CHAPTER 7

The Cognitive Neuroscience of Self-Regulatory Failure

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It is one of the mysteries of human nature that inhibiting a behavior (e.g., not reaching for another piece of cake) can be experienced as more effortful than performing the action that otherwise would be inhibited. The deceptive ease with which people manage to avoid indulging every craving, voicing every thought, or giving in to the vicissitudes of every emotion belies the sheer amount of effort that must be expended to stay in control. Should people's ability to regulate themselves become compromised, the damage to their social lives would be devastating. Even behaviors as trivial as not looking at a mole on an employer's face would become impossible to resist. Although, at first blush, it might seem unfathomable that people could suddenly be robbed of their self-control, the reality is that with certain brain injuries anyone can suffer from the deficits in self-regulation just described.

Although the importance of the brain in enabling self-regulation has long been of interest to neuroscientists and neuropsychologist, many of the other disciplines that study self-regulation (e.g., developmental psychology, educational psychology, social psychology) have long remained agnostic regarding the underlying neural mechanisms that allow self-regulation to occur. In contrast to these disciplines, neuroscientists have long studied the brain mechanisms that underlie elementary forms of motor and cognitive control, generally under the rubric of "executive function." However, this line of research seldom explored how these faculties play out in the sorts of situations that have traditionally been under the purview of social and health psychologists (e.g., desires, prejudice, mood). It is not immediately clear why it took so long for self-regulation researchers to seek out neural mechanisms, as neurologists and neuropsychologists have long recognized the importance of the brain, particularly the frontal lobes, in the organization and regulation of behavior (e.g., Kleist, 1934). Reports of extraordinary cases of dysregulated social behavior following brain injury go back as far as the 19th century (Welt, 1888), and many early neuropsychologists put the prefrontal cortex at the center of their theories of

self-control (Fuster, 1980; Jarvie, 1954). Although neuropsychologists have made great strides in understanding the relationship between brain and behavior, it is often the case that these theories are blind to the social contexts in which most of our thoughts and actions are embedded. It is only recently have researchers begun to apply modern cognitive neuroscience methods to the problem of how the brain enables self-regulation, as well as what happens in the brain when self-regulation fails.

In this chapter we present a brief overview of the functional neuroanatomy involved in self-r egulation in social and emotional domains, focusing on neuropsychological research that elegantly demonstrates the dramatic failures of self-regulation that can result from damage to specific brain regions. Following this, we turn to studies of the neural substrates of self- regulation and self- regulation failure across three domains: moods and emotions, thoughts and prejudices, and appetitive behaviors (e.g., desires and temptations). Finally, we review recent neuroscience-based models of self- regulation failure.

Neuropsychological Insights into the Functional Organization of Self-Regulation

When it comes to the neural substrates of self-regulation, no region has been more consistently implicated than the prefrontal cortex (PFC). The PFC supports a host of mental operations that fall under the rubric of *executive function* (e.g., working memory, response inhibition, attentional selection, decision making, planning), enabling organisms to adaptively adjust their behavior to external demands and internal goals (Miller & Cohen, 2001). The most widely accepted definition of PFC is that it is the portion of the frontal lobe that lies anterior to primary and secondary motor cortex. The PFC, unlike other regions of the brain, is unique in that it shares connections with a wide range of systems involved in generating and modulating behavior (e.g., motor and sensory systems, subcortical regions involved in emotion and reward, and medial temporal regions involved in learning and memory).

Evidence that the PFC plays a critical role in organizing and controlling behavior stretches back as far as the mid-19th century (although less systematic accounts can be traced back to the 14th century; e.g., Lanfranchi, 1315). Early case reports of patients with damage to the PFC revealed deficits so bizarre that many doubted their veracity. For example, the famous case of Phineas Gage was initially dismissed as a "Yankee invention" by a noted English surgeon of the time. Early case studies focused on the striking personality changes exhibited by these patients, with many examples of formerly pleasant people becoming profane, egoistic, and insensitive to social norms following damage to the PFC. Reflecting the general tone of these patients' behavior, one early observer termed this constellation of symptoms *Witzelsucht*, which roughly means facetiousness and refers to a patient's tendency to make inappropriate jokes (Oppenheim, 1890). Another type of symptom commonly observed after damage to the PFC was a dramatic loss of motivational drive. These patients had great difficulty with spontaneously generating behaviors and lacked initiative to such a degree that they often failed to wash or dress themselves. Early theorists of prefrontal function assumed these two distinct types of self-regulation failure were manifestations of the same underlying "prefrontal syndrome," but as diagnostic techniques improved and the number of patient studies

increased, it became clear that the different neuropsychological deficits observed in these patients had their origin in damage to distinct regions of the PFC.

