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EXECUTIVE RESOURCES

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Abstract

Executive resources allow for flexible, adaptive, goal-directed responses to environmental circumstances in essentially all facets of daily living. Executive function is composed of related, but separable, components. This article will highlight three essential aspects of executive function: (1) working memory, (2) planning and organizing, and (3) inhibitory control. Working memory is the system by which information is maintained in an active mental state so that it can be used for other purposes. Planning and organizing of behavior involves the way in which individuals optimize the execution of multistep tasks to achieve a goal. Inhibitory control allows an individual to inhibit inappropriate responses and to shift responses when necessary. These aspects of executive function appear to depend in part on large-scale neural networks that are centered in distinct areas of prefrontal cortex, working in concert with other brain regions, such as parietal cortex and the basal ganglia. Executive function is a fundamental aspect of human cognition that is compromised in patients with a wide range of medical conditions.

INTRODUCTION

Executive resources are defined as higher-order processes involved in the control of cognition and goal-directed behavior. Intact executive functioning supports a multitude of behaviors, underscoring the ubiquitous involvement of executive resources in human behavior and cognition. Examples of executive functions include initiation of goal-directed behavior, planning and sequencing of complex tasks, performing more than one task simultaneously (multitasking), shifting attention to salient items or events, strategic decision making, extracting the gist of a scenario, sustaining behavior despite distraction or interference, overriding automatic responses with more appropriate behaviors, and terminating behavior at an opportune time.[1] In short, executive resources allow for flexible, adaptive, goal-directed behavioral responses to environmental circumstances. Indeed, executive resources are fundamental to success in the wide range of cognition domains covered in this issue of CONTINUUM.

Individuals with executive dysfunction can exhibit a broad range of manifestations in their daily lives.[2] Patients may have difficulty grocery shopping or preparing a meal. They may have trouble keeping up with demands at work. They may become distressed when the day's plan changes and exhibit difficulty switching situations, behaviors, or thoughts. Because the ability to appreciate the larger picture, manage multiple options, and assess consequences may be compromised, patients show impaired judgment in daily decision making and problem solving. Their stories and conversations may be poorly organized and difficult to follow. They may not grasp jokes or puns because of limited capacity for abstract thinking.

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Many report memory loss, as forgetfulness can result from inattention, perseveration, and poorly planned information retrieval. Thus it is evident that, for patients and their loved ones, the functional consequences of executive dysfunction are far-reaching and devastating.

In general, executive functions are attributed to the frontal lobes, in particular to the prefrontal cortex. In fact, this association is so strong that the literature commonly conflates the terms *executive function* and *frontal function*. Growing evidence, however, demonstrates that frontal structures are part of larger cortical-cortical and cortical-subcortical networks that subserve executive functioning. For instance, functional neuroimaging studies have implicated frontoparietal networks in various executive functions, including working memory, set shifting, and inhibition.[3,4] In addition, functional neuroimaging provides evidence for basal ganglia involvement in executive tasks such as planning.[5] Disruption of frontal-striatal circuitry or the basal ganglia is thought to underlie executive difficulties in patients with movement disorders, such as Parkinson disease,[6] Huntington disease,[7] and progressive supranuclear palsy.[8]

Some authors have argued for a common mechanism underlying the various aspects of executive function. Candidate mechanisms include general intelligence,[9] working memory,[10] processing speed,[11] and behavioral inhibition.[12] However, the observation that various facets of executive function can be affected independently in patients with diseases involving different brain regions suggests that executive function is not a unitary phenomenon.[13] Indeed, studies demonstrating relatively low correlation in performance across various executive tasks suggest that executive function is composed of related, but separable, components.[14] This dissociability of executive functions underscores the need to test a range of executive skills at the bedside or in the clinic.[15] Although executive functioning can be partitioned in many different ways, we will discuss three essential aspects of executive resources in this article: (1) working memory, (2) planning and organizing, and (3) inhibitory control.

WORKING MEMORY

Definition

Working memory is the system by which information is maintained in an active mental state during the course of processing so that it can be used for other purposes. It is this system that allows us, for instance, to understand a lengthy sentence or to retain a phone number long enough to run to the telephone and dial it. The working memory system is intimately related to various aspects of executive function: information must remain in an active state so that it is accessible for use in higher-order behaviors, such as planning and organizing, decision making, and problem solving. Working memory dysfunction in the patient described in Case 10-1 did indeed interfere with many facets of her daily functioning, such as shopping and managing the household finances.

