

CHAPTER 8

The Common Neural Basis of Exerting Self-Control in Multiple Domains

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ABSTRACT

People regularly exert control over impulsive thoughts and behaviors in order to make appropriate decisions and take appropriate actions even when they are more difficult or less pleasant than alternative choices. A common theme in mental illnesses characterized by impulsivity, such as ADHD and substance abuse, is an impaired self-control mechanism. Therefore, understanding the mechanisms underlying an intact control mechanism can not only shed light on how healthy people exert self-control over their thoughts and behaviors, but help us to understand what is impaired in patient populations as well. The right ventrolateral prefrontal cortex (VLPFC) is a region in the brain that is commonly activated when people are exerting many different forms of self-control. It is noted that other prefrontal regions also consistently activated when one exerts self-control, such as the dorsolateral prefrontal cortex, anterior cingulate cortex, orbitofrontal cortex, and medial prefrontal cortex, may be recruited for other task demands and not self-control specifically. Although the right VLPFC has been linked to other functions as well, this review will focus on the hypothesized general role that it plays during acts of self-control.

There are infinite manners in which one can exert self-control. We limit our discussion to six forms of conscious, explicit control that are commonly addressed in the literature: motor response inhibition, suppressing risky behavior, delaying gratification, regulating emotion, memory inhibition, and thought suppression. First, we review the literature exploring the involvement of the right VLPFC in each type of self-control separately. Next, we explore the small amount of literature comparing different forms of self-control to each other and discuss the possibility that these forms of self-control are related constructs. We also discuss the anatomical positioning of the right VLPFC and point out that it is well suited to serving a key role in exerting self-control. Finally, we conclude that although more direct research must be conducted before firm conclusions can be made, there is evidence that the right VLPFC is utilized when exerting self-control regardless of the specific domain of control.

Keywords: Self-control, fMRI, right VLPFC

Self-control can be defined as “the overriding or inhibiting of automatic, habitual, or innate behaviors, urges, emotions, or desires that would otherwise interfere with goal directed

behavior” (Muraven et al., 2006). Without self-control, capricious and enjoyable decisions would be made, statements uttered, and actions taken. For example, if one has a

deadline at work for an unpleasant project, he or she may have the inclination to leave work and do something fun instead of taking the responsible, yet dull, path of meeting the deadline. Or, if one has a strong urge to disclose to one's boss his or her opinion of that horrendous project, the person may instead remain silent and sensibly agree to work late in order to competently finish the task at hand. Whereas it is sometimes more desirable to follow one's own whims, those actions could occur at the expense of practical and boring yet sensible decisions. Clearly it is important that some sort of internal control system be implemented in order to inhibit such impulses so that more appropriate decisions can be made and actions taken. When that control system is impaired problems occur, such as impulsive behavior in ADHD, gambling, poor financial decisions, substance abuse, etc. The negative behavioral and clinical manifestations of a lack of self-control underscore the importance of thoroughly understanding the basis of an intact control mechanism at many different levels of analysis, including cognitive, clinical, social, and neural. This review concentrates on the vast base of literature exploring the neural basis of self-control. This review demonstrates that the right ventrolateral prefrontal cortex (VLPFC) is a common neural region recruited for successful self-control in a variety of domains. The existence of this common neural mechanism implies that the different forms of self-control may be parts of a unitary concept.

It is important to point out that the right VLPFC has been associated with a number of diverse tasks and cognitive processes, such as executive self-control in a variety of domains (as discussed in this chapter), stimulus-driven, bottom-up attention and automatic alerting to unexpected, salient stimuli (Corbetta & Shulman, 2002), memory retrieval when one must differentiate between relevant and irrelevant aspects of a stimulus (Kostopoulos & Petrides, 2003), both object-oriented (Courtney et al., 1996) and spatially oriented (Rizzuto et al., 2005) working memory, and the interpretation of emotions (Kober et al., 2008). This chapter will focus on the association between

the right VLPFC and self-control processes as one possible role of the right VLPFC. Although other right VLPFC roles are not discussed here, this review is not excluding the possibility that the right VLPFC plays a part in multiple functions. Moreover, other prefrontal areas, such as the dorsolateral prefrontal cortex (DLPFC), medial prefrontal cortex (mPFC), and anterior cingulate cortex (ACC) are often involved in tasks requiring control as well. However, they may be recruited for other task demands and are not thoroughly discussed here.

The extent and diversity of problems that can occur when self-control is impaired highlights the fact that various forms of self-control do exist. There is disagreement, however, as to whether the varieties of self-control and its assumed converse, impulsivity, are one construct (Monterosso & Ainslie, 1999) or many constructs (Evenden, 1999). Many personality and clinical psychologists have assumed that impulsivity can be decomposed into multiple independent parts, however there is disagreement as to the number and specifics of each and limited evidence to support those claims (Evenden, 1999). Although Ainslie, Evenden, and their colleagues have focused on temporal aspects of impulsivity, such as the inability to withhold responses or to wait for delayed rewards, and their research involves animals, their approaches to dissecting impulsivity and self-control can be expanded to other domains. A notable difference between self-control research with humans and animals is that humans have the advantage of being able to consciously and explicitly exert self-control, something that is much more difficult to observe or measure in animals, if it exists (Monterosso & Ainslie, 1999).

There are infinite manners by which to study self-control in humans. Control processes can either be unconscious, such as priming or speech control, or conscious and explicit. This chapter focuses on literature exploring a number of different forms of explicit self-control to determine if seemingly very different modes of control are in fact subserved by the same underlying process and therefore utilize similar neural mechanisms.