While there remains debate concerning the precise anatomical boundaries of the PFC and its subregions, researchers are largely in agreement on three principal subdivision of the PFC: the ventromedial PFC (VMPFC), the lateral PFC (LPFC; dorsal and ventral convexities), and the anterior cingulate cortex (ACC). Knowledge of the underlying pattern of anatomical connectivity between regions of the PFC is essential to understanding how these regions come together to make self-regulation possible. We turn now to an overview of the neuroanatomy and psychological changes wrought by damage to each of these three regions.

Ventromedial Prefrontal Cortex

The VMPFC consists primarily of the inferior aspect of the medial PFC and the orbitofrontal cortex, both of which are cytoarchitecturally similar structures (Ongur & Price, 2000). Patients with damage to the VMPFC have difficulty regulating social, affective, and appetitive behaviors. This is borne out by the connectivity pattern in the VMPFC, which is highly interconnected with subcortical limbic areas, such as the amygdala (Carmichael & Price, 1995). In addition, the VMPFC shares connections with reward-processing regions in the ventral striatum (Haber, Kunishio, Mizobuchi, & Lynd-Balta, 1995), as well as regions involved in appetite and visceral sensation, such as the hypothalamus and the insula (Barbas, Saha, Rempel-Clower, & Ghashghaei, 2003). As a result of its connectivity with brain regions involved in emotion and reward, the VMPFC is thought to be important for the self-regulation of emotional, social, and appetitive behaviors (Beer, Shimamura, & Knight, 2004; Fehr & Camerer, 2007; Hare, Camerer, & Rangel, 2009; Quirk & Beer, 2006).

Prior to the 20th century, there were few systematic studies of the changes in personality and behavior brought about by damage to the PFC. Most early examples are case studies, such as that of Phineas Gage, the American railroad foreman whose tamping iron (an iron bar approximately 3 inches in diameter) was propelled through his cranium when the explosive charge he had been preparing accidentally ignited. A less widely known, but no less compelling, case for social disinhibition following damage the VMPFC was made in 1888 by Leonore Welt, who describes the case of a man who sustained severe head trauma after falling 100 feet from a window. This patient showed personality changes similar to those of Phineas Gage, becoming moody and threatening, and often playing cruel practical jokes on the other patients (Welt, 1888). Shortly after his release from the hospital, the patient succumbed to an unrelated illness and his brain was subject to a postmortem examination. Studying his brain, Welt found evidence of extensive VMPFC damage and posited that this injury was the source of the patient's personality changes. This particular case is important for being the first published report of a brain injury as the basis for poor self-control that was confirmed by postmortem examination. Moreover, it inspired others to consider the importance of the precise location of damage to the etiology of personality changes following brain injury.

Since these early case reports, a large number of studies have confirmed the basic finding of social disinhibition following damage to the VMPFC. While initially neurologists had difficulty arriving at a precise description of the symptoms, focusing on certain aspects of the disorder, such as inappropriate humor and use of profanity (Oppenheim,

1890) or the tendency to boast (Brickner, 1934), display aggression (Rylander, 1939), steal and lie (Kleist, 1934), engage in sexual exhibitionism (Ackerly, 1937), more recently it has been shown that the patients have impaired decision making, preferring risky but disadvantageous outcomes over safer ones (Sanfey, Hastie, Colvin, & Grafman, 2003). Over time neuropsychologists converged on the view that damage to the VMPFC leads to a breakdown in self-control and restraint, with a particular emphasis on failure to obey social norms (Beer et al., 2004; Blumer & Benson, 1975; Jarvie, 1954). Interestingly, these patients do not lack knowledge of common social norms (Saver & Damasio, 1991). Theirs is a problem not of memory but of maintaining control over their behavior in everyday situations.

Lateral Prefrontal Cortex

The LPFC, unlike the VMPFC, has no direct connections to limbic regions involved in emotion; instead the LPFC projects primarily to other regions in the PFC, namely, to secondary motor regions involved in action planning (Petrides & Pandya, 1999), the basal ganglia (Nambu, 2008) as well as the VMPFC and ACC (McDonald, Mascagni, & Guo, 1996). With regard to function, although the LPFC is thought to play an important role in elementary executive processes, such as working memory (Curtis & D'Esposito, 2003), planning (Stuss & Alexander, 2007), response selection (Thompson-Schill, Bedny, & Goldberg, 2005) and inhibition of responses (Aron, Robbins, & Poldrack, 2014), it would appear that the LPFC, through its rich connections with ACC, VMPFC, and secondary motor areas, is principally involved in planning and maintaining behaviors. For self-regulation, this means holding regulatory strategies in mind and ensuring that these are not derailed by distractions, such as when a restrained eater suddenly finds him- or herself ambushed by appetizing foods. Thus, the LPFC is thought to be vital for supporting self-regulation in multiple domains (Cohen & Lieberman, 2010).

