

The use of reward cue-reactivity in predicting real-world self-control failure

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Humans, like all animals, are strongly motivated to approach stimuli that signal a potential reward and avoid those that may lead to harm. The expectation of receiving a reward or punishment is fundamental to nearly all forms of learning and, through repeated exposure, can become associated with environmental cues. For example, when an abstinent smoker hears the distinctive crackling sound a cigarette makes when someone nearby inhales one, this sound alone, through its long history of being associated with smoking, can lead to increased craving and desire for a cigarette. This impulse to consume the tempting item, once activated, can enter into conflict with the abstinent smoker's goal of remaining tobacco free. As reviewed in this chapter, exposure to reward cues such as these can have a host of physiological and psychological effects on the individual: from increased attention toward the desired item and suppression of competing goals, through to increase heart rate, salivation, and activity in the brain's reward centers. These downstream effects of cue-exposure may precipitate failures of self-control as individuals abandon long-term goals in favor of indulging their immediate cravings and impulses.

Unfortunately, humans exist in an environment teeming with cues that signal all manner of pleasurable experiences. At no other time in history have people been so enveloped by advertisements and technological nudges vying for their attention. With respect to food, this has led to the theory that humans are presently living in an obesogenic environment whereby the ease of acquiring high-calorie food and the constant cues and advertisements reminding us of its existence are thought to underlie the current obesity epidemic (Berthoud, 2012). However, our environment is not only composed of cues reminding us of that we could, right this minute, eat something delicious, smoke a cigarette, or drink ourselves into a stupor (or all of the above). With the rise of mobile technology, people also face a plethora of electronic nudges inviting them to engage in pleasurable activities, from binge watching television shows or playing electronic games to sharing photos on social media. Indeed, in addition to food and sleep, it is precisely these types of media experience that rank among the most difficult of temptations to resist (Hofmann, Baumeister, Förster, & Vohs, 2011).

In recent years there has been an increasing interest in understanding the brain mechanisms underlying reward-seeking and its regulation (e.g., Heatherton & Wagner, 2011). In particular, there has been a surge of recent research exploring how individual differences in reactivity to reward cues are related to reward-seeking behavior and poor self-regulation. In this chapter,

we review the latest cognitive neuroscience findings on the neural systems involved in reward-related processing, focusing on research that takes a “brain-as-predictor” approach (e.g., Berkman, Falk, & Lieberman, 2011; Gabrieli, Ghosh, & Whitfield-Gabrieli, 2015) whereby individual differences in brain activity are used to predict behavioral and health outcomes. We begin this chapter with a brief overview of the behavioral research on reward cue-reactivity, followed by a description of the brain systems involved in representing reward incentives and value. In the remaining sections of the chapter we review recent research demonstrating how an understanding of individual differences in reward cue-reactivity and self-control can shed light on why some individuals succeed or fail at regulating their temptations and desires.

A brief overview of cue-reactivity research

Imagine, for a moment, that you were a devout bread aficionado who has embarked upon an ill-advised plan to cut down on carbs. For a former bread lover, the smell and sight of freshly baked bread can serve as an activating stimulus, reminding you of the taste and pleasure you formerly derived from toasts, crumpets, and bagels. These visual and olfactory cues can generate a host of physiological and psychological effects that can interfere with an individual’s ability to resist consuming a tempting food item. Research in this area typically involves exposing individuals to tempting food cues in the form of olfactory cues, such as the smell of pizza or visual cues such as the sight of chocolate or an image of an ice cream sundae. For example, when individuals are exposed to olfactory food cues, they exhibit increased craving and desire for the cued item (Federoff, Polivy, & Herman, 1997). Other research has shown that reward cue exposure may also lead to a variety of physiological effects including increased salivation (Legoff & Spigelman, 1987), heart rate (Nederkoorn, Smulders, & Jansen, 2000), and a reactivity in the brain’s reward circuitry (Tang, Fellows, Small, & Dagher, 2012).