The specific forms of explicit self-control examined here are motor response inhibition, suppressing risky behavior, delaying gratification, regulating emotion, memory inhibition, and thought suppression. They are vastly different on the surface. However, it is possible that they are different manifestations of the same construct, namely the exertion of self-control over actions or cognitions while engaging in goal-directed behavior. If that is the case, the neural networks subserving each of these subtypes of self-control may be overlapping, if not identical. Although very little research has directly compared different forms of self-control to each other, there is evidence that the individual subtypes may rely on similar prefrontal networks. The right VLPFC, DLPFC, mPFC, and ACC are commonly activated in neuroimaging studies exploring the different self-control subtypes, although the right VLPFC is the region most consistently involved in such studies (Anderson et al., 2004; Aron & Poldrack, 2006; Elliott et al., 2000; Kalisch et al., 2005; Levesque et al., 2003; Matthews et al., 2004; McClure et al., 2004; J. P. Mitchell et al., 2007; Ochsner, 2004; Wyland et al., 2003). This review first focuses on the involvement of the right VLPFC in each variety of self-control separately. Next, it integrates the relevant literature and discusses the possibility that these forms of self-control are related constructs. Finally, it will conclude that although more direct research must be conducted before firm conclusions can be made, there is evidence that the right VLPFC is utilized when exerting self-control regardless of the specific domain of control. The commonly noted DLPFC and ACC activation, on the other hand, may subservise more general control mechanisms such as rule monitoring (Bunge, 2004) and conflict monitoring (Botvinick et al., 2004) respectively, whereas mPFC activity may be related to self-referential or emotional processing (Lieberman, 2007; Ochsner & Gross, 2005).

MOTOR INHIBITION

Arguably one of the most thoroughly studied forms of self-control is motor response inhibition. Motor response inhibition can be simple, requiring the suppression of an action with no

alternative response necessary, or more complex, requiring both the suppression of an action and the execution of a different action. For example, a baseball player must exert simple inhibitory control in order to stop an already-initiated swing when realizing the pitch being thrown will be a ball. If, however, one is driving and a child runs in front of the car, both inhibitory control must be exerted to remove pressure from the gas pedal and a different, unexpected response must be executed in order to slam on the brakes.

Both the go/no-go (Casey et al., 1997) and the stop-signal (Logan, 1994) tasks are simple motor inhibition paradigms that test one's ability to exert self-control by inhibiting a button press to a stimulus at the occurrence of a signal to immediately stop responding. The level of prepotency of responding can be manipulated by altering the proportion of stimuli not to be responded to; the fewer of those stimuli, the harder it is to inhibit a response. The dependent variable in the go/no-go task is either number of commission errors—responding to a no-go stimulus, or number of omission errors—not responding to a go stimulus. The dependent variable in the stop-signal task is stop-signal reaction time (SSRT), a measure of the time a participant needs to be able to inhibit his or her response. The main difference between the two tasks lies in the signal to stop: in the go/no-go task it is the stimulus itself (i.e., an “X” in a string of other letters), whereas in the stop-signal task it is a signal that occurs after the onset of the primary stimulus (i.e., a tone or a change in color of the primary stimulus). Successful performance on the stop-signal task reflects inhibitory self-control of an already-initiated response and may reflect a more pure form of response inhibition than that in the go/no-go task, which may more accurately reflect response selection. In the go/no-go paradigm participants are given the signal to inhibit their response before the response is actually initiated, since the stimulus itself is the signal to inhibit (Rubia et al., 2001). Importantly, however, imaging results with both tasks are very similar. The right VLPFC is consistently engaged in both go/no-go and stop-signal tasks when participants are inhibiting prepotent responses. It should be noted that other prefrontal and subcortical

regions, namely the DLPFC (Garavan et al., 2002; Liddle et al., 2001; Rubia et al., 2001), ACC (Garavan et al., 2002; Rubia et al., 2001), and subthalamic nucleus (STN; Aron & Poldrack, 2006) are often found to be active during motor inhibition tasks. Although these regions are likely involved in cognitive control in addition to the right VLPFC, because this review focuses on the role of the right VLPFC in inhibitory self-control, they are not discussed further.

Early lesion work in rhesus monkeys demonstrated that the inferior frontal convexity, corresponding to the VLPFC in humans, is necessary for successful performance on go/no-go tasks, whereas the mPFC is not (Iversen & Mishkin, 1970). Single-cell recording in macaque monkeys has found neurons in the inferior DLPFC (analogous to the human VLPFC) that respond selectively either to go or to no-go stimuli (Sakagami & Niki, 1994).

Human neuroimaging studies have consistently found a similar reliance on right-lateralized VLPFC (or the inferior frontal cortex within the VLPFC; IFC) during successful no-go (Garavan et al., 2002; Garavan et al., 1999; Konishi et al., 1998; Liddle et al., 2001; Menon et al., 2001) and stop-signal (Aron & Poldrack, 2006; Chevrier et al., 2007; Rubia et al., 2003) performance (for a review, see Aron et al., 2004). In further support of the key role of the right IFC in successful stopping, it has been found that the right IFC and the STN, a subcortical region thought to be critical for successful stopping as well, were the only two regions correlated with SSRT; greater activity in each area was associated with faster SSRT and therefore better response inhibition (Aron & Poldrack, 2006).

Both human lesion studies and transcranial magnetic stimulation (TMS) studies have reinforced that not only is the right VLPFC utilized in successful motor response inhibition, but that it is necessary. One study examined stop-signal performance in patients with focal lesions in varying locations in the prefrontal cortex (Aron et al., 2003). The authors found that the extent of lesions in the right inferior frontal gyrus (IFG) was more correlated with slowing of SSRT than any other frontal lobe lesion. When regressing out effects resulting from right IFG damage no

other frontal region damage correlated with SSRT, including the left IFG (Aron et al., 2003). Another study found that temporary disruption of the right IFG using TMS increased SSRT and decreased percent inhibition at a given stop-signal delay, regardless of what hand the subjects were using to respond (Chambers et al., 2006).

In conclusion, studies utilizing the go/no-go and stop-signal tasks consistently and fairly specifically implicate the right IFC in controlling simple motor response inhibition (Aron et al., 2004).

Reversal learning is a more complex form of motor inhibition that requires both the inhibition of a prepotent response and the substitution of that response with an alternate response that subjects had previously been instructed to avoid. Often, reward and punishment are used to develop prepotent responses and to signal when those responses must be overridden in favor of the opposite response (Clark et al., 2004).

Animal literature implicates the orbitofrontal cortex (OFC), a region within the larger VLPFC, as necessary for reversal learning. Lesioning the OFC consistently impairs reversal learning in a variety of species, including rats and primates (Clark et al., 2004). Early studies exploring focal frontal lesions in rhesus monkeys noted that the VLPFC/lateral OFC was crucial for reversal learning, whereas other frontal cortical regions such as the medial OFC, anterior OFC, and DLPFC were not (Butter, 1969; Dias et al., 1996; Iversen & Mishkin, 1970). Moreover, single unit recording from cells in both medial and lateral OFC in monkeys indicates that a population of cells responds to rewarded stimuli and that these same cells reverse their firing to the previously punished but newly rewarded stimulus after a reversal (Rolls et al., 1996; Thorpe et al., 1983).

