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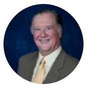

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Cognitive Rehabilitation Interventions for Executive Function: Moving from Bench to Bedside in Patients with Traumatic Brain Injury

Keith Cicerone[1], Harvey Levin[2], James Malec[3], Donald Stuss[4], and John Whyte[5]

Abstract

■ Executive function mediated by prefrontally driven distributed networks is frequently impaired by traumatic brain injury (TBI) as a result of diffuse axonal injury and focal lesions. In addition to executive cognitive functions such as planning and working memory, the effects of TBI impact social cognition and motivation processes. To encourage application of cognitive neuroscience methods to studying recovery from TBI, associated reorganization of function, and development of interventions, this article reviews the pathophysiology of TBI, critiques currently employed methods of assessing executive function, and evaluates promising interventions that reflect advances in cognitive neuroscience. Brain imaging to identify neural mechanisms mediating executive dysfunction and response to interventions following TBI is also discussed. ■

INTRODUCTION

The National Institute of Neurological Disorders and Stroke (NINDS) is encouraging a shift in research objectives from diagnosis and descriptive analysis of neuropsychological assessment of the cognitive impairments in traumatic brain injury (TBI) to the development of evidence-based interventions in the evaluation and treatment of patients with TBI. To further that goal, an NINDS workshop highlighted a limited set of neurological conditions in which progress in the rehabilitation of higher thought processes would benefit from formal partnerships between basic cognitive neuroscientists and clinicians in assessing residual capacity within specified lesioned circuits and potential for functional return. In this article, the TBI cognitive rehabilitation working group provide a comprehensive analysis of the pathophysiology of TBI, the resulting executive function (EF) deficits in adults, the current methods used to assess these impairments, and promising strategies for enhancing both the quality of research and cognitive remediation.

PATHOPHYSIOLOGY OF TBI IN RELATION TO EF

The prefrontal areas and frontal systems are particularly vulnerable to TBI, which produces primary brain damage of two broad types: diffuse axonal injury (DAI) and focal cortical contusions (FCCs). DAI is a microscopic shearing injury of axons and small blood vessels that occurs throughout the brain but disproportionately involves the deep frontal white matter (Povlishock, 1993). DAI may also involve subcortical structures with critical frontal projections, such as the ventral tegmental area of the midbrain (Adair, Williamson, Schwartz, & Heilman, 1996) and the anterior or medial thalamus. Prefrontal, but not extrafrontal hypometabolism, measured by resting positron emission tomography (PET) correlated with executive, behavioral, and memory dysfunction in TBI patients with DAI (Fontaine, Azouvi, Remy, Bussel, & Samson, 1999).

FCCs are caused either by a direct blow to the skull transmitted to the brain or by powerful acceleratory/deceleratory inertial forces causing the brain to be abraded by adjacent skull (primarily the ridges and confines of the anterior fossa and middle fossa). These contusions are primarily confined to the basal frontal and anterobasal temporal regions (Gentry, Godersky, & Thompson, 1988). Dorsolateral prefrontal cortex (DLPFC) FCCs are less common, but the functions associated with this region may be compromised by disconnection effects secondary to DAI. That is, secondary damage to frontal systems after focal injury may result from (a) delayed neuronal injury (as occurs after diffuse injury) including the effects of excitoxicity and inflammation, (b) herniation syndromes (especially frontal transfalcine herniation that may compromise medial frontal lobes and anterior cerebral artery perfusion) and (c) hypoxic–ischemic injury.

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The effects of TBI on EF are dynamic in the sense that these abilities are impaired immediately after injury and recover at a variable rate depending on severity of focal and diffuse effects. Traditionally, the initial period of recovery following the resumption of consciousness has been referred to as posttraumatic amnesia (PTA) because of an obvious absence of the capacity to form new memories. However, many other cognitive processes including EF are also initially disrupted by TBI (Stuss, Binns, et al., 1999).