Patients suffering from damage to lateral portions of the PFC present a very different symptomatology than do patients with VMPFC damage. These patients display profound difficulties in planning behavior and inhibiting goal-irrelevant distractions. One early case illustrating these deficits was described by noted Canadian neurosurgeon Wilder Penfield and is of a patient who underwent a neurosurgical resection involving lateral portions of the PFC. Following recovery, it was noted that the patient demonstrated much difficulty playing games that involved the maintenance of multiple goals in memory, such as bridge (Penfield & Evans, 1935). Moreover, the patient appeared to lose all initiative, displaying a profound apathy toward seeking employment. This case is remarkably similar to one reported half a century later, in which a college student, having recovered from damage to the right PFC, repeatedly failed classes and eventually dropped out of college. He later reported that despite understanding the material, he simply could not muster the interest it would take to be successful (Stuss & Benson, 1986). Unlike patients with damage to the VMPFC, patients with LPFC damage have no problem engaging in social interactions or understanding social and emotional cues (Bar-On, Tranel, Denburg, & Bechara, 2003). Their deficits are more in line with the core faculties of what has come to be known as *executive function* (Miller & Cohen, 2001), and their difficulty in organizing and regulating behavior can be traced to deficits in working memory, task switching, and inhibitory control. Accordingly, these patients have difficulty in tasks that have changing demands, and they often perseverate in behaviors

that have become irrelevant to the current goals of the task (Barceló & Knight, 2002; Milner, 1963). These patients also perform poorly on tasks relying on inhibitory control. For instance, patients with LPFC damage are impaired on the Stroop task (Perret, 1974; Vendrell et al., 1995), in which they have to read the name of a color word printed in a conflicting ink color (e.g., the word *red* printed in blue ink). These patients also have difficulty generating novel items, such as nonverbalizable designs, and tend to perseverate on the same type of design throughout the task (Jones-Gotman & Milner, 1977).

Perhaps the best overall example of the constellation of deficits exhibited by patients with LPFC damage comes from observing their performance on everyday tasks outside the laboratory. In a cleverly designed study, Shallice and Burgess (1991) instructed patients to perform an array of real-world errands (e.g., shopping for items on a list, asking for directions, and meeting someone at a specified time) while being unobtrusively tailed by two observers who made note of their performance. Patients showed a remarkable inability to complete even the most rudimentary daily errands; for instance, patients failed to purchase items on their list, entered the same shop multiple times, and even left a shop without paying (Shallice & Burgess, 1991). This clever, real-world neuropsychological test serves to illustrate how the many facets of LPFC function must work together to allow us to accomplish even the most mundane of goal-directed behaviors.

More recently, studies using transcranial magnetic stimulation, which can cause local disruptions of neural activity within a brain region, have shown that inactivation of the LPFC can lead to increased impulsiveness and risky decision making (Chambers et al., 2006; Knoch, Pascual-Leone, Meyer, Treyer, & Fehr, 2006). Conversely, activating (instead of inhibiting) these same regions using a technique known as direct current stimulation, produces the opposite effect. Rather than impairing the ability to engage in self-control, direct current stimulation appears to improve self-control, as evidenced by reduced impulsive behavior during financial decision-making tasks (Fecteau et al., 2007; Jacobson, Javitt, & Lavidor, 2011).

Anterior Cingulate Cortex

The ACC is the rostral portion of cingulate cortex, resting above the corpus callosum. It is interconnected with a wide range of brain structures involved in cognition, emotion, and motor execution. However, unlike other regions of the PFC, the ACC receives little input from regions involved in sensory processing (Carmichael & Price, 1995). The ACC is intimately connected to the LPFC and VMPFC, and the adjacent motor cortex. In addition, the ACC shares many important connections with limbic regions involved in emotion, and ventral striatal regions implicated in reward processing (Ongur, An, & Price, 1998; Vogt & Pandya, 1987). In many ways the ACC sits at the anatomical crossroads of cognitive control, affective control, motor planning, and arousal, and is therefore ideally suited to exert an influence over these regions in response to environmental demands (Paus, 2001).

