulls valence up. Thus, we can only infer the presence of both types of activation from this finding, not the amount each system plays a role in the observed valence ratings is at best speculative in nature. Furthermore, this line of evidence does

not eliminate the possibility that tobacco cravings are simply less intense than food cravings. However, this does not seem particularly convincing, given: 1) the unusually great difficulty of quitting tobacco over and above that of other drugs, which have NA reduced upon each use, but usually do not have extra ‘hits’ besides an initial use (e.g. one injection, one pill or handful of pills), unlike the dozens of ‘hits’ present in a single cigarette (Zhu et al, 2000; Piasecki, 2006); and 2) because participants ate prior to the study. Thus, less hunger should be present than desire for nicotine, especially given that the length of time that should have elapsed since our smoking participants’ last cigarette should have been long enough that they would be in a state of deprivation. Although hunger may have an effect solely on the DMS (given that it’s an unpleasant state of deprivation), it seems more likely that it should have at least some effect on the appetitive nature of food, as is evidenced by the greater biological reaction organisms have to food in a state of hunger (e.g. salivation), which appears appetitive in nature. One could argue that these reactions are based on deprivation, but they only occur in the presence of food, and furthermore, result in greater reported enjoyment of the food when it is eventually consumed. Nonetheless, these arguments are speculative, and this evidence does not confirm the presence of DMS activity with tobacco cravings, it is merely strongly suggestive – as is the case with all self-report measures that examine motivational system activation.

Affect

Unexpectedly, both tobacco and food cravings were linked with positive background affect, rather than the NA that would be expected if cravings were induced by need to escape withdrawal distress. This result was not predicted by any of the three theories. That said, tobacco craving was associated with lower valence than food craving. This could indicate that a certain level of background positive affect must be present for cravings to occur at all, with NA produced by withdrawal existing as a concurrently occurring emotion that lowers overall mood, without eliminating the AMS activation that produced the initial positive affect. In other words, perhaps NA produced by withdrawal is generally “overlaid” on top of background positive affect (at least initially), and it is this continued presence of some approach motivation that allow drug-seeking behaviour. Observations of patients with the melancholic vs. atypical subtypes of depression somewhat corroborate this explanation. Melancholic depression is characterized by a lack of background positive affect, with no mood brightening occurring in response to positive external events (anhedonia). These patients tend to avoid appetitive activities such as eating. Patients with atypical depression (which is

not anhedonic but instead typified by the presence of high levels of NA), on the other hand, instead eat more and likely experience more cravings (APA, 2000). Since our participants were only in the very mildest stages of nicotine withdrawal, this overlaid NA would only be of very low intensity. Thus, the withdrawal-related NA could be small enough to prevent the background approach motivation/positive affect required for the craving to appear from being washed out. If this is the case, then dual AMS-DMS activation during cravings (and thus EIT) is supported.

Nonetheless, this interpretation must be looked at with caution, as there are several alternative explanations for this unexpected relationship between background mood and cravings. Firstly, demand characteristics may have skewed the results. Greater altruism and cooperation is observed in the presence of positive affect (Moore et al, 1973), so this finding may stem from participants who were already in a good mood purposely (though perhaps unconsciously) rating images in a way they think are supportive of the experiment's expected results. This is suggested by the presence of 2 non-smoking participants who reported numerous tobacco cravings. They were clearly not experiencing cravings by any definition given in the instructions (and these scores were thus excluded from the data), but an altruistic desire to create what they felt 'should' be the result may have driven them to rate tobacco images as craving-inducing. Indeed, both participants had very high scores on affect – although this cannot be tested for statistical significance given a sample size of only 2. Secondly, it could be that participants had trouble defining their mood, with cognitive impairment produced by mild nicotine withdrawal (Shoaib & Bizarro, 2005) leading to a further misunderstanding among the smoking group, which could have resulted in mood rating inflation. Our system for rating mood was exploratory in nature, with little (if any) research comparing it to trial-based ratings (unlike all of the other measures), so this issue is not unlikely. Thirdly, participants may have been hiding negative affect (NA), given that this behaviour is prescribed by social norms (Eid & Diener, 2001). This could result in participants who were experiencing higher levels of NA actually rating their mood more positively as a defence mechanism (essentially, self-deception about their own affective state).

Although the only theory that seems able to account for this finding is EIT, this is stated with caution, given all the unexpected nature of the result, and all of the aforementioned potential issues with our mood rating scale. Although the potential presence of some of these issues in mood rating suggest they may have played a role in results obtained using other self-report measures, these issues are mitigated by the inclusion

of ERP measures, as ERP results are generally not affected by such factors as demand characteristics and self-deception (Marks & Isaac, 1995).

Vividness

The higher vividness ratings observed for craving-inducing images than those that were emotionally neutral as well as non-craving-inducing provides converging evidence that cravings were indeed a result by our food and tobacco photos, as the vividness-craving association has been reported in multiple previous studies using drug and UR-related stimuli – albeit not concurrently using both types of stimuli (e.g. Harvey et al, 2005; Tiggemann & Kemps, 2005). Furthermore - although it is not confirmed – the tendency for vividness to be associated with virtually any type of image that produces goal-directed approach behaviour has led numerous researchers to hypothesize that AMS activity in general positively correlates with vividness (e.g. May et al, 2004; Harvey et al, 2005; Kemps & Tiggemann, 2007, 2010). This was even observed in a preliminary study of ours, with food images producing more vivid mental images than threatening, neutral, or pleasant images, with some exploratory results hinting that hunger may increase food vividness ratings. The greater vividness of food (in other words, the purely appetitive stimuli) than threatening photos was particularly telling, as this connected vividness to the AMS more strongly than to the DMS (Faulkner et al, 2011). This lack of connection between very high vividness and DMS activation was also suggested by the present study, as shown by the general positive correlation between valence and vividness irrespective of the presence of craving. Thus, our greater observed vividness for food craving is likely indicative of AMS activation. Slightly – rather than greatly – increased vividness, on the other hand, seems to link with negative valence and the DMS, as was shown by our observation of significantly greater vividness ratings for negative valence (by rating) images than neutral, but less than food images. Tobacco craving sat directly between the defensive and appetitive stimuli (negative valence and food), such that it displayed no significant difference from either, despite the significant difference between food and negative valence. This could mean one of three things for tobacco cravings: 1) the DMS and AMS are concurrently activated; 2) solely the DMS is activated, but to a huge extent; and 3) only the AMS is activated, but weakly. Despite the ambiguity, this provides evidence for motivational system activation, regardless of whether it's AMS or DMS. Furthermore, the concurrent lack of significant vividness differences between tobacco craving and negative valence, and tobacco and food craving, with negative significantly different from food, makes a concurrent activation

hypothesis most plausible, since this suggests that tobacco cravings cannot be dissociated from either the AMS or the DMS, even though the AMS and DMS can be dissociated.

Our vividness results also provide evidence for EIT, beyond its prediction of craving-related activation of both the AMS and DMS. EIT predicts that intensity of craving is correlated with intensity of imagery, and furthermore that the mere presence of craving increases the vividness of a mental image (May et al, 2010). This was observed in our data, with cravings producing higher vividness than any other category, including emotional photos. However, note that the other major theories of craving (AMM and IST) do not examine mental imagery and vividness, and make no predictions about it. Thus, while this finding supports EIT, it is not necessarily inconsistent with other theories of craving.

P300 and LPP

The p300 and LPP's patterns of activation indicated that motivational system activity was linked to cravings. This was suggested by the increased amplitude of both components for food and tobacco cravings vs. no-craving, even when emotional valence was controlled for. These activation patterns occurred in the regions expected for each component: primarily parietal for the p300; and parietal, central, and frontal for the LPP. Also, both components appeared at approximately the latencies expected. Together, this strongly suggests that the significant patterns observed in the regions of interest selected did indeed link to these components, and thus that it is reasonable to interpret our ERP data in the context of p300 and LPP-related research literature.

p300

Our p300 results primarily supported activation of the AMS in conjunction with cravings of all types. Considerably more left hemisphere electrodes than right displayed a significant difference between craving-inducing and neutral images. In fact, very little p300 amplification was observed in the right hemisphere overall, with only a single electrode displaying significance (P8), and only in response to food cravings. Interestingly, Nijs et al (2009) also found electrode P8 to display greater p300 amplitude in response to food – specifically in high “external eaters” – which the study suggested were more likely to experience cravings for food. Thus, this seemingly aberrant finding may in fact stem from a type of neural activation specific to food imagery, rather than something that relates solely to motivational system activation. However, this is a

strictly hypothetical interpretation, and further study would be necessary to determine whether this: 1) actually represents a part of a “food component;” 2) is an erroneous finding; 3) suggests a limitation of treating only the left hemisphere as responding to appetitive stimuli; or 4) demonstrates that some DMS activation does occur in response to food even in the absence of hunger. Note, however, that the latter is unlikely given the definition of the AMS as relating to motivation towards URs such as food, and the lack of any deprivation that the food images could be drawing attention to, which would be the source of any unpleasantness food photos would be able to produce. The second explanation is also unlikely, since our result replicates that of Nijs et al (2009). The first and third explanations seem most reasonable, given the somewhat mixed findings relating to p300 lateralization.

Tobacco cravings produced higher overall p300 amplitude activation in the left hemisphere than food cravings, suggesting that they may in fact be more intense than regular food cravings. The lack of right hemisphere activation in response to tobacco cravings does not, however, provide evidence that the DMS is not involved – it merely suggests that the DMS is not linked to tobacco cravings at this early stage of processing. Furthermore, evidence for differential patterns of activation linking to specific motivational systems (appetitive vs. aversive) is not nearly as strong for the p300 as it is for the LPP (Van de Laar et al, 2004; Cunningham et al, 2005; Gable & Harmon-Jones, 2010), with mixed findings reported in studies examining p300 laterality in this context (Karhunen et al, 2000; Nijs et al, 2009). Indeed, if lateralization in the p300 does not, in fact, strongly link to appetitive vs. defensive motivation, then this too may explain the seemingly strange result seen with electrode P8 in response to food cravings. Also, any link the p300 has to the AMS and DMS could merely be a result of the p300’s temporal proximity to the LPP. It should also be noted that tests of individual electrodes only found significantly greater activation for food than tobacco cravings at one location (and only barely): left-hemisphere electrode P3, which calls into question the actual amount that tobacco cravings are more AMS-activating in nature, especially given the significant activation of the right-hemisphere electrode P8 with food craving.

