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# The Physiology of Executive Functioning

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Executive function (EF) has been defined as a multifaceted construct that involves a variety of high-level cognitive abilities (De Frias, Dixon, & Strauss, 2006). For most of the last century, studies of executive functions originated from neuropsychological research that focused on adults with frontal lobe damage (Stuss & Benson, 1986). Results of these studies suggested that lesions in the prefrontal cortex are associated with difficulties in tasks that require the ability to control impulses, plan strategically, and inhibit behaviors (Luria, 1972). Over the years, major features of executive functions have been identified, and these include abilities such as inhibitory control, attention shifting, working memory, goal-directed behavior, and strategic planning (Barkley, 1997; Miyake et al., 2000; Zelazo & Müller, 2002). Although essential components, such as response inhibition and goal-directed behavior, have been identified as important facets of executive function (Weyandt, 2009), to date, there is no agreed upon definition for this construct (Jurado & Rosselli, 2007).

Despite the fact that there is no universal definition of executive function, many studies have attempted to examine the underlying physiological features of executive functions. The purpose of this chapter is to examine the physiological underpinning of executive functions, as well as the

methodological limitations associated with these studies. Specifically, structural neuroimaging studies that have examined changes across development will be examined, followed by a discussion of functional neuroimaging studies that have focused on five constructs of executive function—planning, verbal fluency, working memory, response inhibition, and set shifting. In addition, common limitations associated with neuroimaging studies and suggestions for future research.

The articles presented in this chapter were obtained by searching two databases, namely, PsycArticles and ScienceDirect. The lists of reference were reviewed for the purpose of the study. Keywords such as executive function (or specific executive functions such as planning, verbal fluency, working memory, response inhibition, and set shifting) and structural imaging *or* functional imaging were used. In order for the article to be included in this review, the study had to be (a) published in a peer-reviewed journal between the years 1991 and 2012. In addition, the study had to (b) use neuroimaging techniques and (c) include a sample size larger than ten to examine the physiology of executive functions.

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## Physiological Underpinning of Executive Functions

Past research has created a false belief that the physiological underpinning of executive functions were allocated to the frontal lobes based on case studies with individuals who had sustained

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damage to the frontal lobes. These individuals often displayed deficits on a range of tasks purported to measure executive functioning; hence, it was presumed that damage to the frontal lobes would result in low performance on executive function tasks (Alvarez & Emory, 2006; Collette, Hogge, Salmon, & Van der Linden, 2006). More recently, however, with the advancement of technology, various methods (e.g., MRI, fMRI, PET) have supported that executive functioning relies on various distributed networks, which include frontal and posterior regions of the cerebral cortex, as well as subcortical regions (Collette et al., 2006; Jurado & Rosselli, 2007; Marvel & Desmond, 2010).

### Structural Neuroimaging Findings

A handful of structural neuroimaging studies have provided support that prefrontal and parietal regions are involved in executive functions (Badre & Wagner, 2007; Collette, Olivier et al., 2005; Gilbert, Bird, Brindley, Frith, & Burgess, 2008; Jacobs, Harvey, & Anderson, 2011; Keller, Baker, Downes, & Roberts, 2009; Raposo, Mendes, & Marques, 2012; Rypma, 2006; Tamm, Menon, & Reiss, 2003; Tamnes et al., 2010; Van Petten et al., 2004). For example, structural differences in the prefrontal cortex have been investigated. Keller et al. (2009) found volume atrophy in the dorsal prefrontal cortex with individuals with temporal lobe epilepsy, and performance on tasks of executive functioning (i.e., working memory index of the Wechsler Memory Scale and the Controlled Oral Word Association Test) was positively correlated with the volume of the dorsal prefrontal cortex. It is important, however, to note that results differ substantially among different age groups. For example, Jacobs et al. (2011) recently reported that along with the prefrontal cortex, the *entire brain* (p. 810) may play a crucial role in performing executive functioning tasks in childhood. On the other hand, studies conducted with older adults have also found that the prefrontal cortex appears to play a crucial part in executive functioning task performance. Specifically, some researchers have found positive

correlations between prefrontal lobe volumes and executive functioning task performance (Gunning-Dixon & Raz, 2003; Salat, Kaye, & Janowsky, 2002).