Knowledge of the cognitive and behavioral effects of ACC damage is constrained by the relative paucity of patients with pure focal damage to the ACC. It is uncommon for this region to be damaged in closed-head injuries, and damage caused by strokes tends to encroach upon surrounding cortex (e.g., the medial PFC and secondary motor cortices). Of the few case studies of patients with focal ACC damage, their symptoms are marked by general apathy, blunted affect, and difficulty in maintaining goal-directed behavior

(Cohen, Kaplan, Moser, Jenkins, & Wilkinson, 1999; Cohen, Kaplan, Zuffante, et al., 1999; Cohen, McCrae, & Phillips, 1990; Laplane, Degos, Baulac, & Gray, 1981; Wilson & Chang, 1974). Family members report that these patients appear to have lost their "drive" and frequently note patients' dramatic loss of interest in activities and hobbies they formerly found pleasurable (Cohen, Kaplan, Moser, et al., 1999; Tow & Whitty, 1953).

Given the paucity of patients with focal ACC damage, much of the theorizing concerning ACC function is built on recent findings from cognitive neuroscience. One of the most consistent findings from brain activation studies is that the ACC is involved in detecting conflict among competing responses and monitoring for errors in performance (Carter et al., 1998; Gehring & Knight, 2000; MacDonald, Cohen, Stenger, & Carter, 2000). This has led many to theorize that the primary role of the ACC is to detect situations in which response conflict is likely, then to signal the need for increased cognitive control, such as when overriding habitual behaviors or overcoming temptations (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Kerns et al., 2004; Paus, 2001; Peterson et al., 1999). Moreover, it is hypothesized that under situations of cognitive conflict, the ACC communicates directly with the LPFC to bring current behavior in line with overarching goals (Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004).

The Neural Basis of Self-Regulatory Failure

In the previous section, we reviewed neuropsychological case studies demonstrating the roles of VMPFC, LPFC, and ACC in self-regulation. This research demonstrates that damage to any one of these regions can have profound effects on a person's ability to regulate behaviors across a variety of domains, from following social norms to carrying out mundane, everyday tasks. The ability to maintain our goals in mind, to correct for errors in performance and, ultimately, to bring our thoughts and behaviors in line with our intentions, relies on the complex interplay between each of the aforementioned PFC regions. This ability to remain in control of our behavior is proposed to rely on a balance between self- control capacity and the strength of impulses and desires. Self-regulation can therefore fail when faced with a strong desire or when the individual's self-control capacity is reduced or the motivation to engage in effortful control is lacking (Heatherton & Wagner, 2011). Careful study of the deficits exhibited by patients with focal brain damage can give us important insights into the underlying cognitive operations that these damaged regions normally support. However, to understand how the healthy PFC enables self-regulation and what happens in the brain when self-regulation fails, we must turn to the study of healthy populations and the methods of cognitive neuroscience. In the following section we examine how these methods have been used to investigate the neural substrates of self-regulation and self-regulation failure in three separate domains: emotions, thoughts and stereotypes, and appetitive behaviors.

Neural Bases of Emotion Regulation

Keeping emotions in check is a vital part of maintaining harmonious social relationships. Were our ability to do so suddenly knocked out, our relationships would likely turn very ugly indeed. Research on the neural substrates of this complex ability has honed in on a model of emotion regulation involving top-down regulation by the PFC of limbic regions

involved in affect (Davidson, Putnam, & Larson, 2000; Ochsner & Gross, 2005). A consistent finding across a wide range of studies is an inverse correlation between the PFC and activity in the amygdala, a limbic region sensitive to emotionally arousing stimuli. The precise region of PFC involved in modulating the amgydala varies across studies but is invariably either the LPFC (Hariri, Mattay, Tessitore, Fera, & Weinberger, 2003; Ochsner, Bunge, Gross, & Gabrieli, 2002; Ochsner et al., 2004) or the VMPFC (Johnstone, van Reekum, Urry, Kalin, & Davidson, 2007; Urry et al., 2006). In light of the earlier discussion of the anatomical connectivity of these two regions, specifically regarding the fact that the LPFC has no direct connections to limbic regions, it would appear that the LPFC exerts its regulatory influence indirectly. Evidence for this indirect pathway was reported by Johnstone and colleagues (2007), who found that the relationship between LPFC and the amygdala during emotion regulation is mediated by the VMPFC.