Baddeley and Hitch proposed an early and influential model of working memory stipulating two distinct limited-capacity buffers for temporarily storing different types of information and a third component to coordinate the buffers.[16] The first buffer, the *phonologic loop*, involves temporary storage of sound-related information (eg, words, digits, and musical elements) and a rehearsal mechanism that maintains information in an active state so it can be used. The second buffer, termed the *visuospatial sketch pad*, is responsible for storage and rehearsal of nonverbal information. The third component of the model is the central executive, thought to orchestrate higher-order operations, such as shifts of attention between the two buffer systems and strategic retrieval of information for appropriate use.

Anatomy of Working Memory

The Baddeley and Hitch working memory system depends on a network of structures with specialized functions. The phonologic loop has been localized to left perisylvian structures, including the left inferior parietal area for storage of verbal information and the dorsal portion of Broca area for rehearsal of material to be maintained in an active state.[4] The visuospatial sketch pad is housed in the right hemisphere, including inferior parietal and prefrontal structures. As described for the phonologic loop, it is thought that anterior-posterior distinctions between storage and rehearsal processes exist within the nonverbal working memory system as well.[4] The central executive is thought to be contained within prefrontal cortex.[17,18] According to an influential hierarchical two-stage model, ventrolateral regions of prefrontal cortex are involved with retrieval and online maintenance of information stored in more posterior cortical areas, while dorsolateral prefrontal structures are involved in more active monitoring and manipulation of those representations.[19]

Assessment of Working Memory

Testing working memory involves tasks that require information to be held in an active state so that it can be manipulated or used in some way. In the digit span task, the patient repeats progressively longer number sequences in the forward or the reverse direction. Although digit span is affected by both age and education, typical adult performance is about seven digits forward with a reverse span that does not differ by more than two digits.[20] Visuospatial working memory can be tested with an analogous pointing span task (an examiner points to a series of circles of increasing number; the patient is asked to point to the items in the same or the reverse order). Typically, pointing span is one to two items shorter than digit span.[20] Other working memory tasks involve spelling *world* forward and backward, reciting the days of the week or the months of the year in reverse order, or subtracting a specified number (usually 3 or 7) serially from 100 (eg, 100, 93, 86, and so on). Patients referred for formal neuropsychological testing may be given the Paced Auditory Serial Addition Test.[21] In this task, single digits are presented at regular intervals and patients are asked to add each digit to the one preceding it and state the sum before hearing the next number.

PLANNING AND ORGANIZING

Definition

In this section, we discuss the ability to plan and organize complex behavior—that is, how individuals carry out multistep tasks, such as making coffee or going grocery shopping. Planning is the ability to identify and organize the many elements required to achieve a goal. Planning is often needed to help optimize the execution of complex tasks. Patients with impaired planning may exhibit difficulty developing a flexible plan appropriate to the circumstances, initiating the plan, carrying out a series of steps in the correct order, maximizing efficiency and time management, adjusting the plan in real time, and completing the series of actions.[22] Studies of patients with executive dysfunction resulting from Alzheimer disease and frontotemporal degeneration (FTD) have shown difficulty understanding the organization of steps in familiar activities, such as making coffee.[23] In daily life, impairment of planning and organizing can compromise the ability to multitask, resulting in difficulties at home and at work. Difficulty organizing complex activities also can interfere with social interactions that require the appreciation of subtle cues in a continually changing and highly interactive environment. With more severe deficits, everyday behavior breaks down with devastating consequences for the ability to live independently. Even the simplest of routine actions, such as brushing one's teeth or making a sandwich, can be impossible without prompting from others.

Like other daily activities, aspects of language can be conceptualized as complex multistep tasks that require planning and organizing. Words and phrases must be organized into sentences and story events into coherent narratives.[22] Nonaphasic patients with executive dysfunction related to Parkinson disease and FTD show impaired production and comprehension of grammatically complex sentences.[24,25] Moreover, nonaphasic patients with FTD and traumatic brain injury have difficulty with narrative functions, such as telling an organized, coherent tale or comprehending the gist of a story, related to their executive limitations.[26,27] The manifestation of executive dysfunction in language interferes with patients' ability to interact with others, compromising independence and quality of life.