Similar to the animal literature, human lesion studies consistently implicate the OFC as crucial for successful reversal learning (Fellows & Farah, 2003; Rolls et al., 1994). Because naturally occurring lesions in humans are not precise, a lateral/medial distinction cannot be made in these studies. Neuroimaging studies in healthy volunteers are beginning to elucidate the separable roles of specific sections of the OFC in reversal learning.

Tasks with healthy adults tend to use probabilistic reversal learning, meaning that subjects are given incorrect feedback on a certain percentage of responses, often 20%–30%, so as to increase the difficulty of the task and the number of reversal errors to be analyzed in event-related fMRI designs. Additionally, reversals occur after a range of correct responses in a row, for example, anywhere between 10 and 15, so the switch is not predictable (Cools et al., 2002). When comparing the final incorrect trial after a reversal, just before subjects reverse their response tendencies, to correct trials, trials where subjects did not subsequently change their response, or control tasks not requiring a decision to be made, the VLPFC/lateral OFC is consistently active (Cools et al., 2002; Kringelbach & Rolls, 2003; O'Doherty et al., 2003; Remijnse et al., 2005).

Crucially, in one study that further explored the presence of VLPFC activity during reversal learning, it was not more active for initial errors after a reversal (when the response was not subsequently changed) as compared to correct trials, or for probabilistic errors as compared to correct trials (Cools et al., 2002). This indicates that the main role of the VLPFC was to exert behavioral control over responses to inhibit the previously rewarded response so that a different response could be made. This purported VLPFC role is similar to that in go/no-go and stop-signal studies, where it has been implicated in inhibiting a prepotent response.

A theory that is largely supported by the aforementioned neuroimaging data is that the ventral PFC, and specifically the OFC, may be separated into functionally distinct areas, lateral and medial (Elliott et al., 2000). Given the diverse afferent and efferent connections between the OFC and other brain regions, including other prefrontal areas and limbic and subcortical areas, functional heterogeneity is not surprising. The medial OFC may keep track of reward contingencies in a dynamic environment, thus allowing for the realization of a necessary change in response if reward contingencies change, while the lateral OFC may exert behavioral control based on those contingencies (Elliott et al., 2000).

In conclusion, evidence is fairly consistent supporting a role for the right VLPFC, the IFG/lateral OFC in particular, in the behavioral inhibition of prepotent responses, whether the task requirement is simply to inhibit a response (Aron & Poldrack, 2006; Garavan et al., 2002; Rubia et al., 2003) or to inhibit a previously rewarded response in order to be able to make a different one (Cools et al., 2002; Elliott et al., 2000; Kringelbach & Rolls, 2003). When task demands include reward contingencies, as in most reversal learning paradigms, the mPFC is further recruited, particularly the medial OFC, which has been implicated both in processing reward-related information and in mediating emotion-related behavior, which may be relevant to reward monitoring as well (Elliott et al., 2000; O'Doherty et al., 2003).

RISK-TAKING BEHAVIOR

When describing someone who engages in risky behavior, be it sensation-seeking such as sky diving, health-related such as drug use, or finance-related such as gambling, it seems intuitive to use adjectives and phrases such as “reckless”, “impulsive”, or “lacking self-control”.

Although many self-report questionnaires have been developed to assess risky behavior, they are not ideal because subjects may not fill them out accurately due to lack of insight or self-presentational concerns (Lejuez et al., 2002). Thus, a handful of tasks have been designed to assess risky behavior in the laboratory while avoiding the pitfalls of self-report measures.

One of the earliest tasks designed to assess risky behavior was the Iowa Gambling Task (IGT; Bechara et al., 1994). Performance on the IGT is often impaired in patients with ventromedial PFC lesions, meaning that they tend to make risky choices that result in potentially higher gains in the short term, but a lower overall payoff (Bechara, 2004; Bechara et al., 1994; Bechara et al., 1998). However, there are interpretations of the processes involved in the IGT other than impaired self-control that can explain impaired performance on this task, such as learning outcome probabilities of each of the decks, developing a long-term strategy (Manes et al., 2002;

Wu et al., 2005), or reversal learning (Dunn et al., 2006; Fellows & Farah, 2005).

Many other studies have explored risky versus safe decision making in simpler gambling-related tasks with inconsistent results. In a recent meta-analysis, Krain and colleagues (2006) concluded that the lateral OFC and the mPFC are involved in risky decision-making. However, the involvement of these regions was task-general and was not related to whether the participants made risky or safe choices in the tasks. Some studies have examined risky versus safe choices more specifically. Although some have found that the right OFC/VLPFC was more active for risky as compared to safe trials (Cohen et al., 2005; Ernst et al., 2004; Eshel et al., 2007), a similar region has also been found to be more active for safe as compared to risky trials (Matthews et al., 2004). Moreover, lateral OFC activity has also been correlated positively with risk aversion (Tobler et al., 2007) and negatively with number of risky choices (Eshel et al., 2007), both relationships implying that greater lateral OFC activity is related to a tendency toward making safer choices.

The Balloon Analogue Risk Task (BART) is another procedure with which to explore risk-taking (Hunt et al., 2005; Lejuez et al., 2002). In this task, participants are shown a balloon and told to push one button to inflate it and another to end the trial. For each pump, a temporary bank of money is increased by a constant amount (e.g., five cents). With each additional pump, however, there is an increased chance that the balloon explodes. If the balloon explodes, the subject loses all the money in the temporary bank. If the subject chooses to end the trial before the balloon explodes, the money in the temporary bank becomes permanent winnings. The average number of pumps and the amount of money provided with each pump can be varied. In the first study using the BART, participants were healthy controls who varied on risk-taking tendencies as indexed by a variety of self-report measures (Lejuez et al., 2002). Number of pumps was correlated with a variety of risk-related concepts as indexed by the Barratt Impulsiveness Scale, the Eysenck Impulsiveness Scale, the Sensation Seeking Scale, and actual risky behavior including smoking, drinking,

drug use, gambling, stealing, unprotected sex, and not using seatbelts. The correlation of performance on the BART with self-report scales was specific to risky behavior; it was not correlated with anxiety, depression, or empathy. This task is a good alternative to the gambling tasks because it is simple, provides immediate feedback, and, as sometimes occurs in the real world, risky behavior is rewarded up to a point before it is punished (Lejuez et al., 2002).