Mood disorders, such as major depressive disorder (MDD) and borderline personality disorder (BPD), present interesting cases of impaired emotion regulation. Research on patients with these mood disorders has consistently shown a breakdown in the inverse functional coupling between VMPFC and the amygdala, leading to exaggerated activation of the amygdala in response to negative emotional material (Donegan et al., 2003; Johnstone et al., 2007; Silbersweig et al., 2007). This finding of a dysfunctional VMPFC–amygdala circuit finds additional support in a recent study of patients with BPD, using fludeoxyglucose–positron emission tomography (FDG-PET), a neuroimaging method that allows for the measurement of resting glucose metabolism. In contrast to healthy controls, patients with BPD showed no coupling of metabolism in the VMPFC and amygdala (New et al., 2007). These findings demonstrate that even when patients with BPD are not actively regulating emotions, the normal functional coupling between the VMPFC and amygdala is impaired.

A final example of the uncoupling of this VMPFC–amygdala circuit comes from a study of the deleterious effects of sleep deprivation on emotion regulation. In this research, sleep-deprived and control participants underwent functional magnetic resonance imaging (fMRI) scanning while viewing negative emotional material. As in the patients with mood disorders mentioned earlier, sleep-deprived patients demonstrated an exaggerated amygdala response compared to control participants and impaired functional connectivity between the VMPFC and amygdala (Yoo, Gujar, Hu, Jolesz, & Walker, 2007).

Regulation of Thoughts and Prejudices

Cognitive neuroscientists have long studied the neural basis of response inhibition, relying primarily on tasks such as the the go/no-go task, in which certain cues indicate a go response (usually a button press), while others require the participant to inhibit responding. Research using this task has consistently found activation in both the ACC and LPFC (Casey et al., 1997; Kiehl, Liddle, & Hopfinger, 2000; Somerville, Hare, & Casey, 2011). The ACC in particular is thought to be involved in response competition between conflicting cues, and in monitoring for errors in performance, while activity in the LPFC reflects the actual inhibition of responses during the no-go trials (Liddle, Kiehl, & Smith, 2001). Surprisingly, few attempts have been made to apply this framework to the problem of thought suppression.

In perhaps the first study to examine the neural substrates of actively suppressing thoughts, Wyland, Kelley, Macrae, Gordon, and Heatherton (2003) found increased ACC activity during periods of active thought suppression compared to periods of

unrestrained thought. One problem with interpreting these results is that because subjects were not instructed to report thought intrusions during the suppression period, it is unclear whether ACC activity was related to failures of thought suppression or was instead signaling the need for additional cognitive control (see Botvinick et al., 2001). To parse out these two interpretations, Mitchell and colleagues (2007) conducted a similar study. However, this time, participants were instructed to respond whenever they experienced intrusions of a prespecified thought. Results from this study are in agreement with the previously described research on response inhibition, demonstrating increased activity in the LPFC during periods of thought suppression, while the ACC was found to respond only during instances of thought intrusions. These findings provide converging evidence that the ACC monitors for conflict, while the LPFC is involved in actively regulating and suppressing thoughts (Mitchell et al., 2007).

Controlling attitudes and prejudices differs from thought regulation in that stereotypes are often automatically activated upon encountering outgroup members (Devine, 1989; Devine, Plant, Amodio, Harmon-Jones, & Vance, 2002; Fiske, 1998; Greenwald, McGhee, & Schwartz, 1998; Payne, 2001). Moreover, outgroup members, particularly racial outgroup members, are often perceived as threatening (Brewer, 1999; cf. Ackerman et al., 2006). Research examining the neural correlates of prejudice has largely focused on prefrontal top-down regulation of amygdala activity to members of a racial outgroup, although similar findings exist for members of stigmatized groups, such as unattractive people and the obese (Krendl, Macrae, Kelley, Fugelsang, & Heatherton, 2006). An important factor to keep in mind when reviewing this research is that people differ in implicit racial attitudes, and this difference has been shown to moderate amygdala activity in response to racial outgroup members (Cunningham et al., 2004; Phelps et al., 2000). An excellent example of this comes from a study examining the depleting effects of interracial interactions on the propensity to recruit control regions of the PFC when evaluating racial outgroup members. In this study, participants engaged in an interracial interaction with a black confederate, in which they were asked to discuss racially charged topics. Following the interaction, participants completed a Stroop task. Interestingly, participants with more negative implicit attitudes toward blacks showed decreased performance on the Stroop task, indicating that, for them, the interracial interaction was cognitively depleting. Participants also participated in an ostensibly unrelated fMRI study in which they viewed black and white faces. As with other similar studies (e.g., Cunningham et al., 2004), they showed increased recruitment of the LPFC and ACC when viewing black faces. More importantly, activity in these regions was positively correlated with both participants' scores on the Implicit Association Test (IAT) and with their Stroop interference scores (Richeson et al., 2003). These results suggest that for those with fewer implicit attitudes toward blacks, there is less need to recruit PFC regions involved in cognitive control to override stereotypes that they simply do not seem to have.