In 2010, Tamnes and colleagues studied neuroanatomical correlates of executive functions in Norwegian children and adolescents (50 males/48 females), ages 16–19. In the study, the relationships between three executive functions—namely, updating, inhibition, and shifting—and cortical thickness were examined via magnetic resonance imaging (MRI). During childhood and adolescence, cortical maturation is believed to be associated with thinning of the gray matter (Shaw et al., 2006), so it was hypothesized that rapid thinning would be associated with greater cognitive gains. Therefore, the primary research question focused on whether cortical maturation of the prefrontal cortex was associated with higher levels of executive functioning. Specifically, the researchers hypothesized that there would be a negative relationship between cortical thickness and executive functions and higher levels of performance would reveal stronger negative associations with cortical thickness and age.

In the study, six different executive function tasks were used (keep track task, letter memory task, plus-minus task, Trail-making test, antisaccade task, and Stroop task). Updating was assessed by keep track task (adapted by Miyake et al., 2000) and the letter memory task (also adapted by Miyake et al., 2000). Both tasks required the participant to update their working memory by recalling the last few words or letters from a sequence of words/letters. Two tasks were used to measure shifting, namely, the plus-minus task (adapted by Miyake et al., 2000) and the D-KEFS Trail-making test (Delis, Kaplan, & Kramer, 2001). In these tasks, the participant had to shift their attention to follow directions. For the former task, the participants were asked to complete a number of mathematical problems by adding 3 and then another problem set that required them to subtract 3. After these two problem sets, participants were given the third problem set, which required alternating between adding 3 and subtracting 3. For the latter task, three conditions—number sequencing, letter

sequencing, and number-letter sequencing—were administered. Specifically, participants were instructed to connect the numbers in numerical order in the number sequencing task. Similarly, participants were asked to link the letters in alphabetical order in the letter sequencing task. In the number-letter sequencing task, the participant had to connect both numbers and letters in ascending order (e.g., 1-A–2-B). Finally, inhibition was measured by the antisaccade task (adapted by Miyake et al., 2000) and the Stroop task (Delis et al., 2001). Both tasks required the participant to inhibit reflexive responses and focus on the target stimuli.

Before controlling for age, cortical thinning was observed across most parts of the cortical mantle, and negative associations were found between EF tasks (keep track, letter memory, antisaccade task) and cortical thickness. However, after controlling for age, results revealed that the keep track task (updating) was associated with cortical thinning in the parietal and frontal regions of the brain. In addition, thinning in the areas of the left inferior frontal gyrus (LIFG) and the right superior medial parietal areas was associated with better working memory updating performance. These results are consistent with functional magnetic resonance imaging (fMRI) findings showing that working memory is associated with the prefrontal cortex, anterior cingulate, and parietal and occipital regions of the brain (Honey, Bullmore, & Sharma, 2000). The antisaccade task (inhibition) was related to more thinning in the occipital (posterior) and parietal regions. The authors suggested that the antisaccade task might tap into visual detection and attention processes than inhibition ability in children and adolescence. Finally, there was no evidence supporting the hypothesis that individual differences in levels of executive functioning were related to structural maturation differences in the prefrontal cortex. The researcher speculated that the occipital and parietal regions of the brain were associated with basic cognitive processes that would not vary among individuals, whereas the prefrontal circuits, being highly associated with strategic thinking, would vary across participants (Collette, van der Linden et al., 2005).

There were several limitations associated with this study. First, cross-sectional data was used to examine the relationship between executive functioning tasks and structural brain maturation. Ideally, longitudinal studies would be used to investigate this relationship by including multiple time points and mapping developmental and maturational trajectories within participants. Next, individuals who participated in this study revealed relatively high cognitive functioning, which may not be representative of the general population. In addition, the executive functioning tasks used in the research was only limited to six tasks. Therefore, different results might emerge when different tasks are used. Finally, there was some possibility that other cognitive processes may have influenced task performance. For instance, the researchers did not control for non-executive abilities such as motor and processing speed that may have differed across age. Collectively, these studies suggest that improvement on executive functioning tasks is associated with structural maturation of the brain, with regional development of the cerebral cortex, sub-cortical structures, and white matter showing ongoing development from early childhood to adulthood (Giorgio et al., 2010).