Whereas the BART has been related to impulsivity and presumably a lack of inhibitory control (Lejuez et al., 2002), its neural correlates have only begun to be explored. Preliminary data suggests that when suppressing prepotent responding on the BART, the right VLPFC is active (Stover et al., 2005; Cohen et al., 2009).

In conclusion, the risky decision-making literature provides support for the involvement of the lateral OFC and mPFC when confronted with risky choices (Krain et al., 2006). The involvement of the mPFC may result from the processing of reward-related information (Elliott et al., 2000). Although there is some support for the involvement of the right VLPFC in suppressing risky choices (Eshel et al., 2007; Matthews et al., 2004; Stover et al., 2005; Cohen et al., 2009; Tobler et al., 2007), the current literature is inconsistent. This phenomenon must be explored more thoroughly before any conclusions can be made regarding whether the suppression of a risky response is subserved in part by the same self-control mechanism that subserves successful motor response inhibition.

TEMPORAL DISCOUNTING

Another focus of the literature exploring impulsivity regards temporal discounting. If given the choice of receiving \$100 today or \$110 tomorrow, many individuals choose to receive \$100 today, even though it is a smaller reward. This may be viewed as impulsive behavior; people are sometimes unable to control their desire for an immediate payoff even though it would be beneficial to do so in the long run.

There have not been many studies exploring the neural basis of temporal discounting in humans. Research conducted with animals

such as pigeons, rats, and primates, supports hyperbolic discounting models, in which the tendency to choose immediate rewards drops off steeply with time. Many animal studies have focused on the effects of lesions on temporal discounting behavior. When administering focal neural lesions to animals and then testing them on temporal discounting tasks, two regions consistently emerge that are associated with impulsive behavior when lesioned: the nucleus accumbens (NAcc) core and the OFC (Cardinal, 2006; Mobini et al., 2002). Moreover, single cell recordings in intact nidopallium caudolaterale (NCL) in pigeons, which corresponds to the human prefrontal cortex, have identified cells that fire during the delay between decision and reward when choosing the larger, delayed option. Activity in these cells was negatively correlated with length of delay, until a preference shift from the larger, later to the smaller, sooner reward. At that point, when the delay was zero for all decisions, cell activity remained constant (Kalenscher et al., 2005). Such cells, whose activity was negatively correlated with delay length, have also been identified in rhesus monkeys (Roesch & Olson, 2005). In both pigeons and monkeys, the same cells whose activity is negatively correlated with delay length fire more for greater reward magnitudes. In other words, OFC cells appear to code for overall subjective value of the rewards, incorporating both delay, which decreases subjective value, and reward, which increases subjective value (Kalenscher et al., 2005; Roesch & Olson, 2005). These cells are specific to the OFC, as cells in other prefrontal areas in the monkey, such as the DLPFC, frontal eye fields, supplementary eye fields, premotor area, and supplementary motor area did not code for delay length (Roesch & Olson, 2005).

In short, the animal literature has identified specific neural networks that seem to be involved in successful temporal discounting in a variety of species. This can provide clues as to which brain areas to study in humans in similar paradigms.

To date, there have been very few functional neuroimaging studies in healthy humans directly examining the neural systems underlying immediate as opposed to delayed rewards using choices between smaller rewards sooner

or larger rewards later. In one such study, the authors hypothesized that a quasi-hyperbolic function, incorporating the two parameters δ (constant weighting of all delays) and β (larger weight given to immediate outcomes), underlies temporal discounting (McClure et al., 2004). Other temporal discounting studies in humans have been more focused on exploring subjective value and other mental processes that will not be discussed here (see Kable & Glimcher 2007).

McClure and colleagues (2004) found that two dissociable neural systems were active during a temporal discounting task. The first was active for all trials where an immediate option was available (corresponding to β). This network included limbic areas such as the ventral striatum, medial OFC, and mPFC. These areas have been associated with reward preference and visceral, emotional reactions. This limbic network can be seen as the neural parallel to Metcalfe and Mischel's (1999) "hot", emotional system. The second network was active during all decisions regardless of delay (corresponding to δ), but more active for difficult than for easy decisions. Level of difficulty was defined by closer relative magnitudes of the two choices and greater variability in subject responses. This network included multiple PFC areas, including the right VLPFC, lateral OFC, and DLPFC. This lateral prefrontal network, which has been associated with response inhibition and rule representation, may be seen as the neural parallel to Metcalfe and Mischel's "cool", cognitive system. A dissociation between these two networks was seen when comparing their relative activation during trials where one option was immediate. When subjects chose the delayed option, the lateral prefrontal network was more active than the limbic network; when the immediate option was chosen, there was a trend toward the limbic network being more active than the lateral prefrontal network. While the use of a quasi-hyperbolic instead of a true hyperbolic function has been questioned (Ainslie & Monterosso, 2004), these results provide evidence that a right-lateralized prefrontal network, including the right VLPFC, is utilized when exerting self-control over temporal decision-making (McClure et al., 2004).

A similar paradigm was used in a neuroimaging study comparing methamphetamine abusers to healthy controls. The neural response to the task was qualitatively similar in the two groups even given the expected behavioral difference that methamphetamine abusers chose more impulsively than did healthy controls (Monterosso et al., 2007). Comparing hard choices to easy choices revealed significantly greater activation in the right VLPFC region found in other studies of self-control. Moreover, participants who chose the delayed option more had greater right VLPFC activity. (Monterosso et al., 2007).