Control of Cravings and Appetitive Behaviors

As noted earlier, the VMPFC and ACC share many reciprocal connections with midbrain regions that are important for reward (e.g., nucleus accumbens). The nucleus accumbens, along with the ventral tegmental area (VTA), form part of what is known as the *mesolimbic dopamine system*. Both animal neurophysiology and human neuroimaging work have shown that a seemingly universal feature of rewarding stimuli, be they natural rewards or

drugs of abuse, is that they activate dopamine release in the nucleus accumbens (Carelli, Ijames, & Crumling, 2000; Di Chiara & Imperato, 1988; Pfaus et al., 1990) or, in the case of neuroimaging work, lead to increased activation in this same region (Berns, McClure, Pagnoni, & Montague, 2001; Breiter et al., 1997; O'Doherty, Dayan, Friston, Critchley, & Dolan, 2003). This holds true even when participants are simply viewing photographic "cues" of rewarding stimuli, such as attractive members of the opposite sex (Cloutier, Heatherton, Whalen, & Kelley, 2008), food images (Demos, Heatherton, & Kelley, 2012; Wagner, Boswell, Kelley, & Heatherton, 2012) or images of drugs (David et al., 2007; Garavan et al., 2000; Myrick et al., 2008). This paradigm, given the name *cue reactivity*, has become an important tool in research on the neural correlates of craving and control in drug addicts (Childress et al., 1999; Garavan et al., 2000; Maas et al., 1998; Wexler et al., 2001), smokers (David et al., 2007; Due, Huettel, Hall, & Rubin, 2002; Wagner, Dal Cin, Sargent, Kelley, & Heatherton, 2011), and obese persons (Rothemund et al., 2007; Stoeckel et al., 2008). For instance, in dieters, cue reactivity to foods is prospectively correlated with future weight gain over the following 6-month period (Demos et al., 2012) and in another study has been shown to be associated with daily food desires, as measured by experience sampling (Lopez, Hofmann, Wagner, Kelley, & Heatherton, 2014). Within the domain of smoking, cue reactivity to smoking cues predicts the degree to which smokers attempting to quite are able to stay abstinent (Janes et al., 2010). In addition, research on people's ability to delay gratification (e.g., Mischel, Shoda, & Rodriguez, 1989) has shown that people who had trouble delaying gratification during childhood demonstrated greater brain cue reactivity to appetitive stimuli over 40 years later (Casey et al., 2011).

What happens when participants try to inhibit their response to food or drug cues? As might be expected from results in other domains, self-regulation of appetitive desires recruits PFC control systems regardless of whether the rewarding stimulus is food (Stoeckel et al., 2008), erotic images (Beauregard, Levesque, & Bourgouin, 2001), cigarettes (Brody et al., 2007; David et al., 2005; Kober et al., 2010), drugs (Garavan et al., 2000; Wrase et al., 2002), or money (Delgado, Gillis, & Phelps, 2008). Moreover, activity in these regions appears to be related to whether people are successful at inhibiting cravings. For example, successful dieters have been shown to recruit the LPFC spontaneously when viewing images of appetizing foods, whereas unsuccessful dieters do not (DelParigi et al., 2007). This finding suggests that what makes these dieters successful is that they appear to recruit regulatory regions spontaneously in response to food cues, and that this automatic regulation strategy helps to control food cravings.

A well-known finding in research on restrained eating is that forcing chronic dieters to break their diet, usually by having them consume a high-calorie milkshake "preload," can lead to bouts of unrestrained eating (Heatherton, Herman, & Polivy, 1991, 1992; Heatherton, Polivy, Herman, & Baumeister, 1993; Herman & Mack, 1975). Theories of drug addiction suggest that the reason why drug addicts fail to control their consumption is that midbrain reward areas become hypersensitized to drug cues (Stoeckel et al., 2008) and are uncoupled from top-down control regions in the PFC (Bechara, 2005; Koob & Le Moal, 1997, 2008). This notion was examined in a study that compared cue reactivity to appetizing foods in restrained and unrestrained eaters, half of which drank a high-calorie milkshake preload, effectively breaking the restrained eaters' diets. Restrained eaters whose diets were broken by the milkshake preload demonstrated increased food-cue-related activity in the nucleus accumbens compared to both unrestrained eaters and restrained eaters whose diet had not been broken (Demos, Kelley, & Heatherton, 2011),

a finding that mirrors the earlier behavioral studies (e.g., Heatherton et al., 1991, 1992; Herman & Mack, 1975).