Although the notion that exposure to reward cues can precipitate reward-seeking behavior has been around for a long time, one of the first to investigate the psychology of this phenomenon was Stanley Schachter (1971). In his theorizing about the causes of obesity, Schachter posited that obese individuals are more *stimulus-bound* than non-obese individuals; that is to say they are more susceptible to external environmental influences on behavior (Schachter, 1971; Schachter & Friedman, 1974). Along the way, Schachter conducted experiments examining how environmental triggers could be manipulated to increase or decrease eating behavior among obese individuals. For example, Schachter and his then graduate student Lee Ross devised an experiment to test whether obese individuals were more susceptible to food cues than non-obese individuals. To do this, they had individuals sit at a table which happened to contain a tin of cashews that was either under high or low levels of illumination. This simple manipulation served to highlight the salience of the food cue in the environment and led to the finding that overweight individuals consume more cashews – as measured by covertly weighing the tin before and after the experiment – in the salient condition than did non-obese individuals (Ross, 1969). This finding of cue-salience was later taken up in the domain of smoking, where a similar study showed that nicotine-deprived smokers were more likely to smoke following exposure to salient smoking cues (Herman, 1974).

This early work was followed by a surge of research on cue-reactivity and its relationship to craving, drug addiction, obesity, and other health-related behaviors. For example, in the addiction literature it has been demonstrated that exposure to cigarette or drug cues increases craving for – and consumption of – the desired items (Sayette, Martin, Wertz, Shiffman, & Perrott, 2001). Similarly, in dieters, exposure to appetizing food cues leads to craving and consumption compared

to non-dieters (Harris, Bargh, & Brownell, 2009), although even normal-weight individuals are susceptible to the lure of appetizing foods cues (Cornell, Rodin, & Weingarten, 1989). Other work has shown just how quickly these cue–reward associations can be formed. For example, a neutral cue can, over a single session of repeated pairings, become associated with chocolate food rewards and subsequent exposure to this neutral cue can elicit increased craving for chocolate (e.g., Van Gucht, Vansteenwegen, Van den Bergh, & Beckers, 2008).

Across multiple meta-analyses, cue-exposure proves to be a common and reliable predictor of craving in the domains of drug addiction and eating (Gass, Motschman, & Tiffany, 2014). Moreover, a recent meta-analysis on food cue-reactivity has shown that, across multiple studies, visual representations of cues (images, videos) are just as effective at eliciting cue-related craving and consumption as the sight and smell of actual foods (Boswell & Kober, 2016). This last point is worth highlighting as we turn to the neuroscience research where the consumption or sight of actual food or drugs is made difficult by the restricted neuroimaging environment.

Beyond the effects of cue-reactivity on craving and consumption, research has shown that exposure to reward cues can also have subtler effects that may operate outside an individual's awareness. For instance, when dieters are exposed to food reward cues on a computer monitor, they typically display an attentional bias toward the spatial location these cues last appeared on the screen (Papies, Stroebe, & Aarts, 2008a). Exposure to reward cues has also been shown to impair working memory capacity; for instance, work by Kemps and colleagues (2008) has shown that, among participants who had abstained from eating chocolate, performance on a working memory task was impaired when it was performed in the presence of chocolate cues (Kemps, Tiggemann, & Grigg, 2008). This last finding suggests that desired food cues can occupy cognitive resources and impair performance on other tasks. Other research has shown that exposure to tempting food or cigarette cues may also lead to the activation of positive hedonic thoughts for the tempting items such as the thought of partying and letting loose upon exposure to alcohol cues (Hofmann, van Koningsbruggen, Stroebe, Ramanathan, & Aarts, 2010). Moreover, exposure to appetizing food cues has also been shown to inhibit long-term dieting goals among dieters (Papies, Stroebe, & Aarts, 2008b). However, it appears that exposure to reward cues need not always lead to craving and consumption. For instance, counteractive control theory posits that, in some individuals, exposure to tempting cues may serve to activate self-regulation goals, particularly for people who have a history of successful self-regulation in the face of temptations (Fishbach, Friedman, & Kruglanski, 2003).