These misgivings aside, the fact that the p300 displays an increase in amplitude solely in the left hemisphere for tobacco cravings does still suggest – albeit non-definitively - that tobacco cravings have greater AMS-activating properties at this early stage. This supports IST, and somewhat contradicts AMM. In regards to EIT, it is neither contradictory nor supportive, as EIT suggests that AMS activation tends to occur

earlier in the course of a craving than DMS, especially when severe deprivation is not present (Kavanagh et al, 2005).

LPP

The LPP results, on the other hand, were strongly suggestive of activation in both systems, and furthermore, had much larger effects and were overall more robust than our p300 or self-report results. We were also able to confirm that our LPP results were likely motivational system-related, as there was significantly greater LPP area under the curve for both the negative and positive valence (by participant rating) trials than for neutral valence at most electrodes (albeit not all). Also, there were significant differences between the negative and positive conditions, showing that the AMS and DMS produced alterations in the LPP that could be differentiated.

Unlike the p300, tobacco- and food craving-containing trials had significantly larger LPP amplitudes than no-craving trials in *both* hemispheres, which provided evidence for DMS activation associated with cravings (as this is the pattern generally produced by DMS activity). Our strong (and consistent, though not always significant) correlations between the left-hemisphere and right-hemisphere patterns of LPP activity for the craving conditions suggested that the same underlying neural mechanism was likely responsible for activation in both hemispheres. Also, visual inspection of the difference waves between tobacco cravings in smokers and images of tobacco viewed by non-smokers (Figure 7 contains examples) suggested that a similar pattern of increase in amplitude occurred in both hemispheres between 400 and 1000ms. AMS activity was evidenced by the even greater increase seen in left-hemisphere amplitude than right for both tobacco and food cravings vs. no cravings.

It was initially somewhat surprising that both food and tobacco cravings produced bilateral activation in the LPP, as we expected food to link solely to the AMS. Nonetheless, this was one of the two possible outcomes predicted by EIT – but not any other theory (Table 6, Hypothesis 21) – as tobacco cravings still produced greater overall activation than food cravings, in both hemispheres. EIT views food cravings as also being both AMS and DMS activating, but only when at least some deprivation is present. It thus follows that the amount of time between the last time participants ate and the presentation of food photos was still too long to ensure that no hunger whatsoever was present. This was likely caused by the rough nature of our

method for selecting the 2 hour interval, which was necessary due to the paucity of research examining this in humans. EIT still predicted this greater level of overall LPP activation for tobacco cravings (than food cravings) under this circumstance. This was because the smoking group should be experiencing much greater feelings of deprivation (from nicotine) and thus more DMS activation during tobacco cravings, as the time between their last cigarette and the experiment (2 hours) should have almost ensured the presence of mild affect-related nicotine withdrawal symptoms. The validity of our timing for tobacco was demonstrated much more directly by earlier research (Hughes et al, 1994; Maurice et al, 2005), so fewer assumptions were required when setting this interval.

One could argue that the greater LPP amplitude for tobacco than food cravings may have instead been due to the aforementioned consistent association of nicotine reward with a single stimulus (cigarettes), while food reward is associated with numerous stimuli (Zhang & Luck, 2009; Versace et al, 2010). However, this seems unlikely, as adding the negative valence (by rating) and food craving areas under the curve together did not produce a result significantly different from the area under the curve produced by tobacco craving at most electrodes where both conditions displayed a significant effect. The vast majority showed mean differences less than 100 microvolts, which is miniscule. In other words, adding the DMS-related pattern of activation (negative valence) to the primarily AMS-related pattern (food) resulted in a waveform closely resembling that produced by tobacco craving when ERP activity not relating to either motivational system was removed. Also, the additive condition (negative plus food craving) significantly – and often strongly – correlated with the pattern and level of activation produced in the tobacco condition. Furthermore, the difference between food and tobacco craving was *symmetrically* bilateral, suggesting all extra activation was DMS-related. These findings provided evidence that the greater LPP amplitudes for tobacco were a result of a much greater level of deprivation (and thus DMS activation) experienced by our participants when craving tobacco than when craving food. In fact, these results suggest that AMS activation may produce an increase in LPP activation in both hemispheres, simply to a much smaller degree in the right hemisphere. Indeed, because ERP signals propagate across the entire skull, the significant effect observed in the right hemisphere may actually be due to activation that originated in the left hemisphere. Given all of this, our LPP findings seemed to demonstrate concurrent DMS and AMS activation in tobacco cravings, and likely concurrent

activation of both systems in our observed food cravings as well, but with only extremely weak activation in the DMS.

Limitations

Although there were numerous lines of converging evidence supporting our primary hypothesis, a number of issues were present in our design that prevented it from examining certain measures that could provide further support for our claims. Firstly, there was only a 100ms pause between the participant rating of craving and the presentation of the next image. While this was not a problem for the ERPs on which this study focused, it prevented examination of a potentially interesting component: the stimulus preceding negativity (SPN). This is an ERP that occurs in anticipation of an emotionally-relevant stimulus, when participants are motivated to attend to it. It occurs within the 2 seconds prior to presentation of an image under conditions where other emotionally-relevant pictures have been shown in a sequence of stimuli, and participants are cued that a relevant image is impending (Hillman et al, 2000; Takeuchi et al, 2005). Two earlier studies found a significantly (and considerably) larger SPN in smokers than in non-smokers in anticipation of tobacco-related images (Parker & Gilbert, 2008). It would have been logistically impractical for us to include the required 3-4 second pause (Costell et al, 1972) between the final rating and the next image – this would have added a considerably amount of time to the experiment, and thus introduced problems with participant attention.

Two inter-stimulus self-rating measures lacked necessary details to fully confirm the affective- and craving-related results. Firstly, on the emotional scale, participants were not asked to rate either the “arousal” or “dominance” of the stimuli displayed (only the valence), which forced us to completely rely on the initial IAPS ratings for these other 2 measures. Thus, most of our tobacco images were left without scores on either dimension. These measures would have been valuable for examining the salience of the addiction-related stimuli in our participants. In the case of arousal, rating this in tandem with valence should produce results with a much closer link to craving than either measure used alone, given the previously observed link between craving and arousal (Weinstein et al, 1997; Kavanagh et al, 2005). Dominance would have been particularly interesting to examine, as loss of control plays a large role in addiction, and is, in fact, one of the defining features (Lyvers, 2000). Also, dominance is frequently ignored in the ERP literature on emotion, despite some preliminary studies showing it may have profound effects on EEG, especially regarding

lateralization (Demaree et al, 2005). Thus, utilizing it could have provided more information about the measure itself, on top of helping support hypotheses about craving. Furthermore, a number of previous studies have shown it to potentially have a very strong link with cravings (Munoz et al, 2009). Secondly, while subjects were asked if a craving was present after images were displayed, and of what type, we did not include a measure of craving intensity. Although information from a yes/no paradigm of that sort is still of value, considerably more sensitive results would be obtained from a Likert-type rating scale. A future study will include an inter-stimulus question on image arousal, and another on craving intensity (if a craving is reported).

Demand characteristics were not strongly controlled for in the self-ratings. The inter-stimulus questions made it obvious what the study was examining, especially when coupled with negative, tobacco, and food imagery. A future study should include a more implicit test of craving, such as eye tracking or a visual dot probe task (Mogg et al, 2003). While ERP measures are not affected by demand characteristics, it would have been valuable to have a second measure free of this effect for the sake of better validation of the craving results.

While our number of smokers ($n=16$) was sufficient to test our primary hypotheses, having a greater number – and a larger sample size overall – would have allowed us to look for comparisons with other measures shown to have relationships with ERP components and cognitive processing, such as socioeconomic status (Kishiyama et al, 2009) and political orientation (Amodio et al, 2007). More selective recruiting, better control for technical issues that cause discarding of data due to noisy waveforms, and a larger number of participants will allow us to probe the relationship craving has with these measures in future research.

No test besides self-report was used to test if participants had followed directions to eat and smoke 90 minutes prior to the study. Thus, we could not ensure that participants were not in fact hungry, nor could we ensure that the smokers were in a state of mild nicotine deprivation. A salivary swab and/or breath sample test for nicotine and blood glucose level should be used in future studies to provide biological evidence corroborating these participant reports.

There were numerous technical problems with electrode Cz. It produced unusually large amplitudes in a large number of our participants, which were too great in magnitude to be due to ERP effects. Cz amplitudes were often in the realm of thousands of microvolts greater than any other electrodes. This was consistently entirely limited to Cz, without the Cz readings affecting any surrounding electrodes. Interpolating Cz was not always possible if any other electrodes also required interpolation, because Cz's central location meant interpolating both Cz and another midline electrode resulted in the distortion of numerous surrounding electrodes' waveforms. We were thus forced to remove Cz from certain analyses. Furthermore, this makes any significant results we found for Cz somewhat questionable.

Summary and conclusions

Regardless of the study's limitations, our results nonetheless primarily favoured the hypothesis that tobacco cravings involve the activation of both the AMS and DMS, especially since multiple types of evidence we gathered concurrently supported this hypothesis. Thus, the intrusion aspect of elaborated intrusion theory (Kavanagh et al, 2005) was relatively well-supported. Convergent evidence for EIT was also provided by our results relating to mental imagery vividness (Table 6). Nonetheless, future research is needed to confirm this finding through other experimental modalities, and to fill in gaps left by certain limitations of the current study.

Tables

Table 1: P300 - post-hoc results from 2-way within-subject repeated measures ANOVA comparing self-report conditions across 11 electrodes, for p300

(I) Condition	(J) Condition	Mean Difference (I-J)	Std. Error	Sig.
No Craving	Food craving	-.198***	.056	.001***
	Tobacco craving	-.460***	.139	.002***
	Negative valence	.074	.049	.136
	Neutral valence	-.061**	.027	.035**
	High valence	-.055	.080	.496
Food craving	Tobacco craving	-.262*	.151	.066*
	Negative valence	.124	.073	.103
	Neutral valence	.137**	.057	.023**
	High valence	.143	.105	.185
Tobacco craving	Negative valence	.386**	.153	.018**
	Neutral valence	.399***	.136	.007***
	High valence	.405**	.152	.013**
Negative valence	Neutral valence	.014	.051	.789
	High valence	.020	.072	.787
Neutral valence	High valence	.006	.074	.938

Significance indicated by asterisks: * $p < 0.1$ (approaching significance); ** $p < 0.05$; *** $p < 0.01$

Based on estimated marginal means, with Sidak adjustment for multiple comparisons utilized.