Recently, Burzynska et al. (2011) examined the relationship between cortical thickness and executive function performance. Specifically, Burzynska et al. examined the relationship between cortical thickness and executive functioning as assessed by performance on the Wisconsin Card Sorting Test (WCST; Heaton, Chelune, Talley, Kay, & Curtiss, 1993). The WCST is a neuropsychological card sorting task that requires attention, inhibition, and set-shifting skills. In this study, researchers hypothesized that cortical thickness would be positively associated with WCST performance. This hypothesis was based on the theory that cortical thickness in adulthood may involve more neurons and synaptic connections, high degree of complex circuitry and myelination, and higher metabolic efficiency in the brain (Deary & Caryl, 1997). Seventy-three healthy young adults (32 women/41 men) between ages 20 and 32 and 56 healthy older adults (27 women/29 men) between ages 60 and

71 participated in the study. All participants achieved at least 8 years of education and had no history of neurological or psychiatric disease. Structural neuroimaging results (MRI) revealed that higher accuracy on the WCST was related to thicker cortex in the lateral prefrontal and parietal regions. Specifically, thicker cortices in bilateral middle frontal gyrus (MFG), right inferior frontal gyrus (RIFG), postcentral gyrus (PCG), precentral gyrus (preCG), and the superior parietal gyrus (SPG) were associated with higher percentage of correct responses on the WCST. The results of this study contradict the findings of Tamnes et al. (2010), which limited their research findings to young children. Studies that have investigated cortical changes in childhood agree that cortical thinning during this period is associated with better performance on executive functioning tasks, as well as academic outcomes (Shaw et al., 2006; Sowell et al., 2004). However, during adulthood, Miller, Alston, and Corsellis (1980) have suggested that the human brain undergoes a gradual reduction in volume. Perhaps the fact that cortical thinning is related to better performance on executive functioning tasks in childhood and adolescence no longer holds for older adults, since these individuals are experiencing reductions in brain volume. Therefore, with older adults, the maintenance of cortical thickness could be associated with *better* executive functioning. These ideas are speculative, of course, and warrant empirical investigation.

To further explore executive functions in the elderly population, Weinstein et al. (2011) investigated how aerobic fitness may impact executive functioning outcomes. In this study, participants completed two executive functioning tasks: the Stroop task and the spatial working memory assessment. Aerobic fitness was measured by maximal graded exercise test (VO<sub>2</sub> max), which is an indicator of cardiorespiratory fitness (CRF) (American College of Sports Medicine, 1991). To assess CRF, participants were asked to speed walk on a motor-operated treadmill within 2 weeks after the completion of the executive functioning tasks. Results of the study indicated that higher CRF levels were associated with better outcomes on the Stroop task and the spatial working

memory task. In addition, individuals with higher CRF level had greater gray matter volume in the dorsolateral prefrontal cortex (DLPFC). Specifically, the volume of the right IFG and preCG mediated the relationship between fitness level and Stroop interference, whereas non-overlapping regions of the DLPFC mediated the association between fitness level and spatial working memory.

This study had several strengths in that it used a relatively large homogeneous sample, which allowed the researchers to test mediation models. In addition, this study used two validated cognitive tasks to examine the hypothesis. However, the cross-sectional design does not allow for causal inferences and longitudinal studies are needed. Moreover, other variables such as genetic factors that affect the production of neurotrophins may in turn influence executive functioning performance.

In summary, a number of neuroimaging studies suggest that broad areas of the anterior and posterior regions of the brain are likely associated with executive functions (Perry et al., 2009). Although the specific regions of activation differed across tasks (and studies), preliminary studies support that increased activation in the DLPFC, as well as the parietal regions (i.e., SPG), is associated with better executive functioning performance on tasks including the Stroop task, spatial working memory, and the WCST.

## Functional Neuroimaging Findings

Numerous studies of executive functions have been conducted with functional neuroimaging techniques, i.e., those that assess regional cerebral blood flow (rCBF) or glucose metabolism (Weyandt, 2006). Most of these studies have used a cognitive subtraction method to deduce which particular regions of the brain are associated with the executive processes (Salmon & Collette, 2005). Specifically, this method compares regions of brain activity while participants engage in an executive functioning task compared to when the participant solves a nonexecutive control task.

By measuring regional brain activation patterns between executive and nonexecutive tasks, the activation patterns specific to the executive tasks are believed to represent the brain regions specifically recruited for executive processes (Collette et al., 2006). To improve on the cognitive subtraction methodology, several studies have extended these findings by applying “conjunction” analyses (Collette & Van der Linden, 2002; Collette, Oliver et al., 2005), which measures the common regional activation associated with performance on multiple tasks purported to measure the same executive function.