Planning and organizing also play a crucial role in social interactions. The ability to perceive subtle, nuanced behavior in a social interaction and modify one's behavior accordingly is termed *theory of mind*.[28] Theory of mind involves the ability to switch perspectives to optimize participation in social exchanges. The ability to engage in theory of mind is extraordinarily demanding, yet we take it for granted. Theory of mind is frequently compromised in diseases affecting the frontal lobes, such as FTD[29] and traumatic brain injury.[30]

Models of planning and organizing generally fall into two categories. Some authors argue that complex, multistep actions are processed in a linear-sequential manner. In this case, events within a script are accessed sequentially, according to established knowledge of the order in which they occur.[31] An alternate model stipulates that complex actions consist of clusters of associated events that are arranged hierarchically in order to achieve an outcome or goal.[32,33] For instance, in a multistep activity such as fishing, groups of highly associated actions (eg, open can of worms and place worm on hook) are combined with other event groups (eg, raise the pole and reel in the line) to accomplish the task. The advantage of clustered hierarchical models is adaptability; that is, subroutines within a multistep task can be managed in a flexible manner in response to external circumstances while the overall goal is maintained.

Anatomy of Planning and Organizing

As suggested by Case 10-2, substantial evidence associates the dorsolateral region of the frontal lobes with planning and organizing of complex actions needed to complete a task. Patients with frontal lobe injury observed during everyday activities, such as shopping, have shown impaired plan execution and goal achievement.[34] Lesion studies also have demonstrated an association between particular aspects of multitasking, such as task switching and planning, and damage to prefrontal cortex, including the left polar and right dorsolateral regions.[35,36] Patients with focal neurodegenerative syndromes, such as behavioral variant FTD, show impaired performance on measures of executive control that require planning and organization.[37] Moreover, prefrontal atrophy as measured by structural MRI has been related to difficulty producing coherent narratives and comprehending the organization of task events in patients with FTD[23,27] and focal prefrontal injury.[38]

Functional neuroimaging studies in healthy individuals also implicate the prefrontal cortex in executive tasks requiring planning.[39] Prefrontal cortex activation also has been demonstrated in healthy subjects asked to process the order of events in multistep tasks, such as eating at a restaurant.[40] Moreover, transcranial direct cortical stimulation to the left dorsolateral prefrontal cortex has been shown to improve planning ability, implicating this region in this aspect of executive function.[41] fMRI also has suggested that regions of the frontal lobe, arrayed anatomically in a caudal-rostral fashion, process increasingly complex materials involving decisions based on higher levels of abstraction.[42]

Assessment of Planning and Organizing

In the clinic, planning and organizing can be evaluated as patients carry out a number of tasks. Verbal fluency tasks require patients to list exemplars of a designated category in a fixed period of time (eg, animals or words beginning with the letter *F* in 60 seconds). During this task, one can assess the patient's ability to search the mental lexicon for information in an organized and efficient manner. Impairment in planning and organizing can manifest itself in a disorganized approach to copying a complex design, such as the Rey-Osterrieth figure.[43] The Tower of London task is a classic test of planning and organizing administered during formal neuropsychological evaluations and commonly used in research.[44] In this task, subjects are asked to move colored pieces to achieve an illustrated arrangement in as few moves as possible. The frequent observation that patients exhibit difficulty in everyday functioning out of proportion to their performance on common executive assessments in the office has inspired efforts to utilize more realistic tasks.[15] The Naturalistic Action Task evaluates patients' ability to carry out daily activities (eg, making coffee) using a structured assessment of their actual performance of the task.[45]

INHIBITORY CONTROL AND COGNITIVE FLEXIBILITY

Definition

Here we discuss the crucial ability to inhibit inappropriate responses and to shift responses when necessary. This type of cognitive flexibility prevents one from replaying a certain behavior repeatedly. Failure to inhibit can lead to perseverative and stimulus-bound behavior. As illustrated in Case 10-3, patients may involuntarily repeat what another person says (echolalia) or imitate another person's actions (echopraxia). Patients may fixate on objects in the environment despite attempts to redirect their attention. They may feel compelled to pick up and use an object even if it is unnecessary or redundant (utilization behavior). It is not uncommon for a patient with utilization behavior to pick up a pen on the desk and start writing or take the eyeglasses out of the examiner's pocket and put them on.