All results from data produced by averaging across electrodes C3, C4, CP3, CP4, Cz, Fz, P3, P4, P7, P8, and Pz

Table 2: p300 - 6 condition x 11 electrode repeated measures MANOVA post-hoc Sidak test results

<i>Left hemisphere</i>					
Electrode	(I) Condition	(J) Condition	Mean Difference (I-J)	Std. Error	Sig.
C3	No craving	Food craving	-.912	.223	.001***
		Tobacco craving	-.731	.313	.070*
	Food craving	Tobacco craving	.180	.375	.634
CP3	No craving	Food craving	-.921	.225	.001***
		Tobacco craving	-1.146	.415	.029**
	Food craving	Tobacco craving	-.225	.410	.586
P3	No craving	Food craving	-.743	.293	.049**
		Tobacco craving	-1.805	.483	.002**
	Food craving	Tobacco craving	-1.061	.553	.060*
P7	No significant results				

<i>Right hemisphere</i>					
Electrode	(I) Condition	(J) Condition	Mean Difference (I-J)	Std. Error	Sig.
P8	No craving	Food craving	.511	.224	.052**
		Tobacco craving	-.374	.632	.914
	Food craving	Tobacco craving	-.225	.410	.537
P4	No significant results				
CP4	No significant results				
C4	No significant results				

Midline					
Electrode	(I) Condition	(J) Condition	Mean Difference (I-J)	Std. Error	Sig.
Pz	No craving	Food craving	-.448	.245	.098*
		Tobacco craving	-1.154	.475	.063*
	Food craving	Not significant vs any other conditions			
Cz	No significant results				
Fz	No significant results				

Significance indicated by asterisks: * $p < 0.1$ (approaching significance); ** $p \leq 0.05$; *** $p \leq 0.01$

Table 3: LPP - 6 condition X 18 electrode repeated measures MANOVA post-hoc Bonferroni results: left hemisphere

Electrode	(I) Condition	(J) Condition	Mean Difference (I-J)	Std. Error	Sig.
C3	No craving	Food craving	-188.461***	48.155	.008***
		Tobacco craving	-475.919***	105.727	.002***
	Food craving	Tobacco craving	-287.457	102.442	.133
CP3	No craving	Food craving	-150.433***	32.386	.001***
		Tobacco craving	-356.182***	67.194	.000***
	Food craving	Tobacco craving	-205.749**	63.494	.045**
F3	No craving	Food craving	-164.795***	35.426	.001***
		Tobacco craving	-599.435***	99.605	.000***
	Food craving	Tobacco craving	-434.639***	94.453	.001***
F7	No craving	Food craving	-304.336***	79.198	.009***
		Tobacco craving	-664.714***	110.191	.000***
	Food craving	Tobacco craving	-360.378**	105.141	.028**
P3	No craving	Food craving	-124.315**	35.720	.024**
		Tobacco craving	-377.913**	107.710	.022**
	Food craving	Tobacco craving	-253.598	99.862	.251
FC3	No craving	Food craving	-168.631***	37.694	.002***
		Tobacco craving	-482.061***	94.055	.000***
	Food craving	Tobacco craving	-313.430**	88.351	.020**
P7	No craving	Food craving	-185.932***	45.777	.005***
		Tobacco craving	-588.779***	124.324	.001***
	Food craving	Tobacco craving	-402.847**	114.380	.022**
O1	No craving	Food craving	-162.822**	48.521	.033**
		Tobacco craving	-541.462***	128.811	.003***
	Food craving	Tobacco craving	-378.640*	121.092	.060*

Significance indicated by asterisks: * $p < 0.1$ (approaching significance); ** $p < 0.05$; *** $p < 0.01$

Table 4: LPP - 6 condition X 18 electrode repeated measures MANOVA post-hoc Bonferroni results: midline

Electrode	(I) Condition	(J) Condition	Mean Difference (I-J)	Std. Error	Sig.
Oz	No craving	Food craving	-176.593**	47.213	.012**
		Tobacco craving	-434.643***	109.619	.007***
	Food craving	Tobacco craving	-258.051	105.935	.318
Pz	No craving	Food craving	-117.696	45.007	.210
		Tobacco craving	-361.693***	85.034	.003***
	Food craving	Tobacco craving	-243.997**	70.703	.026**
Cz	No craving	Food craving	-185.932***	41.985	.002***
		Tobacco craving	-465.106***	95.569	.001***
	Food craving	Tobacco craving	-279.175**	87.322	.050**
Fz	No craving	Food craving	-213.369***	46.917	.001***
		Tobacco craving	-547.993***	95.998	.000***
	Food craving	Tobacco craving	-334.624**	103.989	.048**

Significance indicated by asterisks: * $p < 0.1$ (approaching significance); ** $p < 0.05$; *** $p < 0.01$

Table 5: LPP - 6 condition X 18 electrode repeated measures MANOVA post-hoc Bonferroni results: right hemisphere

Electrode	(I) Condition	(J) Condition	Mean Difference (I-J)	Std. Error	Sig.
C4	No craving	Food craving	-146.029***	24.708	.000***
		Tobacco craving	-432.826***	85.075	.000***
	Food craving	Tobacco craving	-286.796**	83.052	.026**
CP4	No craving	Food craving	-125.692**	34.358	.015**
		Tobacco craving	-373.113***	67.386	.000***
	Food craving	Tobacco craving	-247.421***	59.422	.004***
F4	No craving	Food craving	-197.333***	39.180	.000***
		Tobacco craving	-536.041***	112.428	.001***
	Food craving	Tobacco craving	-338.707*	110.187	.069*
F8	No craving	Food craving	-226.754***	43.665	.000***
		Tobacco craving	-574.920***	118.165	.001***
	Food craving	Tobacco craving	-348.166*	115.604	.080*
P4	No craving	Food craving	-124.013	47.178	.203
		Tobacco craving	-404.786***	91.778	.002***
	Food craving	Tobacco craving	-280.773**	85.324	.039**
FC4	No craving	Food craving	-131.183**	40.862	.048**
		Tobacco craving	-495.288***	85.919	.000***
	Food craving	Tobacco craving	-364.105***	76.369	.001***
P8	No craving	Food craving	-185.977**	48.977	.010**
		Tobacco craving	-544.377	190.90.01	.119
	Food craving	Tobacco craving	-358.400	180.009	.840
O2	No craving	Food craving	-188.346***	45.325	.004***
		Tobacco craving	-531.279***	107.227	.000***
	Food craving	Tobacco craving	-342.932**	107.705	.050**

Significance indicated by asterisks: * $p < 0.1$ (approaching significance); ** $p < 0.05$; *** $p < 0.01$

Table 6: Summary of each theory's predictions and whether or not each was observed in our data. Hypothesis # links each prediction to its associated result.

Theory tested	Hypothesis	Observed result?	Hypothesis #
Required to test all theories	No differences between smokers & non-smokers in age, sex, BDI, STAI, hunger, number of addictions present, or preceding night hours of sleep	✓	1
	Considerably greater SPQ tobacco addiction scores in smokers	✓	2
	More tobacco cravings in response to tobacco photos; same for food	✓	3
	Significantly more tobacco cravings in smokers, and equal number of food cravings in smokers and non-smokers	✓	4
	Lower valence ratings for negative than neutral, food & positive images	✓	5
AMS-based tobacco craving (IST)	No valence difference between food & tobacco craving-inducing images	✗	6
	No differences in mood between any conditions	*✗	7
	Tobacco craving activation significantly greater than that of the no craving condition almost solely in the left hemisphere (hemi) for the p300	**✓	8
	Tobacco craving activation significantly greater than that of the no craving condition almost solely in the left hemi for the LPP	✗	9
	Addition of negative and food-craving inducing image LPP areas under the curve significantly greater than tobacco craving at most electrodes	✗	10
DMS-based tobacco craving (AMM)	Lower valence ratings for tobacco craving-inducing than neutral images	✗	11
	Significantly lower mood for tobacco craving than food or no craving	*✗	12
	Tobacco craving activation either greater in both hemis (or just the right hemi) for the p300, but without significantly greater activation in the left than right	✗	13
	Tobacco craving activation greater in both hemis (or just the right hemi) for the LPP, but without significantly greater activation in the left than right hemi	✗	14
	Addition of negative and food-craving inducing image LPP areas under the curve significantly greater than tobacco craving at most electrodes	✗	15
Concurrent AMS & DMS-based tobacco craving (EIT)	Lower valence ratings for tobacco craving than food craving & positive images	✓	16
	Higher valence rating for tobacco craving-inducing than neutral images	✓	17
	Significantly lower mood for tobacco craving than food craving	✓	18
	Significantly lower mood for tobacco craving than no craving	*✗	19
	Tobacco craving activation greater in both hemis for the p300, with significantly greater activation in the left than right hemi	**✗	20
	Tobacco craving AUC bilaterally larger for the LPP than all other conditions, but moreso in the left hemi OR this same pattern for both food & tobacco craving with tobacco AUC still larger than food; must be equally larger in each hemi	✓	21
	Greater vividness for all craving-inducing images	✓	22
	Addition of negative & food-craving inducing image LPP AUCs, with neutral image AUCs subtracted not significantly different from tobacco craving at most electrodes	✓	23

* Finding was that food-related images linked to more positive mood, while tobacco images had no significant differences from neutral mood. No theory predicted this, but EIT can best account for it.

** Does not necessarily counter EIT, as EIT also suggests that DMS activation may come slightly later than AMS in circumstances where severe craving is not present.