Jurado and Rosselli (2007) provided a review of the brain correlates of executive functions using single-photon emission computerized tomography (SPECT) and MRI. Results revealed that studies exploring strategic planning ability using the Tower of London task generally found that the DLPFC, anterior cingulate cortex (ACC), supramarginal gyrus (SMG), and angular and right and left prefrontal cortex were areas of increased activation (Goethals et al., 2004; Lazerou et al., 2000; Morris, Ahmed, Syed, & Toone, 1993). Additionally, various studies have reported that attentional control as measured by the Hayling task, Stroop task, and Wisconsin Card Sorting Test was related to increased activation in DLPFC (Collette et al., 2001; Gerton et al., 2004; Kaufmann et al., 2005; Lie, Specht, Marshall, & Fink, 2006) and the PFC (Collette et al., 2001; Fassbender et al., 2004). Verbal and nonverbal fluency performances were also associated with increased activation in various frontal regions (e.g., LIFG, ACC, and superior frontal sulcus) including the DLPFC (Frith, Friston, Liddle, & Frackowiak, 1991; Jahanshahi, Dirnberger, Fuller, & Frith, 2000). In the section that follows, neuroimaging findings exploring five executive functions—planning, verbal fluency, working memory, response inhibition, and set shifting—will be covered in more detail.

## Planning

Planning is a complex construct, making it difficult to narrow down a specific set of brain regions or networks underlying this ability. For example,

planning has been defined as a large category of responses and processes including, but not limited to, decision-making, judgments, and evaluation of one’s own behaviors and the behaviors of others (Das & Heemsbergen, 1983). Various executive function tasks including variations of the Tower of London test and maze completion test have been used to assess planning (Purdy, 2002; Welsh & Huizinga, 2001). Research using fMRI and positron emission tomography (PET) has found consistent brain activation patterns during participant performance on planning tasks. For example, using fMRI, Unterrainer et al. (2004) assessed the performance of college students on a computerized version of the Tower of London test as a measure of planning ability. Individuals classified as “better problem-solvers” based on overall task performance demonstrated increased activation in the right DLPFC, right superior temporal region, and right inferior parietal region compared to those classified as “worse problem-solvers.” Similarly, across the entire sample, better performance on the planning phase of the Tower of London test was associated with increased DLPFC activation. In addition, increased activation of the ACC was associated with erroneously solved trials. This increase in ACC activation during incorrectly solved trials is consistent with other neuroimaging studies that have found ACC activation to be associated with overriding responses, response-conflict, and errors of commission (Li et al., 2008).

Owen, Doyon, Petrides, and Evans (1996) used PET to examine regional activation during easier and more difficult versions of the Tower of London planning test with 12 healthy adults. Again, increased activation as measured by increased rCBF in the left DLPFC was associated with performance on the more difficult Tower of London task compared to a control task that consisted of identical visual stimuli and motor responses but was considered to be free of planning demands. In addition, statistically significant increased rCBF in the caudate and thalamus was also associated with performance on the more difficult version of the Tower of London test, implicating the involvement of a frontostriatal network during planning. Using fMRI with a

sample of 22 healthy adults aged 21–49 years old, Van den Heuvel et al. (2003) also found increased blood oxygenated levels (BOLD) within the DLPFC, striatum, premotor cortex, supplementary association area, precuneus, and inferior parietal cortex to be associated with planning activity as measured by a variant of the Tower of London test. These studies, as well as others (Dagher, Owen, Boecker, & Brooks, 1999; Newman, Carpenter, Varma, & Just, 2003), consistently demonstrate increased activation in the DLPFC and frontostriatal networks during executive planning tasks.

## Verbal Fluency

Verbal fluency refers to the ability to recall and produce words associated with a particular pre-specified category or beginning with a particular letter. Phelps, Hyder, Blamire, and Shulman (1997) used fMRI and found that the LIFG, ACC, and superior frontal sulcus demonstrated statistically significant increased activation during a verbal fluency task. In a meta-analysis, Costafreda et al. (2006) also found statistically significant increased activation in the LIFG, with increased BOLD response in more dorsal regions associated with phonological verbal fluency as compared to semantic verbal fluency. Costafreda et al. (2006), however, did not find evidence of significant BOLD responses within the antero-posterior or medial-lateral areas of the LIFG during these verbal fluency tests. Using PET, Frith et al. (1991) found increased activity in the left DLPFC and decreased activation in the bilateral temporal cortices. In a more recent fMRI study, Birn et al. (2010) found that increased activation in the LIFG during the letter fluency as compared to the categorical fluency. Alternatively, categorical fluency was more strongly associated with left fusiform and left MFG activity as compared to the letter fluency.