EXECUTIVE FUNCTION: BACKGROUND AND DEFINITION

Terms such as EF, the dysexecutive syndrome, the supervisory system, and frontal lobe functions are challenging to define and measure. The following schema divides what has been loosely termed "executive functions" into four more clearly defined and circumscribed domains that follow anatomy and evolutionary development: (1) executive cognitive functions, (2) behavioral self-regulatory functions, (3) activation regulating functions, and (4) metacognitive processes (Stuss, in press).

Executive Cognitive Functions

Evolutionary theory of cortical architectonics proposes two major functional/anatomical dissociations within the frontal lobes (Pandya & Yeterian, 1996). The DLPFC is part of the hippocampal archicortical trend and is involved in spatial and conceptual reasoning processes. Much of what is known about EF is based on patients with DLPFC lesions (Milner, 1963). However, it is also important to recognize that because of the interconnectivity between the lateral frontal and posterior regions, diffuse pathology such as axonal injury can also cause dysfunction in executive cognitive functions.

Executive cognitive functions are involved in the control and direction (planning, monitoring, activating, switching, inhibiting) of lower level, more modular, or automatic functions. Working memory, a limited capacity process for the short-term storage, monitoring, and manipulation of information (Baddeley, 1992) and inhibition (Bjorklund & Harnishfeger, 1990) are fundamental, age-related processes that mediate EF (Miller & Cohen, 2001).

Behavioral Self-regulatory Functions

The ventral (medial) frontal region is part of the paleocortical trend emerging from the caudal orbitofrontal (olfactory) cortex, closely connected with limbic nuclei involved in *emotional* processing (Nauta, 1971), including the acquisition and reversal of stimulus–reward associations (Rolls, 2000). The ventral prefrontal cortex (VPFC) is involved in reward processing, including *behavioral self-regulation* in situations where cognitive analysis, habit, or environmental cues are not sufficient to determine the most adaptive response (Eslinger & Damasio, 1985).

Activation Regulating Functions

Activation plays a key role in self-regulation by providing initiative and energizing behavior at a level appropriate to the situation and to attaining the individual's goals. More limited medial pathology results in disorders of activation and drive, clinically known as apathy or abulia.

Metacognitive Processes

The frontal poles (possibly more particularly on the right) are most recently evolved and appear to bridge self-regulatory and executive cognitive functions because of their unique position to integrate executive cognitive functions and emotional or drive-related inputs. The frontal poles are involved in metacognitive aspects of human nature: personality, social cognition, autonoetic consciousness, and self-awareness as reflected by the accuracy of evaluating one's own abilities and behavior in relation to objective performance and reports by others.

In summary, we emphasize four domains of EFs for several reasons: (a) The term executive function has historically referred specifically to cognitive abilities such as planning, switching, and monitoring that are related to the DLPFC, and for the sake of operational clarity should be retained as such. (b) Other important behavioral processes, which have been relatively ignored and lumped within the general term as "executive," depend on systems that are anatomically proximal to the DLPFC. (c) Our proposed distinctions do relate to different anatomical regions and systems with distinct behavioral associations. (d) Most importantly, such anatomical/behavioral definitions are essential in understanding the sequelae of TBI and the development of effective rehabilitation.

ASSESSMENT OF EXECUTIVE FUNCTION

Objectives of Assessment

The objective for assessment of function after TBI is to isolate deficient processes to guide rehabilitation. The most commonly used assessment methods in both research and clinical practice (i.e., Trail Making Test, Stroop, Wisconsin Card Sorting Test [WCST]) were developed to differentiate populations with and without gross cerebral pathology and do not reflect the contemporary cognitive neuroscience perspective of brain/behavioral systems. Whereas many of these assessment measures are sensitive to damage in the DLPFC system, their specificity is low. Promising experimental measures of behavioral self-regulatory and metacognitive processes are in development in various laboratories but are not yet widely used.