Note: hemi = hemisphere

Figures

Figure 1: International 10-20 system of EEG electrode placement, as used in our experimental paradigm (image adapted from Pichitpornchai, 2008)

Figure 2: Spectrum analysis of 10s of pink noise (adapted with permission from Tims, 2006). In pink noise, the volume of random sounds generated with higher frequencies is lowered. The effect is similar to that of white noise, but with a “deeper” sound, since higher frequencies are slightly cutoff. In white noise, the spectral graph is flat, so all frequencies that are randomly produced are of the same volume. It was selected due to its better approximation of how the human ear perceives sound: with pink noise, equal volume is perceived per each *octave* rather than per frequency. Octaves are equidistant to the human ear, but not in terms of frequency: doubling the frequency has the effect of going up one octave. Thus, pink noise equally masks all octaves and ranges of hearing equally, while white noise preferentially masks higher octave sound – which to the human ear means preferentially masking “higher” sound. Pink noise was thus a better option for masking all background sound

Figure 3: Experimental setup surrounding participant. Distances not to scale, excepting labelled lengths.

S1, S2, S3, S4: speakers;

PT: participant (chair at location PT)

E: EEG wire box and amplifier – receives wires from participant EEG cap and outputs them to computer containing data acquisition software

RB: response box, through which participants respond to onscreen prompts

SD: Stimulus display – plasma display for showing images.

Figure 4: Participant prepared for experiment. Connected to Quik-cap EEG headset, with EOG electrodes above and below left eye; reference on nasal supratip. Saline insertion point circled, electrolyte solution injected into gap via needle-free syringe to soak electrode directly below insertion point. Image used with participant consent.

Figure 5: experimental procedure.

a: single trial procedure. Order of screens displayed to subject: 1) 350ms blank screen; 2) trial image for 1300ms; 3. 1000ms blank screen; 4. crosshair on which to generate a mental image, which changes upon pressing a key from 1 to 7 to rate the vividness; 5) 350ms blank screen; 6) Request to rate image valence (1 to 9) that stays until keypress rating; 7) 350ms blank screen; 8) Request to report craving, which again remains until keypress. Procedure then repeats for the next trial.

b: Experiment timeline from beginning to end.

i = instructional screens; m = mood self-report rating; b = baseline recording; t = training block for practicing and learning procedure; TB = trial block (randomly tobacco, food, or affectively negative); p = positive block for restoring mood; d = short initial debriefing screen.

Figure 6: Comparison of neutral, food craving-inducing, tobacco craving-inducing, and negative images on average emotional valence. All differences significant at $p < 0.01$ (with Sidak correction). Note that neutral and negative refer to image category based on IAPS valence ratings, not participant valence ratings.

Figure 7: Difference waves for the viewing of photos that were accompanied by tobacco cravings in smokers, minus non-negative photos that did not induce cravings. High-pass filtered at 10Hz, 12db/octave. Horizontal ticks are 100ms. This image focuses on LPP results (from ~400-1100ms), as the p300 was often washed out by filtering and the subtraction of the neutral condition. Notice that from 400-1100ms, the difference waves are primarily positive, demonstrating greater activation in tobacco-craving inducing images.

Figure 8: Vividness ratings for the following conditions:

NoCravNeutVal: neutral valence-rated trials with no craving present
NoCravNegVal: negative valence-rated trials with no craving present
NoCravPosVal: positive valence-rated trials with no craving present
FoodCrav: all trials with a reported food craving
TobCrav: all trials with a reported tobacco craving

Figure 9: P300 wave at electrodes P3 and CP4. Turquoise is in response to tobacco craving-inducing images, green is food craving-inducing images, red is images that did not induce a craving. Significant differences between all conditions at P3. For comparison, there were no significant differences between any conditions at electrode CP4.

Figure 10: black = negative emotional rating plus food craving minus neutral emotional rating. Red = tobacco cravings. No significant differences between them at most electrodes in either hemisphere. This suggests that the addition of AMS- and DMS-specific activation with activation standard to image viewing results in a waveform equal to that displayed by tobacco cravings, which is evidence for concurrent activation of both systems when a tobacco craving is present.

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Appendix A: IAPS images selected

Neutral images: IAPS ID number and associated valence score

1: 1112 - 4.71;	2: 1908 - 5.28;	3: 2384 - 5.92;	4: 2445 - 5.39;	5: 2446 - 4.70;
6: 2880 - 5.18;	7: 2980 - 5.61;	8: 3005.2 - 5.98;	9: 5040 - 5.39;	10: 5390 - 5.59;
11: 5395 - 5.34;	12: 5455 - 5.79;	13: 5471 - 5.21;	14: 5661 - 5.96;	15: 5731 - 5.39;
16: 5740 - 5.21;	17: 5900 - 5.93;	18: 5920 - 5.16;	19: 5950 - 5.99;	20: 6150 - 5.08;
21: 7000 - 5.00;	22: 7001 - 5.32;	23: 7002 - 4.97;	24: 7003 - 5.00;	25: 7004 - 5.04;
26: 7006 - 4.88;	27: 7009 - 4.93;	28: 7010 - 4.94;	29: 7012 - 4.98;	30: 7014 - 5.15;
31: 7016 - 4.76;	32: 7018 - 4.81;	33: 7020 - 4.97;	34: 7021 - 5.21;	35: 7025 - 4.63;
36: 7026 - 5.38;	37: 7030 - 4.69;	38: 7033 - 5.40;	39: 7034 - 4.95;	40: 7035 - 4.98;
41: 7036 - 4.88;	42: 7037 - 4.81;	43: 7041 - 4.99;	44: 7042 - 5.55;	45: 7043 - 5.17;
46: 7045 - 4.97;	47: 7050 - 4.93;	48: 7052 - 5.33;	49: 7053 - 5.22;	50: 7055 - 4.90;
51: 7059 - 4.93;	52: 7062 - 5.27;	53: 7077 - 5.12;	54: 7080 - 5.27;	55: 7090 - 5.19;
56: 7096 - 5.54;	57: 7100 - 5.24;	58: 7110 - 4.55;	59: 7140 - 5.50;	60: 7150 - 4.72;
61: 7160 - 5.02;	62: 7161 - 4.98;	63: 7170 - 5.14;	64: 7175 - 4.87;	65: 7179 - 5.06;
66: 7180 - 4.73;	67: 7184 - 4.84;	68: 7205 - 5.56;	69: 7207 - 5.15;	70: 7217 - 4.82;
71: 7233 - 5.09;	72: 7235 - 4.96;	73: 7236 - 5.64;	74: 7240 - 6.02;	75: 7242 - 5.28;
76: 7490 - 5.52;	77: 7491 - 4.82;	78: 7500 - 5.33;	79: 7504 - 5.67;	80: 7512 - 5.38;
81: 7513 - 5.45;	82: 7546 - 5.40;	83: 7547 - 5.21;	84: 7590 - 4.75;	85: 7595 - 4.55;
86: 7705 - 4.77;	87: 7710 - 5.42;	88: 7820 - 5.39;	89: 7830 - 5.26;	90: 7950 - 4.94;
91: 5120 - 4.39;	92: 5250 - 6.08;	93: 5665 - 6.15;	94: 5726 - 6.23;	95: 7031 - 4.52;
96: 7060 - 4.43;	97: 7509 - 6.03;	98: 7510 - 6.05;	99: 7920 - 4.51;	100: 9210 - 4.53

Negative images

1: 1111 - 3.25;	2: 3001 - 1.62;	3: 3019 - 2.99;	4: 3071 - 1.88;	5: 3103 - 2.07;
6: 3110 - 1.79;	7: 3140 - 1.83;	8: 3191 - 1.95;	9: 6230 - 2.37;	10: 6300 - 2.59;
11: 8485 - 2.73;	12: 9000 - 2.55;	13: 9031 - 3.01;	14: 9140 - 2.19;	15: 9187 - 1.81;
16: 9280 - 2.80;	17: 9295 - 2.39;	18: 9300 - 2.26;	19: 9301 - 2.26;	20: 9405 - 1.83;
21: 9470 - 3.05;	22: 9560 - 2.12;	23: 9570 - 1.68;	24: 9571 - 1.96;	25: 9600 - 2.48;
26: 9611 - 2.71;	27: 9630 - 2.96;	28: 9911 - 2.30;	29: 9925 - 2.84;	30: 9940 - 1.62

Positive images

1: 5210 - 8.03;	2: 5260 - 7.34;	3: 5300 - 6.91;	4: 5480 - 7.53;	5: 5700 - 7.61;
6: 5760 - 8.05;	7: 5780 - 7.52;	8: 5825 - 8.03;	9: 5830 - 8.00;	10: 5982 - 7.61;
11: 8190 - 8.01				

Eleven were used in this category in error – the intended number was 10.

Food images

1: 7200 - 7.63;	2: 7220 - 6.91;	3: 7230 - 7.38;	4: 7260 - 7.21;	5: 7270 - 7.53;
6: 7281 - 6.40;	7: 7283 - 5.50;	8: 7286 - 6.36;	9: 7289 - 6.32;	10: 7291 - 6.35;
11: 7330 - 7.69;	12: 7340 - 6.68;	13: 7350 - 7.10;	14: 7352 - 6.20;	15: 7400 - 7.00;

16: 7402 - 5.98;   17: 7405 - 7.38;   18: 7430 - 7.11;   19: 7440 - 6.32;   20: 7450 - 6.40;
21: 7451 - 6.68;   22: 7460 - 6.81;   23: 7461 - 5.80;   24: 7470 - 7.08;   25: 7475 - 6.33;
26: 7477 - 6.12;   27: 7480 - 7.08;   28: 7481 - 6.53;   29: 7482 - 6.36;   30: 7488 - 6.19

Tobacco images

These were custom made, as the IAPS did not contain enough tobacco-related images to provide the 30 required.

Appendix B: sample images

Neutral:

Negative:

Positive **Food**

Tobacco

Appendix C: PROMIS Questionnaire

The Shorter PROMIS Questionnaire - instructions

Note that you are free to decline answering any of the following questions, should you feel uncomfortable responding. In this event, simply draw a line through the response area. This will not affect your inclusion in the study, or your class credit for research participation. All answers will be kept completely anonymous, as is required by law (and as is common to all questionnaires and responses in this study). Your name will not be attached to or associated with your responses, nor attached to your participant number.

In this questionnaire certain terms are used which have general meanings attached to them. “Tobacco” should be taken to mean tobacco, cigarettes, cigars, snuff, tobacco bags, shisha, and nicorette chewing gum.

“Recreational drugs” should be taken to mean cannabis, heroin, ketamine, inhalants, LSD, magic mushrooms, DMT, kava, GHB, “designer drugs” such as ecstasy (MDMA), PCP, 2C-B, 2C-I, and 2-CE; and methamphetamine, ephedrine, amphetamine, “speed,” cocaine, and other stimulants.