Friedman and Miyake propose three aspects of inhibition: (1) suppression of automatic responses, (2) resistance to irrelevant information that can distract from the task at hand, and (3) prevention of the intrusion of previously relevant information into ongoing behavior.[46] These aspects of inhibition can be applied to control of behavioral responses in both the motor and cognitive domains.[47]

Logan and colleagues propose a "race model," whereby the behavior observed is the response—*go* or *no-go*—that reaches a certain threshold first.[48] Consider the antisaccade test. In this task, the contest takes place between looking at the target (the more automatic response) and looking away from the target (the less automatic, volitional response). Correctly performed antisaccades result when the volitional response "wins" and is able to inhibit the more reflexive action.[47] Moreover, control of behavior involves the ability to "shift set" in response to changing circumstances. In a given task, a cognitive set is established when an individual's behavior is rewarded for being correct, and it ultimately becomes relatively automatic. When circumstances change, an individual must switch set by inhibiting the previously appropriate, more automatic behavior and adopting a new response.[47] An important role of executive control mechanisms is to avoid perseveration by biasing the competition between automatic behaviors and strategic, adaptive responses via shifts of attention, incorporation of feedback, and maintenance of the goal in working memory.[47,49]

Anatomy of Inhibitory Control

Motor response inhibition is thought to be mediated by areas of prefrontal cortex functioning in concert with more posterior cortical and basal ganglia regions.[47] fMRI studies have further shown activation in a distributed frontoparietal network during motor response inhibition tasks.[3,50] In a study by Ford and colleagues, subjects were instructed whether to produce an antisaccade in anticipation of stimulus presentation.[50] The authors noted increased dorsolateral prefrontal cortex activation during this preparatory period for planning trials with correct antisaccades relative to those with errors, consistent with the notion of a frontally generated inhibitory signal that biases the system toward the desired response.[49,50] When motor response inhibition tasks focus on the period of response execution (rather than the preparatory phase), however, studies emphasize the role of right ventrolateral prefrontal cortex in the act of inhibition per se.[51,52] Connections between prefrontal areas and basal ganglia structures, such as the striatum and the subthalamic nucleus, also have been implicated in performance on motor response inhibition tasks.[53,54] Like motor response inhibition, cognitive set shifting is subserved by a network of frontal, parietal, and basal ganglia structures.[3,47] Studies intended to isolate the process of response inhibition during set-shifting tasks have implicated the ventrolateral prefrontal and orbito-frontal cortex.[51,55]

Assessment of Inhibition, Set-Shifting, and Cognitive Flexibility

A commonly used test of response inhibition is the go-no-go paradigm.[56] In this task, the examiner instructs the patient to lift a finger when the examiner taps once, but not to respond when the examiner taps twice, assessing the ability to inhibit response to a no-go stimulus. The antisaccade test is similar in principle. Trail-making tasks evaluate set-shifting and response inhibition.[57] Patients are asked to alternate between letters and numbers in a sequential manner (eg, 1-A-2-B-3-C…), which can be performed orally or by asking the patient to draw a line connecting letters and numbers in the appropriate order. In the Luria alternating hand sequence task, patients are shown a sequence of three hand movements and are asked to repeat the sequence multiple times.[58] A similar task involves drawing an alternating sequence of square and triangular shapes.

The Stroop task is used frequently in research and in neuropsychological evaluations to assess response inhibition.[59] In the interference part of this task, subjects see color words written in a discordant color (eg, the word *blue* written in red ink). They are asked to report the color of the font and inhibit the more automatic response of reading the word itself. The Wisconsin Card Sorting Task is employed in similar settings to assess cognitive flexibility, use of feedback, and response inhibition.[60] Individuals are asked to sort cards according to various parameters (color, form, or number). They must deduce the sorting rule based on simple feedback they receive (ie, correct or incorrect). Throughout the task, the sorting rule changes without warning after a sorting principle has been deduced, and subjects must inhibit the old sorting rule and ascertain the new rule.