While very little neuroimaging research has been conducted on temporal discounting, what does exist suggests that a network involving lateral prefrontal areas such as the VLPFC and DLPFC operates when deciding whether or not to delay gratification for a larger future payoff. This network is similar to that implicated in self-control and rule monitoring in both motor and behavioral economic domains (Aron & Poldrack, 2006; Cools et al., 2002; Garavan et al., 2002; Krain et al., 2006; Kringelbach & Rolls, 2003; O'Doherty et al., 2003; Rubia et al., 2003), and possibly includes more medial prefrontal areas including the OFC, implicated in emotion and reward processing and emotion regulation (Cools et al., 2002; Krain et al., 2006; O'Doherty et al., 2003).

EMOTION REGULATION

Whereas in many situations it can be adaptive to be in touch with and be able to express one's own emotions, there are some situations in which that is not appropriate. For example, a person who is a good sport may suppress feelings of disappointment and anger at not winning an award in order to congratulate and be happy for the person who beat him or her. Alternately, the winner may inhibit feelings of glee for achieving the award in order to be composed and supportive of the person he or she beat. In situations such as these, it is beneficial to be able to exert control over one's emotional state. Emotion regulation, which is the process by which people influence their emotional

experience and expression (Gross, 1998), has been studied in order to understand the mechanisms behind self-control over affective processes. Successful emotion suppression requires that a person be able to exert self-control over his or her natural emotional response in order to dampen or strengthen it. It is thought that some mental disorders, such as anxiety and depression, may have their roots in the dysregulation of affect, thus there is much interest in discovering the mechanisms behind successful emotion regulation (Gross, 1998).

Although most research has been done on intentional emotion regulation, and that will be the focus in this chapter, unintentional emotion regulation can occur as well (Gross, 2002; Lieberman, 2007). For example, instructing participants to verbally label negative emotional stimuli appears to reduce negative emotion, even without a conscious attempt to do so. Some researchers studying emotion regulation are beginning to incorporate such designs into their research to explore unintentional emotion regulation (Hariri et al., 2000; Hariri et al., 2003; Lieberman et al., 2007).

The rapidly growing literature focusing on the neural correlates of emotion regulation fairly consistently implicates the right VLPFC/lateral OFC when suppressing as compared to maintaining negative emotions as varied as anxiety resulting from the anticipation of shocks, sadness, and viewing aversive images (Harenski & Hamann, 2006; Kalisch et al., 2005; Kim & Hamann, 2007; Levesque et al., 2003; Ochsner, 2004; Phan et al., 2005). Furthermore, the stimuli and emotion regulation strategies used vary greatly between studies, further emphasizing that the right VLPFC may play a role in exerting self-control in different contexts. Finally, an association between the magnitude of right VLPFC and right lateral OFC activity and self-reported decrease in negative emotion has been found, implying that this region is involved in controlling one's emotions (Ochsner et al., 2004; Phan et al., 2005). These results were specific to inhibiting negative emotion—when subjects were asked to decrease negative emotion, a more right-lateralized network involving the right lateral OFC was involved as compared to when

they were asked to increase negative emotion. The left amygdala was more active when increasing as compared to decreasing negative emotion, upholding findings regarding its assumed role in the subjective experience of negative emotions (Ochsner et al., 2004). Multiple studies have found a negative correlation between right VLPFC activity and amygdala activity, implying that perhaps the right VLPFC has a role in suppressing the amygdala's natural response in negatively valenced situations (Hariri et al., 2000; Hariri et al., 2003; Lieberman et al., 2007; Phan et al., 2005).

The right VLPFC is consistently active when instructing subjects to suppress their emotions using a variety of stimuli and strategies. This suggests that inhibitory self-control, believed to be localized to the right VLPFC in a variety of self-control domains such as motor response inhibition, risk-taking, and temporal discounting, may be at work during emotion regulation as well.

MEMORY INHIBITION

Although having good memory is adaptive, and forgetting information is often accompanied by negative consequences, there are situations in which it may benefit someone to forget something. For example, it is crucial to know one's own address and phone number. If people remembered every address and phone number they have ever had, however, it could make quickly recalling the current one more difficult or prone to error. In this case, it is adaptive to "forget" outdated information. Much research has been conducted exploring goal-oriented directed forgetting (MacLeod, 1998). The typical procedure displays a series of stimuli to participants, who are instructed to either remember all the stimuli or to forget some of them. Various stimuli have been used, such as strings of digits or consonants, individual words, word-pairs, and sentences. The cues to forget range from colored dots to the word "FORGET" being displayed. The recall and/or recognition of all stimuli is then tested, with "forget" stimuli consistently being remembered less than "remember" stimuli (MacLeod, 1998).

It has recently been asserted that the control of memory may involve a self-control process similar to behavioral inhibition as measured by stop-signal or go/no-go tasks (Levy & Anderson, 2002). In a memory-focused analogue to the go/no-go task, the think/no-think paradigm requires participants to suppress the memory for certain, previously learned unrelated word pair associations (no-think), while trying to remember others (think). The no-think condition results in successful directed forgetting (Anderson & Green, 2001).

Very little research exists to date exploring the neural basis of directed forgetting. The only neuroimaging study to explore directed forgetting utilized the think/no-think paradigm (Anderson et al., 2004). After the scanning session, participants were tested on cued recall of all the words, with an emphasis that they should recall think as well as no-think words. Behaviorally, the think/no-think manipulation worked. Participants recalled significantly fewer no-think words than think words in both recall tests (Anderson et al., 2004). When comparing the neural activity of no-think versus think trials, activity in the typical control network seen in studies of motor response inhibition was observed (Aron & Poldrack, 2006; Garavan et al., 2002; Rubia et al., 2003). Prefrontal activity included bilateral DLPFC and VLPFC (including the right inferior frontal gyrus), as well as the ACC, presupplementary motor area (preSMA), and dorsal premotor area. Supporting the theory that memories were actually suppressed during this task, bilateral hippocampal activation was less for the no-think trials than the think trials, possibly indicating that memory encoding was occurring during the think trials but not during the no-think trials. Correlational analyses were also conducted between activity during the scan and post-scanning recall. Activity in bilateral DLPFC and VLPFC was correlated with successful suppression—words that were not recalled were associated with greater lateral PFC activity during no-think trials. Hippocampal activity, on the other hand, was greater for think items that were later recalled as compared to those that were later forgotten (Anderson et al., 2004).