“Prescription drugs” includes all medicines that have a mood-altering effect, especially tranquilisers, antidepressants, sleeping tablets, painkillers, cough mixtures and cold cures, slimming pills, prescription stimulants, and antihistamines.

Common examples: Ativan (lorazepam), Xanax (alprazolam), clonazepam, Valium (diazepam), temazepam, oxazepam, Dexedrine (dextroamphetamine), Ritalin (methylphenidate), Adderall (amphetamine), Imovane (zopiclone), Percocet (oxycodone), codeine, morphine, Vicodin (hydrocodone), Dilaudid (hydromorphone), fentanyl, Demerol (pethidine), Zoloft (sertraline), Prozac (fluoxetine), Effexor (venlafaxine), Celexa (citalopram), Lexapro (escitalopram), Cymbalta (duloxetine), Robitussin (dextromethorphan), Desyrel (trazodone), selegiline, Wellbutrin (bupropion), amitriptyline

“Caffeine” includes coffee, tea, chocolate, caffeinated soda (IE Coke, Pepsi), energy drinks, and caffeine pills.

“Work” includes school/university, hobbies and interests, cults, and sects.

“Gambling and risk taking” includes property ventures, stocks and shares, insurance, and other business risks.

Each question is on a six-point scale. Please read each question carefully before answering. Place a cross on the scale between one and six to indicate the extent to which the statement is 'Like' you or 'Not like' you.

For example: A cross at the 'Like me' extreme would indicate that the statement definitely applied to you.

i.e., Not like me ____ X Like me

A cross at the 'Not like me' extreme would indicate that the statement definitely did not apply to you.

i.e., Not like me X ____ Like me

A cross in between the two extremes indicates more or less agreement with one extreme. e.g., If you felt that 'Like me' is more appropriate than 'Not like me' you would answer as follows:

i.e., Not like me ____ X ____ Like me   or

i.e., Not like me ____ X ____ Like me

If you felt that 'Not like me' is more appropriate than 'Like me' you would use one of the remaining two points as follows:

i.e., Not like me ____ X ____ Like me   or

i.e., Not like me ____ X ____ Like me

If you think that a question is just not applicable or incomprehensible to you please answer 'Not like me', as follows:

i.e., Not like me X ____ Like me

Do not leave any answers blank.

Questions were as follows:

- 1) I have had an intimate relationship with caffeine so that in a strange way I have felt that I became a real person only when I used it.
- 2) I have found it difficult to pass over opportunities for casual or illicit sex.
- 3) I have often been so tired with exercise that I have found it difficult to walk or to climb up stairs.
- 4) I have found that feeling light-headed has often been irrelevant in deciding when to stop drinking alcohol.
- 5) I have tended to look for, or take on, positions of power or influence so that I rise to a position of emotional or practical power over others as rapidly as possible
- 6) I have preferred to use nicotine throughout the day rather than only at specific times.
- 7) I have found that the amount that I have won or lost has often been irrelevant in deciding when to stop gambling or risk taking
- 8) I have felt uncomfortable when shopping with other people because it has restricted my freedom.
- 9) I have particularly enjoyed getting a really strong effect from recreational drugs.
- 10) I have tended to think of food not so much as a satisfier of hunger but as a reward for all the stress I endure.
- 11) I have been afraid that I would be thought of as (and perhaps become) a callous person if I do not show my capacity for self-denial and caretaking on a daily basis.
- 12) I have taken on a piece of work that I actively disliked not so much out of necessity but more simply to keep myself occupied
- 13) In a restaurant or even at home I have often tried to persuade others to choose dishes that I knew I would like even though I would probably refuse to eat them
- 14) I have tended to pride myself on never being a burden to others
- 15) I have felt an increased tension or awareness when it has come to the time when I normally take my prescribed medication.
- 16) I have tended to be upset when someone close to me takes care of someone else.
- 17) I have particularly enjoyed buying bargains so that I often finished up with more than I need.
- 18) I have found that having one drink tended not to satisfy me but made me want more.
- 19) I have preferred to exercise alone rather than in company.
- 20) Other people have expressed repeated serious concern over my sexual behaviour.
- 21) I have tended to use nicotine as both a comfort and strength even when I feel that I did not want any.
- 22) I have preferred to take caffeine on my own rather than in company.
- 23) I have tended to use food as both a comfort and a strength even when I have not been hungry.
- 24) I have had a sense of increased tension and excitement when I knew that I had the opportunity to get some drugs.
- 25) The things I have done for others have often resulted in there being not much left of my personal life.
- 26) I have tended to work faster and for longer hours than any other people of my own ability so that they have found it difficult to keep up with me
- 27) I have felt that I become a real person only when I am being totally looked after by someone else
- 28) I have felt it would be more painful for me to give up caffeine than to give up a close friendship.
- 29) I have found it difficult not to take up a position of power or influence when it is available, even when I do not really need it and can see no particular use for it.

- 30) I have prided myself on the speed with which I can get to have sex with someone and I have found that sex with a complete stranger is stimulating.
- 31) I have regularly stolen or helped myself to other people's caffeine even though I had enough money to buy my own.
- 32) I have preferred to look after other people on my own rather than as part of a team.
- 33) I have often tried to take exercise several times a day
- 34) When I have eaten in company I have liked to be with special friends or family members whom I can rely on to finish off some foods for me
- 35) Other people have tended to express concern that I am not doing enough for my own pleasure
- 36) When I have definitely overworked and got myself irritable and overtired I have tended to feel defiant as well as slightly ashamed
- 37) I have had a complete blank of ten minutes or more in my memory when trying to recall what I was doing after drinking alcohol on the previous day or night
- 38) Other people have expressed repeated serious concern about my use of prescription medicines
- 39) I have tried to avoid all risks of upsetting other people.
- 40) I have tended to tidy up the mess that someone else has got into at work, even when I have not been asked to do so.
- 41) Other people have expressed repeated serious concern about some aspects of my drug use.
- 42) I have taken more than the prescribed dose of my prescription medication as and when I feel it necessary.
- 43) I have used alcohol as both a comfort and a strength.
- 44) I have found that being full has often been irrelevant in deciding when to stop eating.
- 45) I tended to give (an act of service to others) and not count the costs even though the costs mount progressively.
- 46) I have found that finishing a specific project is often irrelevant in deciding when to stop working.
- 47) I have been afraid that I will put on excessive amounts of weight or become particularly irritable or depressed if I give up using nicotine altogether.
- 48) I tend to use shopping as both a comfort and a strength even when I do not need anything.
- 49) I have found life rather empty when someone for whom I was caring gets better and I have felt resentful at times when I am no longer needed
- 50) I have found that I have sometimes put on weight even when I am trying to diet
- 51) I have tended to gulp down the first (alcoholic) drink fairly fast
- 52) I have tended to time my intake of caffeine so that others are not really aware of my total intake.
- 53) I have had a list of so many things that I dare not eat, so that there is very little left that I can eat.
- 54) I have particularly enjoyed getting wringing wet with sweat when I exercise.
- 55) I have found that other people have tended to express progressively more concern about my dependent relationships
- 56) When working with others I have tended to disguise the full amount of time and effort that I put into my work.
- 57) I have often chewed something and then taken it out of my mouth and thrown it away.
- 58) I have tended to remain loyal and faithful regardless of what I may endure in a close relationship.
- 59) I have tended to go shopping just in case I might see something I want.
- 60) I have had a sense of increased tension and excitement when I buy caffeine substances or when I see advertisements for them.

- 61) When I have been shopping with family members, friends, or other people, I have tended to disguise the full extent of my purchases.
- 62) I have liked to make myself useful to other people even when they do not appreciate what I do.
- 63) I have tended to find someone else to be close to when my primary partner is away even for a short time.
- 64) I have often found that having my first use of nicotine in any day tends not to satisfy me, but makes me want more.
- 65) I have stolen or embezzled to cover gambling losses or to cover my losses in risky ventures.
- 66) I have found that getting high tends to result in my going on to take more drugs.
- 67) I have tended to keep reserve projects up my sleeve just in case I find some time, even a few minutes to spare.
- 68) I have often felt a sense of tension and excitement when about to take exercise.
- 69) I have tended to use my self-denial and caretaking for others as both a comfort and strength for myself.
- 70) I have taken opportunities to have sex despite having just had it with somebody else.
- 71) Other people have expressed repeated serious concern about my excessive eating.
- 72) I have preferred to have power and influence in all my relationships rather than allow myself to be vulnerable.
- 73) I have regularly covered other people's work and responsibilities even when there was no need for me to do so
- 74) I had a good head for alcohol so that others appeared to get drunk more readily than I did.
- 75) I have found that making a sexual conquest has caused me to lose interest in that partner and led me to begin looking for another.
- 76) I have tended to use drugs as both a comfort and strength.
- 77) I have found it more painful for me to give up gambling and risk taking than to give up a close friendship.
- 78) I have tended to find new close relationships within days or weeks of the failure of the old one.
- 79) I have responded positively to an unexpected invitation to exercise despite having just finished my regular exercise.
- 80) I have often bought so many goods (groceries, sweets, household goods, books, etc.) that it would take a month to get through them.
- 81) I have tended to venture into company only if I have someone to look after me.
- 82) I have found it strange to leave half a glass of (alcoholic) drink.
- 83) I have continued to use nicotine even when I have had a bad cold or even more serious respiratory problem.
- 84) I have preferred to keep my shopping supplies topped up in case of war or natural disaster, rather than let my stocks run low.
- 85) I have often preferred to eat alone rather than in company.
- 86) I have tended to take on more work for someone close to me even if I have not finished the previous batch.
- 87) I have felt an overwhelming sense of excitement when I find a new person to look after my needs or a new way in which an existing partner can look after them better.
- 88) I have often found that I use all of the drugs in my possession even though I had intended to spread them out over several occasions.
- 89) Other people have expressed repeated serious concern over my gambling or risk taking.