Although multiple brain regions appear to be associated with performance on verbal fluency tasks, these neuroimaging studies are consistent with others that suggest the LIFG, as well as temporal and parietal regions, underlies performance

on verbal fluency tasks (Gourovitch et al., 2000; Mummery, Patterson, Hodges, & Wise, 1996).

## Working Memory

According to Baddeley (1992), working memory is the brain system that temporarily provides storage and manipulation of information. Working memory (WM) is usually involved in complex cognitive tasks such as language comprehension, learning, and reasoning. Some constructs of working memory that have been examined in the neuroimaging literature include selection of item representation, selection and updating, updating memory content, rehearsal, and coping with interference (Bledowski, Kaiser, & Rahm, 2010).

Neuroimaging studies examining the physiology of working memory have found both common and unique brain regions associated with working memory performance across different working memory tasks and task parameters (Lepsien, Griffin, Devlin, & Nobre, 2005; Marvel & Desmond, 2010; Rowe & Passingham, 2001; Rowe, Toni, Josephs, Frackowiak, & Passingham, 2000). Research has shown that increases in brain activation in the prefrontal cortex are associated with increased working memory demands (Braver et al., 1997; Bunge, Klingberg, Jacobson, & Gabrieli, 2000). For example, Barch et al. (1997) showed that the DLPFC, the left inferior frontal cortex (IFC), and an area within the left parietal cortex showed significantly increased activation during long-delay (8-s) task conditions compared to short-delay (1-s) task conditions on a modified version of a continuous performance task. This increased activation during long-delay conditions suggests that these regions showing increased activation are specifically associated with the maintenance of information in working memory. Furthermore, because activation of these regions did not show increased activation during task conditions not purported to contain working memory demands, these findings further support the unique role of the DLPFC, left IFC, and a left parietal region in working memory task performance. Along with the prefrontal cortex, Bunge et al. (2000) detected increased activation

in the lateral prefrontal cortex (DLPFC) when participants were engaging in complex task (e.g., reading sentences and trying to retain target words). In 2004, Osaka and colleagues examined the neural substrates of executive functions with individuals who differed in working memory capacities. In this study, the authors hypothesized that the ACC and the LIFG would be the general neural basis for the central executive with reading span test (RST). Ten young adults aged 20–27 were divided into two subject groups: high-span subject (HSS) and low-span subject (LSS). Results of the fMRI indicated that increased activation was found in the ACC and LIFG when both groups were performing the complex RST. In addition, increased signal intensity in the ACC and IFG regions was detected for the HSS group. The cross correlation of signal change between IFG and ACC was higher for the HSS, which suggests that the network system between these two regions were more activated in the HSS than the LSS. The results of this study imply that the HSS have a more active working attention controlling system than the LSS group.

Recently, Fassbender et al. (2011) examined working memory in children with ADHD and found that these children lack specialization of brain function. In this study, the researchers hypothesized that there would be diminished activation in the prefrontal cortex, which is traditionally associated with WM. Researchers recruited 13 participants (ranging from 8 to 14 years) with ADHD combined type and typically developing controls matched on age, IQ, and SES. The Visual Serial Addition Task (VSAT) was used in conjunction with fMRI to examine working memory processes in these children. In this study, the authors hypothesized that participants with ADHD would reveal diminished activation in the prefrontal region of the brain and excess activation in areas that are associated with primary responding instead of higher cortical responding. The fMRI results indicated that the typically developing group had significantly greater activation in the bilateral MFG, right MFG extending into ACC, preCG, bilateral PCG, and the right cingulate when engaging in VSAT, whereas the ADHD group had significantly

greater activation in regions of the brain that were not specific to working memory (i.e., medial prefrontal cortex and bilateral insula extending into basal ganglia). Both children in the typically developing group and ADHD group showed significant activation in the right MFG and the right precuneus. It is important to note that this study has several limitations and the results should be interpreted accordingly. For example, similar to many other neuroimaging studies, this study also had a relatively small sample size which compromises the statistical power of the study as small- and possibly medium-sized effects are unlikely to be detected. In addition, the average IQ level was relatively higher in both the ADHD group and control group, which may limit the generalizability of the study's results. Moreover, some of the participants with ADHD had a history of stimulant medication treatment, which potentially may have long-term effects on specific patterns of brain region activation. In conclusion, research suggests that the prefrontal cortex, specifically, the dorsolateral and parietal regions of the brain (Bledowski et al., 2010), show consistent activation while individuals perform working memory tasks.