Taken together, the findings described above appear, in part, to support Schachter's externality theory of obesity. It is an interesting quirk of history, then, that this theory fell out of favor after the publication of an article by Rodin (1981) that was critical of later incarnations of Schachter's theory that posited that obese individuals were externally sensitive across multiple domains and not just in the domain of eating (e.g., Schachter & Friedman, 1974). As later noted by Stroebe and colleagues (Stroebe, van Koningsbruggen, Papies, & Aarts, 2013), the dismissal of externality theory may have been premature as its earlier incarnations, in which Schachter did not make such strong claims about obese individuals showing a form of a domain-general externality, appears to still be valid. Indeed, this theory finds support in recent cognitive neuroscience research demonstrating the role of neural measures of cue-reactivity in predicting obesity and dietary failures. Thus, the externality theory of obesity may deserve a fresh look as recent neuroscience research uncovers evidence of domain-specific relationships between reward cue-reactivity and poor self-regulation not only in eating, but also in behaviors as diverse as smoking, sexual behavior, and financial decision making.

Functional neuroimaging of reward cue-reactivity

Non-human animal research has demonstrated an important role for both the mesolimbic dopamine system (composed primarily of the ventral striatum/nucleus accumbens and the ventral tegmental area) and the orbitofrontal cortex (OFC) in reward processing. Neurophysiological studies show increased dopamine release and neuronal firing in these regions when non-human animals consume rewards (Di Chiara & Imperato, 1988) and when they are exposed to reward cues (Balfour, Yu, & Coolen, 2004). In humans, electrical stimulation of this region increases feeling of pleasantness (Bishop, Elder, & Heath, 1963) and human neuroimaging research largely corroborates non-human animal studies by demonstrating increased activity in the ventral striatum and OFC during the receipt for food rewards (Kringelbach, O'Doherty, Rolls, & Andrews, 2003) as well as monetary rewards (Knutson, Taylor, Kaufman, Peterson, & Glover, 2005) and even certain social rewards, such as sharing personal information with others (Tamir & Mitchell, 2012). Moreover, brain activity in these regions has been shown to be linearly related to the value and pleasantness of rewards. For example, in one of the first studies to examine food reward, participants underwent functional neuroimaging during receipt of a liquid food (e.g., chocolate milk). Participants' rating of enjoyment for the food was associated with increased activity in the OFC and as participants' enjoyment declined with increasing satiety, so did brain activity in the OFC (Kringelbach et al., 2003). Thus far we have discussed how actual reward receipt is associated with increased brain activity in two key regions of the brain's reward system, but what happens when people view visual cues associated with rewards? Do these same regions show evidence of cue-related increases in brain activity?

Across multiple domains (eating, drugs, and social cues) studies have shown that the same brain structures involved in reward processing during reward receipt also show evidence of increased activity during cue-exposure. For instance, when people view images of highly appetizing foods (e.g., snacks, desserts, high-calorie foods) the OFC and ventral striatum show increased activity relative to less palatable foods or neutral objects (Demos, Heatheron, & Kelley, 2012; Lopez, Hofmann, Wagner, Kelley, & Heatherton, 2014; Rapuano, Huckins, Sargent, Heatherton, & Kelley, 2016; for a meta-analysis see van der Laan, de Ridder, Viergever, & Smeets, 2011). Similar effects are found when drug users view images of drugs (Garavan et al., 2000), alcohol-dependent individuals view alcohol cues (Myrick et al., 2008), or when smokers view images of cigarette smoking or paraphernalia (Wagner, Dal Cin, Sargent, Kelley, & Heatherton, 2011). In addition to these basic findings, a number of studies have demonstrated that reward cue-reactivity may be modulated by a number of individual differences (e.g., body weight, hunger, mood, the presence of peers). For example, OFC reactivity to appetizing food images and commercials shows a linear relationship with hunger (Stice, Burger, & Yokum, 2013) and body mass index (Rapuano et al., 2016). Similarly, negative mood is also associated with increased activity in the left OFC when dieters view appetizing food cues (Wagner, Boswell, Kelley, & Heatherton, 2012) as well as when smokers view smoking cues (McClernon, Kozink, & Rose, 2008).