- 90) I have tended to ensure that I have sex of one kind or another rather than wait for my regular partner to be available again after an illness or absence.
- 91) I have tended to think that a close friendship is when someone else really looks after me.
- 92) If my prescription medicines supply was being strictly controlled I would hang onto some old tablets even if they were definitely beyond their expiry date.
- 93) I have bought things not so much as a means of providing necessities but more as a reward that I deserve for the stresses that I endure.
- 94) I have tended to accept opportunities for further gambling or risk taking despite having just completed a session or a project.
- 95) When I have definitely eaten too much I have tended to feel defiant as well as disappointed in myself.
- 96) I have been afraid that my life will fall apart and that others will take advantage of me if I give up the power and influence that I have held or now hold.
- 97) I have felt that I become a real person only when I am exercising.
- 98) I have tended to make sure that I have the drugs or the money for drugs before concentrating on other things.
- 99) Other people (e.g., doctors) have commented that they would be knocked out by a fraction of the prescription medication that I have regularly taken.
- 100) I have particularly enjoyed eating raw vegetables and also salty or sour things.
- 101) I have regularly undermined other people's positions of power or influence even though they may have significantly less than my own.
- 102) Other people have expressed repeated serious concern over the amount of time I spend working.
- 103) I have felt like a real person only when performing acts of service for someone else.
- 104) I have found that my nicotine consumption goes up or down when I am off alcohol or drugs or when I am on a diet.
- 105) I have tended to use exercise as both a comfort and strength even when I have been perfectly fit and do not need any more.
- 106) I have found that having all the power and influence that I need for my own personal and professional life is irrelevant when deciding when to stop seeking more.
- 107) I have found that my intake of another form of caffeine tends to increase when I am off my own favourite.
- 108) I have preferred to gamble or to take risks in one way or another throughout the day rather than at particular times.
- 109) When I have eaten in company I have tended to time my eating as a form of strategy so that others are not really aware of just how little I am eating.
- 110) I have had repeated affairs even though I had a regular relationship.
- 111) I have found that I tend to adopt a self-denying and caretaking role in many of my relationships.
- 112) I have found that my previous doses of prescription medicines no longer successfully control my symptoms
- 113) I have preferred to graze throughout the day rather than ever allow myself to get hungry.
- 114) I have had three or more regular sexual partners at the same time.
- 115) When I have used too much caffeine I have tended to feel defiant as well as disappointed in myself.
- 116) I have had three or more different sizes of clothes in my adult (nonpregnant, if female) wardrobe.
- 117) I have regularly given unsolicited advice to other people on how to solve their problems.

- 118) I have tended to use a position of power or influence as a comfort and strength regardless of whether there are particular problems needing my attention in other aspects of my life.
- 119) When I have eaten something reasonably substantial I have tended to feel disappointed or even angry with myself as well as slightly relieved.
- 120) I have tended to use gambling or risk-taking as a form of comfort and strength even when I have not felt that I particularly want to gamble or take further risks.
- 121) I have continued to take prescription medication because I find that it helps me, even when the original stresses for which the medication was prescribed have been resolved.
- 122) I have found it difficult to leave any loose ends in a conversation in which I am trying to be helpful.
- 123) I have felt that I become a real person only when I am shopping or spending.
- 124) I have tended to get irritable and impatient when people look after themselves rather than me.
- 125) If I had run out of my prescribed medication I would take an alternative even if I was not sure of its effects.
- 126) I have looked for all opportunities for power and influence as and when they arise.
- 127) I have often stayed up half the night having 'helpful' conversations.
- 128) I have had voluntary sex with someone that I dislike.
- 129) I have often taken exercise just to tire myself sufficiently for sleep.
- 130) In a new relationship I have felt uncomfortable until I hold the most powerful position.
- 131) I have deliberately used nicotine before going out to a place where I may not be able to use it.
- 132) When I ran out of my favourite form of nicotine, I have accepted the offer of an alternative that I do not particularly like.
- 133) I have found that once I start work in any day I find it difficult to get "out of the swing of it" and relax
- 134) I have been irritable and impatient if there has been more than ten minutes of conversation at a meal or social function before my host offers me an alcoholic drink.
- 135) I have gambled or taken risks at the first opportunity in case I did not get the chance later on.
- 136) I have deliberately had an alcoholic drink before going out to a place where alcohol may not be available.
- 137) When my favourite form of gambling or risk taking is unavailable I have gambled on something else I normally disliked.
- 138) I have been aware that once I have consumed certain foods I have found it difficult to control further eating.
- 139) I have become irritable and impatient at meal times if someone has tried to persuade me to eat something.
- 140) I have often drunk significantly more alcohol than I intended to.
- 141) I have been irritable or impatient if my supply of drugs is delayed for 10 minutes or so for no good reason
- 142) I have sometimes rushed through a meal, or skipped it altogether, so that I can have some caffeine.
- 143) I have tended to use more drugs if I have got more.
- 144) I have often avoided meal times by claiming that I have already eaten when it is not true.
- 145) I have often been capable of drinking 20 cups of tea or coffee or cola or lemonade or eating 20 chocolates in a day
- 146) I have often used nicotine to calm my nerves.

- 147) I have been irritable and impatient if there is a complete break of 10 minutes in a gambling session.
- 148) I have tended to change partners if sex becomes repetitive.
- 149) I have often helped someone close to me more than I intended.
- 150) I have felt most in control of my feelings when other people are performing services of one kind or another for me.
- 151) I have often used nicotine significantly more than I intended to.
- 152) Some food has made me wish I could eat it like other people do but I nonetheless find that I could not bring myself to do so
- 153) I have been irritable and impatient if my prescribed medication is delayed for 10 minutes.
- 154) When I have gone out I have often taken sports clothes and equipment with me "just in case" the opportunity to exercise arises.
- 155) I have felt that I have become a real person only when I am tidying up the physical, emotional, and social messes made by someone else.
- 156) I have often gone shopping to calm my nerves.
- 157) I have often found myself taking more prescribed medication than I intended to.
- 158) I have felt most in control of my feelings when performing services of one kind or another for someone else.
- 159) I have deliberately used drugs before going out for a time if I have felt there might not be the opportunity to use them later.
- 160) I have tended to neglect other aspects of my life when I have felt that my position of power or influence is under threat.

Appendix D: General food craving questionnaire

GENERAL FOOD CRAVING QUESTIONNAIRE-STATE

Please indicate by circling the most appropriate response below, to what extent you agree with each of the statements below *right now, at this very moment*.

1. I'm craving tasty food	1	2	3	4	5
2. I have an urge for tasty food					
3. I have an intense desire to eat something tasty	1	2	3	4	5
4. If I ate something, I wouldn't feel so sluggish and lethargic.					
5. Satisfying my appetite would make me feel less grouchy and irritable.	1	2	3	4	5
6. I would feel more alert if I could satisfy my appetite.	1	2	3	4	5
7. If I ate right now, my stomach wouldn't feel as empty.	1	2	3	4	5
8. I am hungry.	1	2	3	4	5
9. I feel weak because of not eating.	1	2	3	4	5
10. My desire to eat something tasty seems overpowering.	1	2	3	4	5
11. I know I'm going to keep on thinking about tasty food until I actually have it.	1	2	3	4	5
12. If I had something tasty to eat, I would not stop eating it.	1	2	3	4	5
13. If I were to eat what I'm desiring, I am sure my mood would improve.	1	2	3	4	5
14. Eating something tasty would feel wonderful	1	2	3	4	5
15. Eating something tasty would make things just perfect.	1	2	3	4	5

Appendix E: STAI

DIRECTIONS: A number of statements which people have used to describe themselves are given below. Read each statement then circle the appropriate number to the right of the statement to indicate how you feel *right now*, that is, *at this moment*. There are no right or wrong answers. Do not spend too much time on any one statement, but give the answer which seems to best describe your present feelings.

	Not at all	Somewhat	Moderately	Very much so
1. I feel calm	1	2	3	4
2. I feel secure	1	2	3	4
3. I am tense	1	2	3	4
4. I feel strained	1	2	3	4
4. I feel at ease	1	2	3	4
6. I feel upset	1	2	3	4
7. I am presently worrying over misfortune	1	2	3	4
8. I feel satisfied	1	2	3	4
9. I feel frightened	1	2	3	4
10. I feel comfortable	1	2	3	4
11. I feel self-confident	1	2	3	4
12. I feel nervous	1	2	3	4
13. I am jittery	1	2	3	4
14. I feel indecisive	1	2	3	4
14. I am relaxed	1	2	3	4
16. I feel confident	1	2	3	4
17. I am worried	1	2	3	4
18. I feel confused	1	2	3	4
19. I feel steady	1	2	3	4
20. I feel pleasant	1	2	3	4

Appendix F: BDI

BECK DEPRESSION INVENTORY- BDI- 21 item scale

This questionnaire consists of groups of statements. Please read the entire group of statements in each category, then pick the one statement in that group that best describes the way you feel. Check off the number beside the statement you have chosen. Do not choose more than one statement in each group.

---

1. ☐ 0 = I do not feel sad.
☐ 1 = I feel sad or blue.
☐ 2a = I am blue or sad all of the time and I can't snap out of it.
☐ 2b = I am so sad or unhappy that it is very painful.
☐ 3 = I am so sad or unhappy that I can't stand it.

2. ☐ 0 = I am not particularly pessimistic or discouraged about the future.
☐ 1 = I feel discouraged about the future.
☐ 2a = I feel I have nothing to look forward to.
☐ 2b = I feel I won't ever get over my troubles.
☐ 3 = I feel that the future is hopeless and things cannot improve.

3. ☐ 0 = I do not feel like a failure.
☐ 1 = I feel I have failed more than the average person.
☐ 2a = I feel I have accomplished very little that is worthwhile or that means anything
☐ 2b = As I look back on my life, all I can see is lots of failures.
☐ 3 = I feel I am a complete failure as a person.

4. ☐ 0 = I am not particularly dissatisfied.
☐ 1 = I feel bored most of the time.
☐ 2a = I don't enjoy things the way I used to.
☐ 2b = I don't get satisfaction out of anything anymore.
☐ 3 = I am dissatisfied with everything.

5. ☐ 0 = I don't feel particularly guilty.
☐ 1 = I feel bad or unworthy a good part of the time.
☐ 2a = I feel quite guilty.
☐ 2b = I feel bad or unworthy practically all of the time now.
☐ 3 = I feel as though I am very bad or worthless.

6. ☐ 0 = I don't feel I am being punished.
☐ 1 = I have a feeling that something bad may happen to me.
☐ 2a = I feel I am being punished or will be punished.
☐ 2b = I feel I deserved to be punished.
☐ 3 = I want to be punished.