## Response Inhibition

Goldman-Rakic, Thierry, Glowinski, Goldman-Rakic, and Christen (1994) defines inhibition as the ability to reject an automatic tendency in a given situation. Inhibition is often considered an executive functioning ability or process (Barkley, 1997; Best & Miller, 2010; Miyake et al., 2000). Several authors have suggested that inhibition is a fractionated construct comprised of several similar yet distinct inhibitory processes (Friedman & Miyake, 2004). For example, some authors (Gray, 1982; Nigg, 2000, 2001) have distinguished between different types of inhibition such as response or motor inhibition, cognitive inhibition, interference control, motivational inhibition, and automatic inhibition of attention. Given the possibility of numerous related but distinct inhibitory processes, it is not surprising that weak correlations

are typically found between measures that tap each of these abilities (Huizinga, Dolan, & van der Molen, 2006; Hull, Martin, Beier, Lane, & Hamilton, 2008). Furthermore, the existence of multiple types of inhibitory process would suggest the likelihood of overlapping yet possibly distinct brain regions underlying these multiple inhibitory processes.

Response inhibition has received considerable interest and research has shown that this is associated with increased activation of the dorsomedial prefrontal cortex, lateral prefrontal cortex, parietal cortex, insular cortex, bilateral precuneus, left angular gyrus, and right middle temporal gyrus (Blasi et al., 2006; Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Mostofsky & Simmonds, 2008). Specifically, Blasi et al. (2006) examined response inhibition and interference monitoring and suppression in 57 healthy adults. In their study, neuroimaging results revealed that performance on a response inhibition task was associated with greater activation in DLPFC, ventrolateral prefrontal cortex (VLPFC), and parietal cortex (PC) as compared to performance on an interference monitoring and suppression task. Bunge et al. (2002) also have found that different inhibitory processes were in fact associated with differential brain region activation patterns. Better performance on an interference control task was associated with increased statistically significant activation of the VLPFC and insular cortex in both children and adults, although children showed increased activation in the left VLPC and insula, while adults showed increased activation in the right VLPFC and insula. Alternatively, regions associated with performance on a response inhibition task included the bilateral precuneus, left angular gyrus, and right middle temporal gyrus, and the right MFG for both children and adults. In adults, the bilateral VLPFC, bilateral DLPFC, and the anterior and posterior cingulate cortices were also significantly activated during task performance. In 2004, Aron, Robbins, and Poldrack found that the DLPFC, IFC, and the orbital frontal cortex are associated with inhibition tasks.

Recently, Carmona et al. (2011) examined response inhibition in medication-naïve adults with ADHD using a within-subject case-control

design. Based on previous research, the authors hypothesized that the unmedicated adults with ADHD would reveal decreased activation in the IFG during response inhibition tasks. Twenty-three right-handed male adults with ADHD and 23 healthy controls participated in the study and the Go/NoGo task was used to measure response inhibition. Contrary to the study's hypothesis, results of the fMRI did not find differences in the bilateral IFG activation during Go/NoGo task performance. These results are consistent with other fMRI studies that have found no difference in brain activation during response inhibition task (Dillo et al., 2010) but are inconsistent with studies that have either found increased or decreased activation in the IFG when compared to controls (Epstein et al., 2007; Kooistra et al., 2010). Hence, the results of the neuroimaging findings warrant further investigation.

It should be noted, however, that several limitations characterized the study (Carmona et al., 2011). For example, the selectivity of the sample could bias the generalization of the results. Specifically, participants in this study were carefully screened for comorbidity and had to have an IQ that fell within one standard deviation of the mean. In addition, the sample size was relatively small in this study. Perhaps the study lacked the power to detect the group differences in the IFG activation due to the small sample size.