These effects of cue-exposure on activation of the brain's reward system appear to occur even when participants are unaware of the nature of the task. For example, in a study by Wagner and colleagues (2011) smokers and non-smokers were asked to view thirty minutes of a motion picture film in a task that was ostensibly about visual perception but happened to contain a number of scenes of actors smoking. Upon examining activity during smoking scenes in the OFC, it was found that smokers had greater OFC activity compared to non-smokers despite being unaware of the nature of the study or explicitly paying attention to the smoking cues in the movie.

Studies of reward cue-reactivity are not restricted to these primary and secondary rewards but have also been conducted on other classes of rewards. For instance, the OFC and ventral

striatum also demonstrate heightened activity to attractive faces (Cloutier, Heatherton, Whalen, & Kelley, 2008), smiling faces (Somerville, Hare, & Casey, 2011), and the recall of pleasant autobiographical memories (Speer, Bhanji, & Delgado, 2014), and are also active when individuals listen to their favorite passages of music (Blood & Zatorre, 2001).

Finally, although this chapter is primarily concerned with studies of reward cue-reactivity, it is worth noting that reward cues may also, in certain instances, lead to increased activation in brain regions involved in representing manual actions and basic motor responses. For instance, when smokers view a movie that contains scenes of smoking, they show evidence of greater recruitment of brain regions involved in the representation of goal-directed actions compared to non-smokers (Wagner et al., 2011; Yalachkov, Kaiser, & Naumer, 2009). Similarly, when individuals view food commercials promoting appetizing foods, they show increased activity in brain regions associated not only with reward, but also with parts of the motor cortex associated with mouth-specific movements (Rapuano et al., 2016). Together, these findings serve as neural evidence for the theory that cue-exposure may not only precipitate craving and desire but can also automatically activate motor schemas for consuming desired items owing to the repeated pairing of actions with food or drug consumption (Tiffany, 1990).

Predicting self-control failure from neural measures of reward cue-reactivity

In the previous sections we described the phenomenon of cue-reactivity and its neural substrates. Here we turn to research aimed at uncovering relationships between brain measures of reward cue-reactivity and various behavioral and health outcomes that can, broadly construed, fall under the umbrella of self-control failures. In particular, we focus on studies that follow a “brain-as-predictor” approach (Berkman et al., 2011; Gabrielle et al., 2015) in which neural measures are used to prospectively predict behavioral, clinical, or health outcomes.

Perhaps the most widely studied relationship between cue-reactivity and health outcomes is research on food cue-reactivity and weight gain. Across several studies, researchers have found that the degree to which adolescents (Yokum, Gearhardt, Harris, Brownell, & Stice, 2014) and adults (Demos et al., 2012) show cue-reactivity to food cues is predictive of subsequent weight gain over the following months. In one such study, incoming college freshmen were invited to participate in a simple cue-reactivity task involving food, alcohol, and sexual images. Participants showed increased activity in the ventral striatum to these various classes of reward cues but more importantly, individual differences in cue-reactivity to food images went on to predict subsequent weight gain measured at a repeat session six months after the initial scan.

Cue-reactivity studies have also examined associations between neural measures of reward processing and self-regulation failures. For instance, heightened neural food cue-reactivity is associated with number of snacks eaten following MRI scanning (Lawrence, Hinton, Parkinson, & Lawrence, 2012) and, perhaps unsurprisingly, with poor success in a subsequent weight-loss program (Murdaugh, Cox, Cook, & Weller, 2012). In the domain of smoking and drug use, studies similarly suggest that elevated cue-reactivity is predictive of future substance use problems at a one-year follow-up (Stice, Yokum, & Burger, 2013). More recently, Lopez and colleagues (2014) combined neuroimaging measures of food cue-reactivity with experience sampling to investigate whether cue-reactivity predicts daily desires for food as well as difficulty resisting food desires. Here, participants came in for an initial neuroimaging session in which individual differences in food cue-reactivity were assessed. Following this, they underwent an experience sampling procedure whereby they were randomly asked to report their food desires, amount of food eaten, and ability to resist acting on food desires at random intervals throughout

the following days. Measures of food desire and enactment of those desires were associated with increased activity in the ventral striatum to appetizing food cues, suggesting that individuals with stronger associations between food and reward were more likely to exhibit self-regulation failures in the domain of eating.