7. ____ 0 = I don't feel disappointed in myself.
 ____ 1 = I am disappointed in myself.
 ____ 2a = I don't like myself.
 ____ 2b = I am disgusted with myself.
 ____ 3 = I hate myself.
8. ____ 0 = I do not feel I am any worse than anybody else.
 ____ 1 = I am very critical of myself for my weaknesses or mistakes.
 ____ 2 = I blame myself for everything that goes wrong.
9. ____ 0 = I don't have thought of harming myself.
 ____ 1 = I have thoughts of harming myself but I would not carry them out.
 ____ 2a = I feel I would be better off dead.
 ____ 2b = I have definite plans about committing suicide.
 ____ 2c = I feel my family would be better off if I were dead.
 ____ 3 = I would kill myself if I could.
10. ____ 0 = I don't cry anymore than usual.
 ____ 1 = I cry more now than I used to.
 ____ 2 = I cry all the time now. I can't stop it.
 ____ 3 = I used to be able to cry but now I can't cry at all even though I want to.
11. ____ 0 = I am not more irritated now than I ever am.
 ____ 1 = I get annoyed or irritated more easily than I used to.
 ____ 2 = I get irritated all the time.
 ____ 3 = I don't get irritated at all at the things that used to irritate me.
12. ____ 0 = I have not lost interest in other people.
 ____ 1 = I am less interested in other people than I used to be.
 ____ 2 = I have lost most of my interest in other people and I have little feelings for them.
 ____ 3 = I have lost all of my interest in other people and don't care about them at all.
13. ____ 0 = I make decisions about as well as ever.
 ____ 1 = I am less sure of myself now and try to put off making decisions.
 ____ 2 = I can't make decisions anymore without help.
 ____ 3 = I can't make decisions at all anymore.
14. ____ 0 = I don't feel I look worse than I used to.
 ____ 1 = I am worried that I am looking old or unattractive.
 ____ 2 = I feel that there are permanent changes in my appearance and they make me look unattractive.
 ____ 3 = I feel that I am ugly or repulsive looking.

15. ____ 0 = I can work about as well as before.
____ 1a = It takes extra effort to get started at doing something.
____ 1b = I don't work as well as I used to.
____ 2 = I have to push myself very hard to do anything.
____ 3 = I can't do any work at all.
16. ____ 0 = I can sleep as well as usual.
____ 1 = I wake up more tired in the morning than I used to.
____ 2 = I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
____ 3 = I wake up early every day and can't get more than 5 hours of sleep.
17. ____ 0 = I don't get tired anymore than usual.
____ 1 = I get tired more easily than I used to.
____ 2 = I get tired from doing anything.
____ 3 = I get too tired to do anything.
18. ____ 0 = My appetite is no worse than usual.
____ 1 = My appetite is not as good as it used to be.
____ 2 = My appetite is much worse now.
____ 3 = I have no appetite at all anymore.
19. ____ 0 = I haven't lost much weight if any lately.
____ 1 = I have lost more than 5 pounds.
____ 2 = I have lost more than 10 pounds.
____ 3 = I have lost more than 15 pounds.
20. ____ 0 = I am no more concerned about my health than usual.
____ 1 = I am concerned about aches and pains or upset stomach or constipation or other unpleasant feelings in my body.
____ 2 = I am so concerned with how I feel or what I feel that it's hard to think of much else.
____ 3 = I am completely absorbed in what I feel.
21. ____ 0 = I have not noticed any recent changes in my interest in sex.
____ 1 = I am less interested in sex than I used to be.
____ 2 = I am much less interested in sex now.
____ 3 = I have lost interest in sex completely.

Appendix G: Demographic and Miscellaneous Questions

Instructions

For answers that require writing a response, place it in the empty box directly to the right of the question, marked "write response below." For answers requiring selecting a response, place a 1 in the box to the right of the answer(s) you select.

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1. **What is your age?**
2. **What is your gender?**
  - a. Male
  - b. Female
  - c. Transgender/Hijira
  - d. Intersex/Hermaphroditic
  - e. Other
3. **Are you right-handed, left-handed, or ambidextrous?**
  - a. Right-handed
  - b. Left-handed
  - c. Ambidextrous
4. **Have you ever participated in an imagery study before?**
  - a. Yes
  - b. No
5. **What is your ethnic category?**
6. **What is your marital/relationship status?**
  - a. Single
  - b. In a relationship
  - c. Engaged
  - d. Married
  - e. Divorced
  - f. Common-law
  - g. In an open relationship
  - h. In a "friends with benefits" relationship
  - i. In a polyamorous relationship
  - j. It's complicated
  - k. Other
7. **What is your weight? Write a simple numerical value in the box to the right representing your unit of measurement of choice**
8. **What is your employment status?**
  - a. Unemployed, non-student
  - b. Unemployed, student
  - c. Employed, student
  - d. Employed, non-student
  - e. Retired, student
  - f. Retired, non-student

- g. Self-employed, non-student
- h. Self-employed, student
- i. Unpaid internship, non-student
- j. Unpaid internship or co-op, student
- k. Other (write what it is in box to the left)

9. Which of the following best describes your political orientation?

- a. Very liberal
- b. Liberal
- c. Moderate
- d. Conservative
- e. Very conservative
- f. Libertarian
- g. Communist
- h. Socialist
- i. Fascist
- j. Christian Theocrat (governance by Christian law)
- k. Sharia (governance by Islamic law)
- l. Anarchist
- m. Fascist
- n. Anarcho-communist
- o. Other (write what it is in box to the left)

10. What was your birth order? (were you the first child? Second child? Etc.)

- a. First
- b. Second
- c. Third
- d. Fourth
- e. Fifth
- f. Sixth
- g. Seventh
- h. Eighth
- i. Ninth
- j. Tenth
- k. 11th, 12th, 13th, 14th, 15th, 16th, 17th, 18th, 19th, 20th, etc.

11. Do you consider yourself to be a religious person?

- a. Yes
- b. No

12. Do you consider yourself to be a spiritual person?

- a. Yes
- b. No

13. What religion are you associated with, if any?

- a. Roman Catholic
- b. Atheist/agnostic/secular/nonreligious
- c. United church
- d. Anglican
- e. Baptist
- f. Lutheran
- g. Presbyterian
- h. Mormon

- i. Jehovah's witnesses
- j. A form of Protestant Christianity not previously specified
- k. Christian orthodox
- l. Islam - Shia
- m. Islam - Sunni
- n. Islam - other
- o. Judaism
- p. Buddhism
- q. Hinduism
- r. Sikhism
- s. New age/spiritual
- t. Baha'i
- u. Jainism
- v. Rastafarianism
- w. Zoroastrianism
- x. Other (write what it is in box to the left)

14. What is/was your university or college major, if any? Include all, if more than one.

15. Which of the following disorders, if any, are you formally diagnosed with? Put a 1 under each of the disorders you have a diagnosis of. Common disorders are in bold. For other, include only psychiatric, psychological, and neurological disorders

- a. ADHD - if known, specify subtype in box to right (predominantly inattentive, predominantly hyperactive, or combined)
- b. Advanced sleep phase syndrome
- c. Agnosia (specify subtype, if known, to the right)
- d. ALS (Amyotrophic lateral sclerosis)
- e. Alzheimer's disease
- f. Anorexia nervosa
- g. Aphagia
- h. Apraxia
- i. Asperger's syndrome
- j. Autism
- k. Bipolar disorder (specify subtype, if known, to the right)
- l. Borderline personality disorder
- m. Brain damage/head injury (specify subtype, if known, to the right)
- n. Brain tumor (specify subtype, if known, to the right)
- o. Bruxism (nighttime tooth grinding)
- p. Bulimia nervosa
- q. Cataplexy
- r. Cyclothymia
- s. Delayed sleep phase syndrome
- t. Dementia (non-Alzheimer's) (specify type, if known, to the right)
- u. Depersonalization disorder
- v. Depression - if known, specify subtype in box to left (IE atypical depression, anxious depression, melancholic depression, vascular depression, psychotic depression)
- w. Dissociative disorder
- x. Dyslexia
- y. Dysthymic disorder
- z. Eating disorder - other
- aa. Epilepsy (specify subtype, if known, to the right)
- bb. Generalized anxiety disorder

- cc. Huntington's disease
- dd. Hypersomnia
- ee. Klein-Levin syndrome
- ff. Migraines (in the box to the right specify with or without aura, or mixed if you get auras inconsistently with migraines)
- gg. Multiple sclerosis
- hh. Narcolepsy
- ii. Obsessive-compulsive disorder (OCD)
- jj. Panic disorder
- kk. Disruptive parasomnia(s) (IE sleepwalking, night terrors, sleeptalking, bedwetting). Further specify in the box to the right.
- ll. Parkinson's disease
- mm. Periodic limb movement disorder
- nn. Post-traumatic stress disorder (PTSD)
- oo. Primary insomnia
- pp. Rapid eye movement behavior disorder
- qq. Restless legs syndrome
- rr. Schizoaffective disorder
- ss. Schizophrenia
- tt. Sleep apnea
- uu. Sleeping sickness
- vv. Social anxiety disorder
- ww. Somniphobia
- xx. Substance dependence/substance abuse
- yy. Tourette's syndrome (specify subtype in box to the right)
- zz. Other (write in box to the right)

16. Do you have any diagnosed physical disorders or disabilities? If yes, specify in the boxes to the right, otherwise, write no.

17. Do you have any phobias? If yes, write them in the boxes to the right. Phobias mean intense fears. Common ones include spiders, snakes, etc.