CONDITIONS INTERFERING WITH EXECUTIVE FUNCTION

As described above, working memory and other executive resources are involved in an enormous range of cognitive processes and behaviors. Given the ubiquitous nature of executive resources, impairment of this kind can be disabling to a wide range of patients encountered by the medical profession. Executive function is particularly susceptible to conditions marked by frontal lobe injury or dysfunction in frontal-parietal and frontal-striatal networks. Perhaps the most common neurologic disorders associated with executive dysfunction are traumatic brain injury; neurodegenerative conditions such as Alzheimer disease, dementia with Lewy bodies, and progressive supranuclear palsy; and conditions that cause hydrocephalus. Table 10-1 summarizes conditions commonly associated with executive dysfunction.

CONCLUSION

We discussed three crucial aspects of executive function: (1) working memory, (2) planning and organizing, and (3) inhibitory control. Although all are clearly associated with prefrontal cortex, components of executive function involve partially overlapping networks of prefrontal, parietal, and basal ganglia structures. Intact executive resources allow us to formulate goals, plan our behavior, and respond in flexible, adaptive ways to contingencies as they arise. As such, executive impairment can have enormous impact on patient independence and quality of life. The need remains for pharmacologic treatments and behavioral strategies for patients with executive dysfunction. Greater understanding of component executive functions and their neural substrates can help guide development of therapeutic interventions.

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KEY POINT

- Executive resources allow for flexible, adaptive, goal-directed behavioral responses to environmental circumstances.
- Executive functions are attributed to the frontal lobes, but growing evidence demonstrates that frontal structures are part of larger cortical-cortical and cortical-subcortical networks that subserve executive functioning.
- Various facets of executive function can be affected independently in patients with diseases affecting different brain regions, suggesting that executive functioning is not a unitary phenomenon. This dissociability of executive functions underscores the need to test a range of executive skills at the bedside or in the clinic.
- Working memory is the system by which information is maintained in an active mental state during the course of processing so that it can be used for other purposes.
- Planning is the ability to identify and organize the many elements required to achieve a goal. Planning is often needed to help optimize the execution of complex tasks.
- Inhibitory control involves the crucial ability to inhibit inappropriate responses and to shift responses when necessary.

Case 10-1

A 75-year-old right-handed woman presented in the outpatient neurology clinic with confusion and forgetfulness. About 4 years earlier, the patient's husband had noted that she was increasingly frustrated. At first he attributed her mood swings to depression and his daily presence at home since his retirement, but she denied these concerns. Over time, she had progressive difficulty managing daily household activities, such as shopping and paying the bills. Her husband took over the household finances after several checks bounced. More recently, she seemed confused when grocery shopping, walking up and down the same aisle, putting items in the cart, and then removing them when she realized she had already obtained a similar item. In conversation, she had intermittent word-finding difficulty and at times lost track of what she had intended to say.

On examination, she was alert and fully oriented. She was mildly distractible but could be easily redirected. On a six-item word-learning task, she had difficulty registering the words, and she recalled only one word after a delay. Her digit span was six forward and two in reverse. When asked to list words beginning with *F* in 1 minute, she named five unique words with multiple repetitions. Language and visuoperceptual/visuospatial functioning were within normal limits for age. The neurologic examination otherwise revealed mildly masked facies and stooped posture.

Over the next year, the patient's husband assumed increasing responsibility for the household. Her inattentiveness worsened, her gait became increasingly characterized as shuffling, and she had several falls. Recently, she admitted to seeing her grandchildren (who live in another city) and small animals in her house, particularly at night.

Comment. This patient has dementia with Lewy bodies. In this condition, patients present with cognitive difficulty preceding or within 1 year of the onset of parkinsonian features. Executive limitations, such as poor working memory and inattention, are common early manifestations of cognitive impairment in dementia with Lewy bodies. Other features of this condition, such as worsening gait dysfunction and well-formed hallucinations, typically emerge over the course of the disease.