Thus far, much of our discussion has focused on cue-reactivity to primary rewards such as food or drugs. Studies from the field of neuroeconomics has generally focused on the same brain structures but has instead examined their relationship to decision making, consumer choice, and risk taking. For instance, reward-related responses in the ventral striatum have been shown to predict subsequent product preferences after viewing images of consumer goods (Levy, Lazzaro, Rutledge, & Glimcher, 2011) as well as subsequently predicting purchasing behavior (Knutson, Rick, Wimmer, Prelec, & Loewenstein, 2007). In each of these examples, participants were not explicitly tasked with making explicit evaluations or purchase decisions, arguing that the predictive power of neural measures of cue-reactivity is not predicated on participants explicitly engaging in decision making.

Are neural measures of reward cue-reactivity domain specific or domain general? Earlier in this chapter, we discussed criticisms of Schachter's externality theory of obesity in which later incarnations suggested that obese individuals may be driven by external cues not just for eating but for other behaviors as well. At the time there was little evidence of this and after a critical paper was published, the theory seems to have fallen into disfavor. As noted in an earlier section, the initial, more constrained version of externality theory in which the eating behavior of obese individuals was driven by external food cues appears to be supported by neuroimaging studies of cue-reactivity, which, by and large, suggest that eating and possibly other behaviors are associated with neural responses to reward cues that are domain specific. Perhaps the best example of this domain specificity is in the study conducted by Demos and colleagues (2012). As mentioned previously, in this study incoming college freshmen participated in a cue-reactivity task in which they viewed multiple categories of reward cues (food, alcohol, and sexual images). The primary finding of this study was that reward cue-reactivity in the ventral striatum went on to predict weight gain at a six-month follow-up session. However, these weight gains were specifically predicted by food cue-reactivity and not by striatal reward-related responses to other classes of rewards (alcohol, sexual imagery). Instead, neural measures of cue-reactivity to sexual images were associated with a self-report measure of sexual desire (Demos et al., 2012). Thus, the data from this study argue against any domain-general reward sensitivity that underlies negative health behaviors in specific domains such as eating. Instead, the associations between the reward system and specific behaviors appear to be tuned to those domains where individuals exhibit difficulty regulating their behavior (eating for dieters, smoking for smokers, etc.).

Does this mean that there's no case of a more general reward sensitivity measure predicting self-regulation difficulty? Other research would suggest that there are instances where individuals may show a more domain-general relationship between reward cue-related activity in the brain's reward system and poor self-control. Perhaps the most striking example of this comes from research following up on a cohort of participants in Walter Mischel's seminal delay of gratification research. In this study, participants from the original delay of gratification research conducted some forty years prior were invited to participate in a functional neuroimaging study in which they performed a go/no-go task involving positive facial expressions. Surprisingly, participants whom, as children, had demonstrated difficulty delaying gratification exhibited an exaggerated response in the ventral striatum to positive cues, despite being measured some forty years later (Casey et al., 2011).

Taken together, the research outlined above suggests that individual differences in reward cue-reactivity can be a reliable measure of reward sensitivity, the surfeit of which makes it difficult

for individuals to control approach behaviors and suppress cravings and impulses, ultimately leading to poor self-control and negative health outcomes.

Individual differences in top-down regulation of reward responses predict self-regulation success