Levels of Analysis in Assessment

Rehabilitation research distinguishes the impairment level (e.g., planning deficit measured by a test) from the activity or participation level, which in the present context refers to performing a task in everyday activities that involves EF more generally defined (e.g., planning a meeting). Participation also refers to categories of involvement in society (e.g., having a job, friends, and other important relationships). These different levels of analysis are interrelated in complex ways (Whyte, 1997). Elemental cognitive processes or operations may be combined in the operation of an EF system (impairment level), but real-world tasks (activity level) invariably require the coordinated operation of multiple sensory, cognitive, and motor systems, even when the task is thought of as tapping executive skills. Multiple tasks and activities combine to determine the overall level of participation in addition to the contribution by an executive deficit.

The following sections on assessment of adults with TBI are divided according to the four anatomical/behavioral distinctions described above. Sections on intervention follow the discussion of assessment. EF in children after TBI has been reviewed recently (Levin & Hanten, 2005).

ASSESSMENT OF EXECUTIVE FUNCTION

All measures reviewed in this article have also been demonstrated to be sensitive to impairment to a greater or lesser degree after at least moderate to severe TBI. Although the right and left dorsolateral frontal areas function in parallel in some ways and asymmetrically in others, lateralized distinctions are not as relevant to the diffuse effects of TBI.

Executive Cognitive Functions

The following measures are most frequently used as executive tests: WCST, Trail Making Test Part B, and specific measures within verbal fluency tasks. They have been shown to be related to focal DLPFC lesions (but not generally to orbitofrontal/ventral medial pathology) provided that other processes that could affect performance are covaried.

Strategic aspects of encoding and retrieval in word list learning tests and working memory are other examples of executive cognitive functions. In memory assessment, one should distinguish between basic associative processes of cue–engram interaction (mediated by medial temporal lobe/hippocampal structures) and strategic processes related to the encoding and retrieval of these associations (mediated by the DLPFC primarily). Memory deficit after TBI can be secondary to impairment of both associative and strategic processes that can be differentiated by tasks such as the California Verbal Learning Test (CVLT) through serial position learning, semantic organization, interference effects, cued recall, recognition, monitoring, and response bias. The role of the frontal lobes in working memory is in the manipulation and control of information held online. The latest updates of the Wechsler instruments have added new tasks stressing manipulation and control, and allow for a separate "working memory" composite score. Executive processing in acquiring visuospatial information is less well understood, and, consequently, there is a paucity of measures that examine learning strategies and working memory manipulation of visuospatial stimuli.

Another set of cognitive processes falling within the broad rubric of executive cognitive functions are mechanisms of attention/intention, such as sustained attention, inhibition of irrelevant information (distractibility), monitoring of information, and variability in reaction time (RT) performance. Different tests of attention assess inhibition and monitoring, using errors and RT as dependent measurements. The right frontal region is important for performance on Continuous Performance Tests, especially when the target complexity is increased (i.e., respond to "O" following "X"; Pardo, Fox, & Raichle, 1991), and the task is slowed. The Sustained Attention to Response Task (SART; Robertson, Manly, Andrade, Baddeley, & Yiend, 1997) and the Elevator Counting Test (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1991) are modern tests of sustained attention. A key impairment found after focal frontal pathology, and following TBI, is increased variability of performance both within a testing session and across sessions (Stuss, Murphy, Binns, & Alexander, 2003). This fluctuation in top-down control is most visible in more complex tasks, including those involving RT and memory tasks.