In addition, results from multiple studies have also implicated right lateralized frontostriatal circuits in effective response inhibition, including the right inferior prefrontal cortex (Aron, Robbins, & Poldrack, 2004; Durston, Thomas, Worden, Yang, & Casey, 2002), presupplementary association area, and the striatum (Congdon et al., 2010). For example, in an event-related fMRI study by Rubia, Smith, Brammer, and Taylor (2003), effective response inhibition measured by performance on the stop task was primarily associated with statistically significant increased activation of the right inferior prefrontal cortex, while poorer task performance was associated with statistically significant increased activation of the ACC and bilateral inferior parietal lobes. In a different study that used the same stop task, Zandbelt and Vink (2010) also found

that successful performance on stop trials was significantly correlated with increased activation of the right inferior prefrontal cortex, as well as the presupplementary motor area and the striatum. In addition to the previously mentioned brain regions, other neuroimaging studies have found statistically significant increased activation of parietal, cerebellar, and thalamic regions during inhibition tasks (Boehler, Appelbaum, Krebs, Hopf, & Woldorff, 2010; Rubia, Smith, Taylor, & Brammer, 2007).

In conclusion, these studies suggest that different inhibitory processes may be associated with different brain region activation; however, the VLPFC and the IFG may be involved across various inhibitory processes (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2004; Bunge et al., 2002). These findings are consistent with other neuroimaging studies showing increased VLPFC activation during the performance of both response inhibition and interference control tasks (Hazeltine, Poldrack, & Gabrieli, 2000; Rubia et al., 2001). Although a number have studies have examined the neural substrates of response inhibition, the delineation of the physiological substrates associated with different types of inhibitory processes remains a much needed area of future research.

## Set-Shifting

Set-shifting is referred to as the ability to flexibly switch back and forth between tasks, operations, or mental sets (Miyake et al., 2000). Neuroimaging studies have shown that activation across prefrontal, parietal, and subcortical structures have been associated set-shifting ability (Salmon & Collette, 2005). For example, Wilkinson, Halligan, Marshall, Büchel, and Dolan (2001) used fMRI and found that performance on a set-shifting task (i.e., local-global task) was associated with statistically significant increased activation of the bilateral inferior parietal cortex, motor and premotor cortex, bilateral putamen, as well as a more general frontoparietal network. It should be noted that these regions showed differential degrees of activation across varying task

parameters. In addition, Zakzanis, Mraz, and Graham (2005) obtained fMRI measures during participant performance on the Trail-making test. These authors found statistically significant increased activation in the left DLPFC, medial prefrontal cortex, and left middle and superior temporal gyrus during the shifting trial compared to the non-shifting trial.

In order to minimize the visuospatial demands inherent to most set-shifting tasks, Moll, de Oliveira-Souza, Moll, Bramati, and Andreiuolo (2002) obtained fMRI measures during participant performance on a variant of the Trail-making test that was intended to minimize visuospatial demands while increasing the verbal requirement. Verbal set-shifting ability was associated with significant increases in BOLD response in the left DLPFC, left supplementary motor area, and bilateral activation of the intraparietal sulci. Other neuroimaging studies using set-shifting tasks requiring minimal visual and spatial cognitive abilities have implicated the superior posterior parietal cortex (Gurd et al., 2002).

In 2004, Wager, Jonides, and Reading conducted a meta-analysis with 31 fMRI and PET studies to examine the neuroimaging studies of set-shifting. As a result, the researchers found that seven regions that showed significant activation across various set-shifting tasks. Specifically, the regions associated with set-shifting were the medial prefrontal cortex, right premotor cortex, bilateral posterior intraparietal sulcus, bilateral anterior intraparietal sulcus, and the left occipital region. Although both posterior (parietal and occipital) and frontal (DLPFC and anterior insula) regions were involved in set-shifting, the involvement of DLPFC was weaker than expected.

In conclusion, there were no specific brain regions that showed activation during set-shifting tasks. Instead, neuroimaging studies revealed that set-shifting is extended to multiple regions of the brain. Increased activation of the parietal cortex has been commonly reported, however, which may suggest that this region of the brain may play a core role in set-shifting (Gurd et al., 2002; Wager, Jonides, & Reading, 2004; Zakzanis et al., 2005).

## Limitations and Future Directions

During the past decade, neuroimaging studies have provided additional information about brain structures and areas of functioning that may be involved with executive functions. This body of work is not without methodological problems, however, that ultimately limit the extent to which solid conclusions can be deduced.