Negative Affect and Social Distress

In the previous section we reviewed the role of prefrontal brain regions in the regulation of emotion. In this section, we instead turn the tables on the PFC and examine research suggesting that emotions can serve as a catalyst for self-regulation failure (for a larger review, see Wagner & Heatherton, 2013a). The experience of emotional and social distress has often been cited as precursor to self-regulation failures in domains such as binge eating (Haedt-Matt & Keel, 2011), drinking (Witkiewitz & Villarroel, 2009), and gambling (Raviv, 1993). Experimental inductions of negative affect and social distress have similarly found that these may lead to increased consumption of unhealthy foods, reduced persistence on tasks, impulsive decision making, and even to aggressive behavior toward others (Baumeister, DeWall, Ciarocco, & Twenge, 2005; Heatherton, Striepe, & Wittenberg, 1998; Lerner, Li, & Weber, 2013; Oaten, Williams, Jones, & Zadro, 2008; Twenge, Baumeister, Tice, & Stucke, 2001).

How does negative affect lead to impaired self-regulation? A number of mechanisms have been proposed, many of which center on the notion that experiencing negative affect causes a shift in current goals, such that the individual becomes engaged in affect regulation at the expense of other forms of self-control (Tice, Bratslavsky, & Baumeister, 2001) Alternatively, people may engage in misregulation, deciding instead to attempt to ameliorate their mood, which can occur at the expense of their long-term goals, such as when an abstinent drinker decides to have a drink in order to improve his or her mood after receiving bad news. Another potential mechanism comes from research suggesting that negative affect may increase the strength of desires, rendering them more difficult to control. For instance, experiencing negative affect has been associated with increased craving for carbohydrate-rich foods (Christensen & Pettijohn, 2001) and, among smokers, increases their reported pleasure from smoking a cigarette (Zinser, Baker, Sherman, & Cannon, 1992). Other work suggests that rewards such as money may increase in value in so far as they are perceived as a means of relieving the negative affective state (e.g., Duclos, Wan, & Jiang, 2013).

Functional neuroimaging studies have similarly shown that emotional distress may heighten reward cue reactivity and impair self-regulation. For instance, research has shown that social distress is associated with increased reward cue reactivity to appetitive positive and appetitive images (Chester & DeWall, 2014) and increased risk-taking behavior, in conjunction with reduced lateral PFC activity, during a driving simulation task (Peake, Dishion, Stormshak, Moore, & Pfeifer, 2013). Similarly, among dieters, emotional distress has been shown to increase reward cue-reactivity to appetizing foods (Killgore & Yurgelun-Todd, 2006; Wagner et al., 2012).

Self-Regulatory Depletion

Successful regulation of thoughts, emotions, and cravings relies on a common system of prefrontal control regions that comprise the ACC, the LPFC, and the VMPFC. Although

we addressed each of these domains in isolation, there is ample evidence that self-regulation relies on a domain-general resource that can become depleted by successive attempts at self-regulation (Baumeister & Heatherton, 1996; Muraven & Baumeister, 2000; Vohs & Heatherton, 2000). The view that self-regulation is a resource-limited system that can become temporarily exhausted through use has come to be known as the *strength model of self-regulation* (Baumeister & Heatherton, 1996). Over the years this model has received considerable empirical support (for a meta-analysis, see Hagger, Wood, Stiff, & Chatzisarantis, 2010); in addition, research using experience sampling has shown that the disinhibiting effects of depletion also appear to obtain in real-world settings, in that the likelihood of reporting a failure to self-regulate increases as a function of the number of prior acts of self-regulation that participants have attempted (Hofmann, Vohs, & Baumeister, 2012). For instance, research has shown that when people engage in a prior effortful self-regulation task, they subsequently become more likely to consume tempting foods (Vohs & Heatherton, 2000), pay attention to rewards (Schmeichel, Harmon-Jones, & Harmon-Jones, 2010), and show impaired emotion regulation (Schmeichel, 2007).