Although the functional MRI study using the think/no-think paradigm supported the hypothesis that inhibitory self-control, localized to the VLPFC in motor inhibition and other paradigms, is at work in directed forgetting (Anderson et al., 2004), more research must be conducted before firm conclusions may be drawn. Given that a wide range of prefrontal areas were recruited, it is possible that other control mechanisms were at work in addition to self-control during directed forgetting. For example, the DLPFC could have been recruited to monitor the think/no-think rule, while other regions may have been recruited to assist with differential rehearsal or other strategies used to control memory. It is interesting to note that although the think/no-think paradigm does not require motor control, a similar neural network to that seen during behavioral self-control was recruited, including the right VLPFC. This raises the possibility that the self-control network activated fairly consistently in a wide variety of forms of behavioral control such as those discussed above (including motor inhibition, risk-taking, temporal discounting, and emotion regulation), is also recruited for directed forgetting. However, given the dearth of research into this possibility to date, further research into the mechanisms behind and the neural basis of directed forgetting must be conducted before the role that inhibitory self-control plays in this phenomenon can be understood.

THOUGHT SUPPRESSION

Intuitively, it seems there can be advantages to being able to control one's own thoughts. For example, if a joke pops into someone's head at a funeral, it is preferable to be able to suppress thoughts about that joke so as not to smile or laugh inappropriately. In other situations, however, it may be disadvantageous to one's mental health to suppress certain thoughts, which can be an instance of an avoidant coping technique in mental disorders such as Post-Traumatic Stress Disorder (PTSD; Rassin et al., 2000). As a result of these somewhat contradictory effects of thought suppression, much research has been

done in empirical settings to further understand this process.

The study of thought suppression has largely been conducted by Wegner and colleagues (for reviews, *see* Rassin et al., 2000; Wenzlaff & Wegner, 2000). In the classic "white bear" thought suppression experiment, two groups of participants were instructed to spend consecutive 5-minute periods either thinking about a white bear (the expression condition) or inhibiting thoughts about a white bear (the suppression condition) (Wegner et al., 1987). It was found that during suppression, thoughts of a white bear were reduced but not eliminated relative to expression. After suppression, however, a rebound effect occurred and there were increased thoughts about the target relative to control groups who did not have to previously suppress the thought. This pattern of results has been largely replicated (Wenzlaff & Wegner, 2000).

Parallels have been drawn between thought suppression and other domains of self-control (Wegner, 1992). Most similar is memory inhibition perhaps because of its shared reliance on cognitive, as opposed to behavioral control. The goal of both processes is to inhibit something from being consciously retrievable (Bjork, 1989; Rassin et al., 2000). Thought suppression shares some characteristics with other forms of self-control as well, such as emotion regulation and temporal discounting. When suppressing an emotion, subjects may rely on similar strategies, such as distraction, as when suppressing a thought (Gross, 2002). Subjects may also rely on distraction and attentional control when attempting to delay gratification (Mischel et al., 1989). Therefore, exploring the neural basis of thought suppression and how it may relate to the neural basis of other forms of self-control is a logical path to pursue.

There has been some research on the neural basis of thought suppression. Only two studies have directly explored the effects of thought suppression in a neutral, non-emotional setting (Mitchell et al., 2007; Wyland et al., 2003). The results of these two studies are not consistent. When contrasting thought suppression with free thought, Mitchell and colleagues found right VLPFC and right DLPFC to be active.

When contrasting clear-all thought with free thought, Wyland and colleagues found a large network of prefrontal areas to be active, including the bilateral insula, left IFC, and ACC. The lack of activity noted in the right VLPFC during self-control (the thought suppression condition) could be due to multiple reasons. First, it is possible that the right insular region they reported active in the clear-all thought versus free-think contrast overlaps with the right VLPFC noted in other self-control paradigms (Aron & Poldrack, 2006; Remijne et al., 2005). Second, perhaps the right VLPFC is required for behavioral but not cognitive self-control. Both the current study and the memory-inhibition study also reported greater left VLPFC activity in the control versus no-control contrasts (Anderson et al., 2004; Wyland et al., 2003), although the other thought suppression study did not (Mitchell et al., 2007).

In support of the above theory of lateralization of the VLPFC, when comparing lateral and medial frontal EEG resting baseline activity in repressors as compared to nonrepressors, repressors have more left-lateralized activity than do nonrepressors, who show equivalent amounts of activity in both hemispheres (Tomarken & Davidson, 1994). Assuming that repressors are better able to suppress their thoughts, this finding could indicate that cognitive self-control may be localized to a left-lateralized frontal network. Additionally, when exploring thought suppression in an emotion regulation context, left lateral PFC has been found to be more active during thought suppression than during free-think conditions (Gillath et al., 2005; Kalisch et al., 2006). The authors hypothesized that the left VLPFC may have been recruited to produce distracting thoughts, a role consistent with the function attributed to Broca's area, found in the left VLPFC (Kalisch et al., 2006). This strategy may also have been used by subjects in the memory inhibition study (Anderson et al., 2004), thus providing an explanation for the left VLPFC activity noted during no-think as compared to think trials. This is in contrast to cognitive reappraisal, which recruits right anterolateral prefrontal regions (Kalisch et al., 2006). Although cognitive reappraisal is a cognitive self-control

technique, it results in more directly observable/behavioral changes (i.e., changes in emotional intensity) than does thought suppression, thus this could explain why emotion regulation via cognitive reappraisal demonstrates right VLPFC activity, whereas emotion regulation via thought suppression does not. Clearly, however, more research must be conducted before any conclusions may be drawn from these data.

SYNTHESIZING THE LITERATURE

Although the vast majority of studies exploring various forms of inhibitory self-control do not attempt to directly relate one variety to another, some research has been conducted with that goal in mind. Muraven and Baumeister in particular have conducted a series of studies relating multiple forms of self-control (for a review, see Muraven & Baumeister, 2000). They conducted a series of studies in which subjects were given a task involving any of a number of forms of self-control (such as emotion regulation, thought suppression, the stop-signal paradigm, the Stroop task, solving impossible anagrams, grasping a resistant handgrip for an extended period of time, or resisting sweets or alcohol) and were then tested on a second, completely different measure of self-control. Their performance was compared to a second group of participants who performed a task matched for effort and frustration as measured by self-report questionnaires that did not require self-control, such as solving mathematical problems or quickly typing a paragraph without feedback. The results consistently demonstrate that subjects who exerted self-control in an initial task were worse at the subsequent self-control task than those who initially performed a difficult initial task not requiring self-control, implying that not only is self-control a unified process, but that it is a limited resource that can be fatigued (Muraven & Baumeister, 2000; Muraven et al., 2006; Muraven et al., 1998).