Case 10-2

A 45-year-old right-handed lawyer was noted by his colleagues to have worsening performance at work. His long-time administrative assistant had assumed increasing responsibility for managing his office. The patient knew he had to call clients and gather information from others for active cases but seemed unable to complete the necessary steps. His assistant made phone calls on his behalf to obtain the information and increasingly assembled case materials for him. Once an avid tennis player, he was less apt to organize matches with his colleagues. Others were concerned that he was “burnt out” or depressed because of his many obligations and responsibilities, but he denied these. Instead, he described enjoying his legal practice but feeling overwhelmed by its rapid pace. Several months later, he had a generalized tonic-clonic seizure at work and was taken by ambulance to the hospital. Head CT in the emergency department revealed a space-occupying mass in the right dorsolateral frontal lobe. Subsequent evaluation was consistent with metastatic melanoma.

Comment. In this case, a tumor in the dorsolateral prefrontal cortex resulted in impaired ability to initiate goal-directed behavior and to plan and organize daily activities. Patients with this type of executive disorder often report feeling overwhelmed at work, as any given task requires substantially more time to complete. Their job performance suffers because of difficulty initiating, organizing, and completing tasks as they arise.

Case 10-3

An 85-year-old right-handed woman was brought to the outpatient neurology clinic by her daughter because of increasing forgetfulness and difficulty with daily activities. Although her home had always been scrupulously clean, unwashed dishes were now piled in the kitchen sink and on the countertops. This change occurred in the context of a 3-year history of increasing memory problems, particularly for recent events. Her daughter said that when she asked the patient a question, she would often repeat the question without answering it.

On examination, the patient echoed the examiner's questions. She demonstrated profound episodic memory difficulty. When asked to name pictures of objects, she got stuck on the name of the first object and repeated it for all subsequent items. When asked to list words beginning with *F*, she provided two words and then repeated the third word over and over. When asked to copy a geometric design, she could not prevent herself from tracing the model. During the motor examination, she seemed to mirror the activities of the examiner.

Comment. The tendency to get stuck on a particular behavior is called perseveration. Perseveration can occur in multiple domains, including repetition of speech (echolalia) and mimicking the gestures of others (echopraxia). Perseverative behavior may be seen with focal disease in ventrolateral prefrontal or orbitofrontal regions, as in traumatic brain injury. Perseverative behavior also occurs in various neurodegenerative conditions as disease affects frontal structures and other areas of the cerebrum. This patient's prominent memory impairment and gradual decline suggest a diagnosis of Alzheimer disease.

TABLE 10-1

Conditions Associated With Executive Dysfunction

► **Structural**
Stroke/vascular dementia
Intracranial hemorrhage (eg, intraparenchymal hemorrhage, subdural hematoma)
Tumor
Normal pressure hydrocephalus
Traumatic brain injury
Multiple sclerosis
Leukodystrophies (eg, adrenoleukodystrophy, metachromatic leukodystrophy, Alexander disease)
Other autoimmune conditions (eg, lupus, CNS vasculitis)
Radiation vasculopathy
► **Neurodegenerative**
Frontotemporal degeneration
Alzheimer disease
Huntington disease
Parkinson disease
Dementia with Lewy bodies
Progressive supranuclear palsy
Corticobasal degeneration
Multiple system atrophy
Motor neuron disease (eg, ALS)
Creutzfeldt-Jakob disease
► **Infectious**
HIV/AIDS dementia complex
Neurosyphilis
Lyme disease
Meningitis
► **Infectious**
Viral encephalitis (including herpes simplex virus encephalitis)
Delirium secondary to systemic infection (eg, urinary tract infection)
► **Toxic-Metabolic**
Hyperglycemia/hypoglycemia
Hypercalcemia/hypocalcemia
Hypernatremia/hyponatremia
Hypercapnia
Hypoxemia
Uremia
Hyperammonemia/hepatic encephalopathy
Hyperthyroidism/hypothyroidism
B_{12} deficiency
Wilson disease

- Lead poisoning
- Medications
- Alcohol
- Illicit/recreational drugs (eg, marijuana, 3,4-methylene-dioxymethamphetamine [ecstasy], phencyclidine, opiates, chronic cocaine and methamphetamine use)
- Withdrawal/delirium tremens

► **Developmental**

- Autism/Asperger syndrome
- Attention deficit hyperactivity disorder
- Mental retardation/developmental delay

► **Psychiatric**

- Depression
- Anxiety and panic disorders
- Schizophrenia
- Bipolar disorder