18. Are you taking any prescription medications? Write all in boxes to the right. Write 1 medication/drug per box. Include the dosage and frequency of use

19. Do you have vision in both eyes?

- a. Yes
- b. Vision only in right eye
- c. Vision only in left eye

20. What is your visual acuity?

- a. 20/20 or near 20/20: perfect or near perfect vision
- b. Nearsighted/myopic, requiring corrective lenses (either contact lenses or glasses); [note: means that objects become blurry or more difficult to see based on distance from you – you have more difficulty seeing distant objects]
- c. Farsighted/hyperopic, requiring corrective lenses (reading glasses) [Note: this means that objects become blurry or more difficult to see based on distance from you – you have more difficulty seeing nearby objects]
- d. Both nearsighted/myopic and farsighted/hyperopic, both requiring corrective lenses (or bifocals)
- e. Such that you require trifocals
- f. 20/20 due to laser surgery
- g. Other (specify what it is in the box to the right)

21. What is your height? Write a numeric value beside your chosen unit of measurement

22. What is your opinion of smoking?

- a. Strongly dislike
- b. Dislike
- c. Neither like nor dislike/No opinion
- d. Like
- e. Strongly like

23. Do you consider smoking disgusting?

- a. Yes
- b. No

24. Do you feel disgusted when you see people smoking, or images of people smoking?

- a. Yes
- b. No

25. Have you had a family member die from smoking? (IE from lung cancer, emphysema, coronary heart disease, stroke, abdominal aortic aneurysm, etc. among smoking family members)

- a. Yes
- b. No
- c. Unknown

26. How many siblings do you have?

27. Would you consider yourself to be a smoker?

- a. Yes
- b. No

28. Have you ever been a smoker in the past?

- a. Yes
- b. No

29. Are you a casual smoker (you only smoke very occasionally, ie only at social events)

- a. Yes
- b. No

30. Which of the following recreational drugs have consumed at any point? Note that this refers only to non-medicinal use. IE, if you were prescribed Adderall for ADHD, it should be written above in prescription medications. However, if you used one of your prescribed medications recreationally, it should still be marked in this question.

- a. Caffeine / Coffee / Caffiene pills / Pep pills / energy drinks / non-decaf tea / energy gum / etc.
- b. Tobacco / cigarettes / cigars / shisha / nicotine / snuff
- c. Alcohol/beer/wine/hard liquor/brandy/tequila/etc.
- d. Marijuana/cannabis/hashish
- e. MDMA/Ecstasy/MDA/love drug
- f. LSD
- g. "Magic" mushrooms
- h. Ketamine / Special K / K
- i. Amphetamine / speed / meth / methamphetamine / Adderall / Dexedrine /
- j. Salvia divinorum
- k. Any opiate besides heroin: IE oxycodone, morphine, methadone, tramadol, tramacet, dilaudid, vicodin, percocet, hydcodone, hydromorphone, etc. [non-medicinal use]

- l. Benzodiazepines (IE Ativan/lorazepam, Klonopin/clonazepam, Xanax/alprazolam, Valium/diazepam, chlordiazepoxide/Librium, zopiclone/Imovane, midazolom, Restoril, temazepam, Halcion, triazolam, Flurazepam, Dalmane, estazolam, Ambien/Zolpidem, zaleplon/Sonata, Lunesta, etc.) (non-medicinal use)
- m. Cocaine
- n. Heroin
- o. Any barbiturate
- p. Methcathinone/M-cat/Cathinone
- q. Peyote/psychedelic cactus/mescaline
- r. Methylphenidate/Ritalin/Concerta/Focalin (non-medicinal use)
- s. DMT/"businessman's trip"/dimethyltryptamine
- t. Ephedrine
- u. Nitrous oxide
- v. 4-MTA
- w. Steroids/Anabolic steroids
- x. Khat
- y. Solvents (ie huffing gas)
- z. Alkyl nitrates
- aa. Buprenorphine
- bb. Any hallucinogenic/psychedelic research chemicals, IE: 2CB, 2CI, 2CE, 2CT, 2CT2, 2CT4, 2CT7, 2CT15, 2CD, 2CE-FLY, 2CB-FLY, DOB, DOC, Bromo-DragonFLY, etc.
- cc. BZP/benzylpiperazine/"Party pills"
- dd. GHB
- ee. Kratom
- ff. Foxy methoxy / foxy / MeO-DIPT, or DIPT
- gg. DXM / Dextromethorphan / cough syrup [non-medicinal use]
- hh. Nutmeg / myristicin (in huge amounts to get "high", not as spice)
- ii. Other (specify to the right)

31. Which of the following have you consumed non-medicinally on a regular or semi-regular basis (meaning once per week or more). If you answer yes to any, write approximately when you were commonly using it, and for how long

- a. Caffeine / Coffee / Caffiene pills / Pep pills / energy drinks / non-decaf tea / energy gum / etc.
- b. Tobacco / cigarettes / cigars / shisha / nicotine / snuff
- c. Alcohol/beer/wine/hard liquour/brandy/tequila/etc.
- d. Marijuana/cannabis/hashish
- e. MDMA/Ecstasy/MDA/love drug
- f. LSD
- g. "Magic" mushrooms
- h. Ketamine / Special K / K
- i. Amphetamine / speed / meth / methamphetamine / Adderall / Dexedrine /
- j. Salvia divinorum
- k. Any opiate besides heroin: IE oxycodone, morphine, methadone, tramadol, tramacet, dilaudid, vicodin, percocet, hydcodone, hydromorphone, etc. [non-medicinal use]
- l. Benzodiazepines (IE Ativan/lorazepam, Klonopin/clonazepam, Xanax/alprazolam, Valium/diazepam, chlordiazepoxide/Librium, zopiclone/Imovane, midazolom, Restoril, temazepam, Halcion, triazolam, Flurazepam, Dalmane, estazolam, Ambien/Zolpidem, zaleplon/Sonata, Lunesta, etc.) (non-medicinal use)
- m. Cocaine
- n. Heroin
- o. Any barbiturate
- p. Methcathinone/M-cat/Cathinone
- q. Peyote/psychedelic cactus/mescaline
- r. Methylphenidate/Ritalin/Concerta/Focalin (non-medicinal use)

- s. DMT/"businessman's trip"/dimethyltryptamine
- t. Ephedrine
- u. Nitrous oxide
- v. 4-MTA
- w. Steroids/Anabolic steroids
- x. Khat
- y. Solvents (ie huffing gas)
- z. Alkyl nitrates
- aa. Buprenorphine
- bb. Any hallucinogenic/psychedelic research chemicals, IE: 2CB, 2CI, 2CE, 2CT, 2CT2, 2CT4, 2CT7, 2CT15, 2CD, 2CE-FLY, 2CB-FLY, DOB, DOC, Bromo-DragonFLY, etc.
- cc. BZP/benzylpiperazine/"Party pills"
- dd. GHB
- ee. Kratom
- ff. Foxy methoxy / foxy / MeO-DIPT, or DIPT
- gg. DXM / Dextromethorphan / cough syrup [non-medicinal use]
- hh. Nutmeg / myristicin (in huge amounts to get "high", not as spice)
- ii. Other (specify to the right)

32. Are you currently on any psychoactive substances, medicinally or otherwise? Specify what it is/they are in the boxes to the right. Write "no" if not. Note that many medical drugs are psychoactive (IE antidepressants, anxiolytics, cold medicines, painkillers, etc.) If you are unsure, ask the researcher. Note that caffeine counts.

33. What is your sexual orientation?

- a. Heterosexual
- b. Homosexual
- c. Bisexual
- d. Transgender
- e. Other (write what it is in the box to the left)

34. How many hours of sleep did you get the preceding night?

35. Is English your first language?

- a. Yes
- b. No

36. How would you describe your proficiency in reading and understanding English?

- a. Native speaker
- b. Completely fluent
- c. Almost fluent
- d. Good, but far from perfect
- e. Moderate
- f. Fair
- g. Poor

37. Are you currently wearing anything for vision correction?

- a. Non-bifocal glasses
- b. Bifocals/bifocal glasses
- c. Trifocals/trifocal glasses
- d. Contact lenses
- e. none
- f. Other (write what it is in the box to the left)

38. What is your job title, if any?

- a. Yes
- b. No
- c. Unknown

39. What is your father's profession, if any?

Mother's profession, if any?

40. If known, what is your parents' net annual household income?

- a. Under 20,000
- b. 20,000 to 39,999
- c. 40,000 to 59,999
- d. 60,000 to 79,000
- e. 80,000 to 99,999
- f. 100,000 to 200,000
- g. 200,000 to 500,000
- h. 500,000 to 1,000,000
- i. Over 1,000,000

41. If known, what is your own net annual household income? That is, not your parents, but your own income per year (and that of your spouse if you have one)

- a. Under 20,000
- b. 20,000 to 39,999
- c. 40,000 to 59,999
- d. 60,000 to 79,000
- e. 80,000 to 99,999
- f. 100,000 to 200,000
- g. 200,000 to 500,000
- h. 500,000 to 1,000,000
- i. Over 1,000,000

42. Do you qualify for OSAP?

- a. Yes
- b. No

43. Would you describe yourself as having grown up in poverty?

- a. Yes
- b. No

44. Would you describe yourself as having grown up rich?

- a. Yes
- b. No

Appendix H: Basis studies for selecting ERP time windows

p1 interval (110-180ms)

Mangun & Hillyard, 1991; Smith et al, 2003; Schupp et al, 2003b; Carretie, Hinojosa et al, 2004; Carretie, Mercado et al, 2004; Delplanque et al, 2004; Briggs, 2007; Olofsson et al, 2008; Kissler et al, 2009; Kishiyama et al, 2009; Versace et al, 2010; Franken et al, 2011

n1 interval (110-180ms)

Keil et al, 2001, 2002; Carretie et al, 2003; Schupp et al, 2003a; Rossignol et al, 2005; Olofsson et al, 2008; Key & Dykens, 2008; Rozenkrants et al, 2008; Kishiyama et al, 2009; Kissler et al, 2009; Franken et al, 2011

EPN/n300 interval (200-300ms)

Weike & Alfons, 2004; Laar et al, 2004; Schupp et al, 2004a, b; Schupp et al, 2007; Briggs, 2007; Olofsson et al, 2008; Flaisch et al, 2008; Stockburger et al, 2008; Peyk et al, 2009; Kissler et al, 2009; Versace et al, 2010; Dunning et al, 2011

LPP interval (450-800ms)

Ito, Cacioppo, & Lang, 1998; Ito, Larsen et al, 1998; Schupp et al, 2004a, b; Moser et al, 2006; Hajcak et al, 2006; Codispoti, Ferrari, & Bradley, 2006; Codispoti, Ferrari, Junghofer, & Schupp, 2006; Hajcak & Nieuwenhuis, 2006; Spreckelmeyer et al, 2006; Wood & Kiseley, 2006; Briggs, 2007; Sabatinelli et al, 2007; Bradley et al, 2007; Olofsson et al, 2008; Herbert et al, 2008; Versace et al, 2010; Dunning et al, 2011; Little & Franken, 2011