The above line of research demonstrates that a wide range of measures of self-control all tap a common pool of resources, thus suggesting that they may all be subsumed by one general self-control process. In a different line

of work that also attempts to equate different forms of self-control, a handful of studies have compared subject performance on two different forms in order to directly explore correlations in performance on the two measures, without regard for the effects of self-control fatigue. Overall, the studies have found that impairment in one domain of self-control is associated with impairment in another domain.

Much of this work focuses on motor response inhibition and its relation to other varieties of self-control, because it is arguably the simplest and the most completely studied form of self-control. A series of studies have directly compared the neural mechanisms utilized during stop-signal and go/no-go tasks to those utilized in other tasks that require cognitive control. Tasks used include the flanker task, which requires the suppression of irrelevant distracting information (Bunge et al., 2002; Wager et al., 2005), set shifting during the Wisconsin Card Sorting Test (Konishi et al., 1999), and an incompatible stimulus-response task that requires subjects to press left for a right arrow and vice versa (Wager et al., 2005). Conjunction analyses showed that right IFC and/or right anterior insula were active in adults across all tasks during the inhibition/conflict trials, the region commonly associated with response inhibition in go/no-go and stop-signal tasks (Bunge et al., 2002; Konishi et al., 1999; Wager et al., 2005).

Using a different tactic, some studies of response inhibition using the go/no-go or stop-signal paradigm focused on populations of subjects that have impairments in real world self-control, such as people with high levels of impulsivity (Logan et al., 1997), ADHD (Durstun et al., 2006; Lijffijt et al., 2005; Logan et al., 2000), substance abuse problems (Fillmore & Rush, 2002; Monterosso et al., 2005), and obesity (Nederkoorn et al., 2006). Subjects in each of these impulsive populations performed worse at motor response inhibition (longer SSRTs or more errors in the go/no-go task) than healthy control subjects. Additionally, obese children also acted in a riskier manner than did healthy controls, suggesting that not only is impaired motor response inhibition associated with a

lack of self-control in general, but impaired motor response inhibition may be associated with risky behavior as well (Nederkoorn et al., 2006). Moreover, children with ADHD have less of an increase in BOLD signal when comparing neural activity during no-go trials to that on go trials than do healthy control children in the right IFG (Durstun et al., 2006).

Reversal learning has also been explored in populations at-risk for increased impulsivity, such as psychopaths, who performed worse on a reversal learning task than did healthy controls (Mitchell et al., 2002). The same psychopathic subjects performed worse on the IGT (i.e., chose more cards from the riskier, disadvantageous decks) than did those in the control group, suggesting a potential link between response inhibition as indexed by reversal learning and risky behavior (Mitchell et al., 2002).

Some studies have found a positive relationship between response inhibition and emotion regulation ability, as operationalized by either a greater ability to inhibit negative emotions during go/no-go blocks with negative feedback (Lewis et al., 2006) or less variability in anger ratings over a three- to four-day period (Hoeksma et al., 2004). In one study that invoked prepotent emotional and motor responses simultaneously (Berkman, Burklund, & Lieberman, 2009), intentional motor response inhibition was associated with decreased amygdala responses and the magnitude of these reductions was inversely associated with the strength of right VLPFC activity during response inhibition. In other words, intentionally inhibiting a motor response appears to have produced unintentional inhibition of affective responses as well, suggesting a common regulatory system for both.

Finally, memory inhibition has been theorized to be related to motor inhibition (Levy & Anderson, 2002). As mentioned in the memory inhibition section, the think/no-think paradigm was modeled after the go/no-go paradigm; both no-go and no-think conditions require overriding the natural tendency to either respond to a stimulus or to retrieve the previously studied target word associated with a cue word (Anderson & Green, 2001). Although the

think/no-think paradigm has not been used in concert with the go/no-go paradigm, a similar right VLPFC region was active in an fMRI study utilizing the think/no-think paradigm that is active in motor inhibition tasks (Anderson et al., 2004). This suggests that a similar inhibitory process may underlie at least one aspect of successful memory inhibition.

There has been some research focusing on the link between risky behavior and other measures of impulsivity. As mentioned above, an association has been found between obesity in children, motor response inhibition, and risk-taking behavior (Nederkoorn et al., 2006). Risky behavior has also been found to be increased in other populations with a purported high level of impulsivity, such as psychopaths using the IGT (Mitchell et al., 2002) and those who abuse substances using both the IGT and CGT (Monterosso et al., 2001).

There has also been research conducted relating risk-taking and emotion regulation. When inducing a negative mood in subjects and then asking them to play a lottery game, those who were told to use cognitive appraisal before making their decision acted in a less risky manner than those who were just asked to report their choice (Leith & Baumeister, 1996).

The decision to choose larger, delayed rewards over smaller, immediate rewards has also been linked to impulsivity and mood state. As described in the temporal discounting section, it has been proposed that the steepness of the temporal discounting curve may be an index of overall impulsivity (Monterosso & Ainslie, 1999). Additionally, a large literature exists exploring temporal discounting in populations purported to be impulsive, most specifically those who abuse substances; this literature consistently finds steeper discounting curves in those who abuse substances as compared to healthy controls (for a review, see Bickel & Marsch, 2001).

While there is a wide range of studies directly comparing more than one concept of self-control, there are still many unanswered questions. First, most studies only compare two of the six described varieties of conscious self-control. Second, the neural basis of self-control has not

been explored while directly comparing multiple forms of self-control within a single population of subjects. Such a study design would be useful to note if there are coactivations or dissociations within the right VLPFC during acts of self-control. It is possible that the right VLPFC is involved in self-control generally, but that there are different subregions that underlie different forms of self-control. It is unclear from the existing literature, which uses different methods, different data acquisition tools, different data processing and analysis techniques, and, most importantly, different participants, whether there is a single right VLPFC region activated in all tasks requiring self-control or if there are unique subregions. The existence of behavioral associations between such a wide variety of self-control indices suggests that it would be fruitful to directly examine the extent of a shared neural basis of different forms of self-control.