In our chapter in the previous edition of this handbook, we could only speculate on how depletion affects brain mechanisms involved in self-regulation. However, in the intervening time, a number of researchers have turned to the methods of cognitive neuroscience in an attempt to understand how self-regulatory depletion undermines self-regulation. Consistent with behavioral results, these studies have demonstrated that following effortful self-regulation, people show impairments on effortful self-regulation tasks such as the Stroop task, and these performance decrements in one study were associated with a reduced error-related negativity signal originating in the ACC and thought to be involved in conflict monitoring (Inzlicht & Gutsell, 2007). Other research, using functional neuroimaging, has shown that depletion leads to reduced recruitment of the LPFC during self-regulation tasks (Friese, Binder, Luechinger, Boesiger, & Rasch, 2013; Hedgcock, Vohs, & Rao, 2012; Persson, Larsson, & Reuter-Lorenz, 2013). For instance, in work by Friese and colleagues (2013), participants first completed a difficult or easy emotion suppression tasks, followed by the Stroop task, all while undergoing fMRI. The results of this study showed that participants in the depletion condition demonstrated increased right LPFC activity during the thought suppression task, and, in the same region, they subsequently showed underrecruitment of this region (relative to nondepleted participations) during the Stroop task. Together, these and other findings suggest that the performance decrements observed on subsequent tasks result from a failure to engage self-control systems following depletion. Moreover, they raise the interesting possibility that the aftereffect of depletion on top-down control will be most pronounced in brain regions involved in both the depletion and subsequent self-control task (e.g., Friese et al. 2013).

These last few studies highlight a role for the PFC in self-regulatory depletion during more cognitive tasks, but what happens when people seek to inhibit their desires or regulate their emotions (i.e., so called "hot" cognition; Metcalfe & Mischel, 1999)? Prior behavioral research suggests that another possible aftereffect of self-regulatory depletion is increased attention toward rewards (Schmeichel et al., 2010). Given that self-regulation often involves a balance between impulses and self-control, another possible route through which depletion can bring about self-regulation failure is by changing the strength of impulses directly. Two functional neuroimaging studies lend partial support to this notion by showing that, following a self-regulatory depletion task, people

show exaggerated amygdala reactivity to aversive emotional scenes (Wagner & Heatherton, 2013b), and dieters show increase reward cue reactivity to images of appetizing foods (Wagner, Altman, Boswell, Kelley, & Heatherton, 2013). Moreover, in both cases, depleted subjects also showed reduced functional connectivity between the amygdala and VMPFC on the one hand (Wagner & Heatherton, 2013b), and reward-related regions and the LPFC on the other (Wagner et al., 2013). These studies are consistent with the notion that self-regulatory depletion may have independent effects on desire strength; however, they also support a model whereby self-regulation impairments may come about as a result of a reduced coupling between regions important for reward and reward regulation, such as the LPFC (Delgado et al., 2008; Kober et al., 2010; Somerville et al., 2011), or between limbic regions and prefrontal areas involved in emotion regulation, such as the VMPFC (Johnstone et al., 2007; Somerville et al., 2013). This reduced functional connectivity, then, may be responsible for the observation that self-regulatory depletion leads to enhanced emotional and reward-related cue reactivity.

Conclusions

Failure to maintain control over one's thoughts, emotions, and desires can result in disastrous consequences for the individual. Patients with focal damage to the PFC present an extreme case of what life would be like without the ability to regulate our behaviors. Neuropsychological case studies have provided essential clues to the cognitive operations subserved by the PFC. However, understanding the complex interplay between regions of the PFC involved in regulating behavior and those regions that signal motivational relevance or emotional states necessitates a cognitive neuroscience approach. In this chapter we have focused on three distinct regions of the PFC and how findings from cognitive neuroscience shed light on their role in self-regulation, as well as what happens when self-regulation breaks down. First is the VMPFC, which shares important reciprocal connections with subcortical regions involved in emotion and reward, and is critical for regulating behavior in social, affective, and appetitive domains. Second is the LPFC, which, with its important role in core aspects of executive function (e.g., working memory), is necessary for planning behavior and maintaining regulatory goals. Third is the ACC, a region that is richly interconnected with cognitive, affective, and motor regions; monitors our performance; and signals the need for recruiting control systems to regulate our behavior.

In this chapter we have reviewed recent work examining the brain basis of self-regulation failure across multiple domains. The general framework that emerges from this research is that lapses in control may result from a failure to recruit lateral prefrontal regions involved in self-control that are necessary to complete a task or inhibit a response. Another route through which self-regulation failure can occur is when these same lateral prefrontal regions fail to adequately keep in check stimulus-driven cortical and subcortical responses associated with emotion, threat, and reward. Thus, what the research suggests is that the two classic components of self-control (top-down control vs. impulse strength) can be approximately mapped onto brain systems that are important for cognitive control on the one hand, and onto brain regions involved in subjective value and reward on the other. Although there is surely more complexity to how the brain enables self-regulation, the results thus far point to the importance of prefrontal control systems in monitoring behavior, signaling the need for control, and engaging in effortful inhibition. However,

just as important appears to be the sensitivity of the brain's reward system, individual differences that are predictive of real-world self-regulation failures (e.g., Lopez et al., 2014). It appears that when it comes to understanding how self-regulation is related to brain function, it is important to maintain a balanced view.

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