First, as noted previously, there is no universally accepted definition of executive function (Jurado & Rosselli, 2007). Second, task impurity is a serious issue as many tasks that are commonly used as measures of executive function lack acceptable validity and reliability (Weyandt, 2009). Indeed, Rabbitt (1997) has expressed concerns regarding the low internal and test-retest reliability among executive function measures, and work by Tate, Perdices, and Maggioro (1998) supports Rabbitt's concerns. For example, Tate et al. examined the temporal stability of the Wisconsin Card Sorting Test and found that the stability coefficient was in the .30–.40 range. Others have argued that various executive functioning tasks purported to measure a single construct have low intercorrelations and in many cases are statistically nonsignificant (Barkley, 2011; Collette et al., 2006; Greve et al., 2002; Humes, Welsh, Retzlaff, & Cookson, 1997; Salmon & Collette, 2005). Moreover, executive functioning tasks that are commonly used not only tap into a particular executive function but also other abilities such as general cognitive skills (Barkley, 2011) or nonexecutive skills (Collette et al., 2006). In addition, many executive functioning tasks have very low ecological validity (Ardila, 2008). Specifically, scholars have argued that these tasks are poorly correlated with daily life activities. Some scholars have suggested that the use of rating scales may be a better method of assessing executive functions (Barkley, 2011).

There are also a number of significant limitations associated with brain imaging techniques. First, neuroimaging studies typically involve small sample sizes (less than 20), which often compromises statistical power, and effect sizes

are rarely reported. Confounding factors such as comorbidity are rarely acknowledged (Jacobs et al., 2011) as are potential medication effects (Anderson, Northam, Hendy, & Wrennall, 2001). Replication and reliability studies are virtually nonexistent. Another major limitation of neuroimaging studies is the use of cross-sectional data instead of longitudinal data. Specifically, most studies do not measure the brain activation of individuals across time nor do they measure this with short or long temporal delays (Collette et al., 2006). This one-time one-shot approach may compromise the reliability of the image. Furthermore, methods across studies vary greatly including the type of mathematical algorithms employed, colors representing activation levels, and statistical analysis procedures (Reeves, Mills, Billick, & Brodie, 2003; Weyandt, 2006; Weyandt & Swentosky, 2013), which may ultimately further complicate the interpretation of the results. In addition, researchers often fail to report the baseline activity in their studies and factors such as age, sex, emotional state, and health also could influence the results of neuroimaging studies; however, most studies have not yet considered these factors (Weyandt & Swentosky, *in press*).

Finally, it is important to note that in many of the previously cited studies (e.g., Li et al., 2008), it is unclear whether or not decisions were made a priori regarding the brain regions to be analyzed. In cases where the entire brain is analyzed, statistically significant activation patterns may simply be the result of the large number of regions analyzed (i.e., type I error) (Salmon & Collette, 2005). It should also be noted that in most of the studies previously cited, only significant findings were reported. Therefore, specific brain regions that did not show statistically significant levels of activation were not explicitly described. Furthermore, it is unlikely that specific brain regions are exclusively related to specific types of executive functions as performance on tasks purported to measure different executive functions often shows overlapping regions of activation. For example, significant activation of the LIFG has been found to be associated with performance on both verbal fluency and response inhibition tests

(Birn et al., 2010; Osaka et al., 2004). Significant activation of the DLPFC and the ACC has been found to be associated with performance on both planning and verbal fluency tests (Frith et al., 1991; Phelps et al., 1997; Unterrainer et al., 2004). Lastly, it is crucial to keep in mind that neuroimaging studies are correlational in nature and do not reveal causal relationships between executive functions and areas of increased brain activation.

## Conclusion

During the past decade, the use of neuroimaging techniques to explore the physiological substrates of executive functions has increased substantially. In general, studies suggest that the physiology of executive function is not limited to the prefrontal cortex as hypothesized in previous studies (e.g., Birn et al., 2010; Fassbender et al., 2011; Newman et al., 2003; Osaka et al., 2004; Unterrainer et al., 2004). Instead, a wide range of brain structures and regions appear to be involved and these vary depending on the executive function measure employed. In general, these findings support that executive function is both a unitary and multifaceted construct. Future studies should show attempt to address the methodological limitations that exist in the current literature. For instance, mixed methodologies (e.g., longitudinal designs, neuroimaging subtraction, and conjunction analyses) and larger sample sizes would be beneficial as would attention to sample characteristics (e.g., IQ, sex, ethnicity). Lastly, further refinement of the conceptualization of the construct of executive functioning and the use of psychometrically sound executive functioning measures will contribute to a greater understanding of the neurophysiological substrates of executive functioning.

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