THE VLPFC IS WELL-POSITIONED TO EXERT SELF-CONTROL

The right VLPFC is well suited to serving a key role in exerting self-control over actions. It has close anatomical associations with other control areas in the prefrontal cortex, such as the DLPFC, mPFC including the ACC, and the OFC (Miller & Cohen, 2001). Evidence that the right VLPFC is linked to the amygdala via the mPFC comes from affect labeling studies, which find increased right VLPFC activity associated with decreased amygdala activity (Hariri et al., 2000; Hariri et al., 2003; Lieberman et al., 2007), likely through mediation by the mPFC, which has dense reciprocal connections with both structures (Lieberman et al., 2007).

Recently, white matter connections identified using Diffusion Tensor Imaging (DTI) have been noted between the right VLPFC and the preSMA, an area thought to be involved in conflict detection (Aron et al., 2007). The preSMA may signal when there is a conflict between an intention (e.g., to resist drug use) and an impulse (e.g., craving)—in other words, when a temptation exists that may challenge one's self-control.

Crucially, the right VLPFC also has direct connections with motor output control areas of the basal ganglia such as the STN (Aron et al.). This may be the means through which the right VLPFC may send a signal to exert behavioral control and therefore underlie an act of self-control.

More detailed research on anatomical connections comes from studies of macaque monkeys. While it is not clear how similar human and monkey prefrontal cortices are, evidence exists that the cytoarchitecture of the macaque VLPFC (including the lateral OFC) is similar to that in humans (Ongur & Price, 2000; Petrides et al., 2005). Therefore, it is possible that similar anatomical connections exist. The monkey inferior arcuate sulcus, just anterior to the ventral premotor area, and its surrounding cortex may be the monkey homologue to the human VLPFC, as evidenced by a study comparing the cytoarchitecture of this region in monkeys and humans (Petrides et al., 2005). This region is directly connected in the monkey to many other cortical regions, such as the lateral and medial OFC, the dorsomedial PFC, the DLPFC, the ACC, the insula, the supplementary, premotor and primary motor areas, and areas of the superior temporal lobe (Deacon, 1992).

The lateral OFC receives sensory input from the primary taste cortex, visual areas via the inferior temporal cortex, and somatosensory areas such as the primary and secondary sensory cortices and the insula. It also has reciprocal connections with the amygdala, cingulate cortex, premotor areas, and DLPFC (Kringelbach & Rolls, 2004). Connections with some of those regions, specifically the ACC, DLPFC, preSMA and amygdala, have been noted in humans as well (Aron et al., 2007; Lieberman et al., 2007; Miller & Cohen, 2001). Lastly, the lateral OFC has efferent connections with the hypothalamus, periaqueductal gray area and striatum, the ventral caudate in particular (Kringelbach & Rolls, 2004). A recent DTI study of white matter tracts in humans has reinforced the finding of a direct connection between the lateral OFC and the ventral striatum in humans (Leh et al., 2007).

CONCLUSION

In conclusion, a fairly localized prefrontal network appears to underlie a variety of forms of self-control. Simple motor response inhibition, mostly assessed via go/no-go and stop-signal tasks, consistently activates the right IFC/VLPFC (Aron et al., 2004). This may be accompanied by DLPFC and ACC activity, which are most likely utilized generally for other cognitive processes, such as rule monitoring (Bunge, 2004) and performance/conflict monitoring (Botvinick et al., 2004) respectively. Support for this can be seen when noting the wide variety of tasks that have been associated with DLPFC or ACC activity, such as the Stroop task, the Wisconsin Card Sort Task, the flanker task, verb generation, and reward-related two-alternative forced-choice tasks, in addition to stop-signal and go/no-go tasks (for reviews, see Botvinick et al., 2004; Bunge, 2004; Ridderinkhof et al., 2004).

Most of the other tasks discussed that require self-control recruit a more diffuse prefrontal network. Reversal learning, for example, which requires the processing of reward contingencies in addition to self-control, recruits the reward-sensitive mPFC and medial OFC (Elliott et al., 2000). Risk-taking and temporal discounting similarly require the processing of relative rewards and recruit the mPFC in addition to the right VLPFC (Krain et al., 2006; McClure et al., 2004), although the specific nature of whether right VLPFC is utilized more when making risky or safe decisions is still under debate. Emotion regulation, which requires both self-control and emotion processing, recruits mPFC as well, which has been associated with emotion-related processing in addition to reward processing (Ochsner & Gross, 2005).

Finally, more cognitive forms of self-control, such as memory inhibition and thought suppression may require more monitoring of rules, which can explain the consistent DLPFC activation in these studies, as well as an increased amount of alternate processing needs, which can explain the diffuse and possibly left-lateralized PFC control network utilized during these tasks (Anderson et al., 2004; Mitchell et al., 2007;

Wyland et al., 2003). However, it is important to note that there are very few neuroimaging studies of memory inhibition and thought suppression, thus any conclusions that can be made are tentative.

In short, it is logical to conclude that the right VLPFC is an area commonly related to self-control, while other prefrontal regions may be recruited based on specific task demands during an act of self-control. It is important to note, however, that the right VLPFC is involved in other sorts of tasks, such as attention (Corbetta & Shulman 2002), memory (Courtney et al. 1996; Kostopoulos & Petrides 2003; Rizzuto et al. 2005), and emotion perception (Kober et al. 2008). Therefore, it cannot be concluded that the involvement of right VLPFC in a task means self-control is being exerted without examining theorized task demands (see Poldrack 2006).

Moreover, additional research directly comparing the neural networks recruited during different forms of self-control must be conducted before any conclusions can be drawn regarding the relative unity or segregation of right VLPFC activity. The research to date cannot resolve whether there is a single part of the right VLPFC that is involved in each of the aforementioned forms of self-control or if different subregions are recruited for different forms. Further research combining neuroimaging with multiple forms of self-control in the same population of subjects will help elucidate the specificity of right VLPFC activity as it relates to self-control, an important phenomenon to understand given the role of impaired self-control in a multitude of clinical problems, such as ADHD, substance abuse, gambling, and many others.

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