This chapter has taken a primarily bottom-up approach, focusing on studies whereby reward-related neural cue-reactivity is assessed using relatively simple tasks unencumbered by complex demands or instructions to regulate impulses and cravings. However, real-world self-control conflicts often involve not only a temptation but also attempts to suppress or inhibit approach behavior toward the tempting object. Much of this work focuses on the role of the prefrontal cortex (PFC) in regulating cravings or impulses (for a review see Heatherton & Wagner, 2011). For instance, the lateral PFC and the ventromedial PFC have both been shown to be involved in down-regulating emotional responses in the amygdala. Specifically, when individuals are asked to change their appraisal of a negative emotional stimulus such as, for example, construing an image of a barking dog not as threatening but as being playful, they typically show an inverse relationship between activity in the lateral PFC and the amygdala (for a review see Ochsner & Gross, 2005). Moreover, the habitual use of this *cognitive reappraisal* strategy in daily life has been shown to predict decreased amygdala reactivity to negative facial expressions (Drabant et al., 2009), suggesting that individuals who regularly rely on reappraisal are better able to regulate their response to aversive events. In line with this work, the past several years have seen the application of reappraisal strategies to the domain of reward reactivity, examining how reappraisal can alter neural responses to temptations (e.g., Kober et al., 2010). With respect to our present topic more recent neuroscience research has focused on the role of individual differences in neural indices of self-control and response inhibition, predicting self-regulation success in many of the same domains as covered previously.

For instance, engaging in cognitive reappraisal of smoking cues increases activity in the lateral PFC, a brain region associated with response inhibition and self-regulation more broadly (see Heatherton & Wagner, 2011), and also simultaneously reduces cue-reactivity in the ventral striatum (Kober et al., 2010). Moreover, other studies show that the degree to which smokers attempting to quit activate the lateral PFC when viewing smoking cues (Janes et al., 2010) or during a response inhibition task (Berkman et al., 2011) goes on to predict subsequent success during smoking quit attempts. Finally, in the domain of eating, recent work examined the relationship between recruitment of prefrontal regions implicated in response inhibition when participants viewed appetizing food cues and the ability to successfully resist real-world food desires. Specifically, Lopez and colleagues (2014) had participants engage in a go/no-go response inhibition task in which the stimulus to be inhibited was images of appetizing food cues while undergoing functional neuroimaging. As expected, when participants inhibited their responses to the appetizing food cues, they showed increased activity in the lateral PFC. Individual differences in this neural marker for response inhibition were associated with increased success at resisting food desires as measured by experience sampling over the following week. That is to say that those participants who exhibited a larger neural response in the lateral PFC when engaging in self-control were also better at resisting food desires in their daily lives (Lopez et al., 2014). Together, these studies demonstrate the importance of examining not only bottom-up responses to reward cues but also top-down responses when attempting to use neural measures to predict real-world self-control failure.

A note on the meaning of prediction

In describing research on cue-reactivity predicting self-control, we employed the term prediction to mean those cases where neural measures of reward-related responses were associated with behaviors outside the immediate experimental session (e.g., future weight gain, smoking abstinence). It is important, however, to note that this use of the term prediction is perhaps overly optimistic as these studies still represent within-sample correlations. Truly validating the predictive potential of neural measures of reward-related processes requires the generation of predictive models that make out-of-sample predictions on an independent set of participants. This type of model building and testing is still far from being the norm in this line of research. However, recent reviews highlighting the necessity of just this type of model building and testing (i.e., Gabrieli et al., 2015) will no doubt spur the field to move beyond describing associations between neural measures and prospective health outcomes, and instead attempt to build models that make predictions about the self-control successes and failures of novel sets of participants.

Summary

For both animals and humans, learning which environmental cues predict reward or signal harm is vital for survival and serves to promote behaviors that are evolutionarily important (e.g., food seeking, reproduction). At the same time, these learned associations can become maladaptive when people are surrounded by cues and opportunities to indulge in unhealthy behaviors. In this chapter, we focused on research demonstrating a role for the brain's reward circuitry in representing the value and pleasantness of both actual rewards and cues that are associated with rewards. Moreover, we described studies in which individual differences in neural cue-reactivity were used to prospectively predict a variety of individual differences in health-related behaviors, from body fat weight gain through mood, stress, and product purchasing decisions. In addition, we noted that this focus on bottom-up processing of rewards is only half the picture when it comes to real-world self-control conflicts. Recent work examining the role of brain systems involved in self-control suggests that individual differences in people's propensity to engage this system are associated with self-regulation success in many of the same domains as findings on reward cue-reactivity. Future research designed to bring these two threads of research together and simultaneously examine the balance between motivational and self-control systems during self-control conflicts promises to shed new light on how and why people fail at self-control.

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