To bridge the gap between laboratory tasks of executive cognitive functions and functional outcome measures of everyday activities, investigators have studied naturalistic actions under controlled conditions. Based on a hypothesized disturbance of supervisory attention associated with reduced planning, working memory, and resistance to interference, Schwartz et al. (1998) designed the Multi-Level Action Test (MLAT) to assess everyday, sequential activities such as packing lunch in a lunchbox. These investigators tested 30 TBI patients undergoing rehabilitation under four conditions in which the presence of distractors was orthogonal to the addition of a second, concurrent action that increased the demand on working memory. Although the patients had a higher rate of errors than uninjured subjects, the TBI group was not more susceptible to interference by distractors or the addition of a concurrent task. Although performance by the TBI patients was not related to the presence of frontal lesions, it was moderately correlated with a measure of functional outcome. This naturalistic approach was also evident in a study of planning activities in which the representation of various actions or "script" was assessed by a card sorting technique that evaluated the patient's sequencing of steps and by a spontaneous generation task in which the patient explained the steps necessary to plan, initiate, and complete each activity (Cazalis, Azouvi, Sirigu, Agar, & Burnod, 2001). In both tasks, 12 patients with severe TBI who were at least 6 months postinjury had slower performance than uninjured subjects. On the card sorting task, the TBI patients (but not controls) had intrusions of a given action from one script to another but they were not more susceptible to intrusions and the degree of impairment did not differ for routine (e.g., preparing to go to work in the morning) versus nonroutine (e.g., taking a trip to Mexico) or novel (e.g., opening a beauty salon) scripts. Performance summed across both of the script tasks was correlated with a measure of dysexecutive functioning in everyday activities (Baddeley, Della Sala, Papagno, & Spinnler, 1997). These studies suggest that naturalistic tasks can reveal executive cognitive deficits in patients at least 6 months after TBI. It is unclear whether naturalistic measures increment the information obtained from laboratory tasks and are useful in evaluating the effects of cognitive rehabilitation.

Behavioral Self-regulatory Functions

Patients with damage to the inferior medial frontal cortex have difficulty in understanding the emotional consequences of their behavior despite intact performance on commonly used neuropsychological tests of executive cognitive functioning, and performing normally in structured situations (Eslinger & Damasio, 1985). Assessment of these behavioral self-regulatory functions tends to be more experimental in nature and includes gambling tasks and naturalistic multiple subgoal tasks.

Because of the role of the VPFC in emotional processing (basic drives and rewards that inform and direct high-level decision making), tests assessing the acquisition and reversal of stimulus–reward associations can be used (Rolls, 2000). Reversal learning is dissociable from the impairment in attentional (extradimensional) set shifting found after DLPFC lesions (Dias, Robbins, & Roberts, 1996), reinforcing the distinction between executive attentional and affective/emotional behavioral measures. The Behavioral Dyscontrol Scale (Grigsby, Kaye, Baxter, Shetterly, & Hamman, 1998) has also been shown to be sensitive in cases of TBI (Leahy, Suchy, Sweet, & Lam, 2003).

Activation Regulating Functions

Damage to left or right medial (anterior cingulate and superior) frontal regions results in poor capacity to generate and maintain actions or mental processes. Patients with damage in this region are slow in more demanding RT tasks, deficient in generating lists of words (particularly in the first 15 sec), and have problems maintaining a selected target such as in the Stroop interference test. Patients with DLPFC lesions are often impaired on the same tasks. For EF tasks, superior medial frontal regions appear "upstream" from the DLPFC, providing activation and drive to organize and sustain action without necessarily providing the content of action. Measures most frequently used to assay activation and drive are verbal fluency tasks and the Stroop test. These tasks lack specificity, as they are also sensitive to impairment in nonexecutive cognitive functions.

Metacognitive Processes

The frontal polar region has been related to theory of mind and self-awareness, humor appreciation, and episodic (autonoetic or self-knowing) memory (Stuss, Gallup, & Alexander, 2001). Self-awareness implies a metacognitive representation of one's own mental states, beliefs, attitudes and experiences. Making inferences about the world and empathizing with others are fundamental to accurate social judgment and appropriate social behavior.

The neuropsychological assessments in this domain include reactions to verbal and cartoon humor, visual perspective-taking tasks, and comparison of performance on remember–know memory tasks. It is important to recognize that for some individuals these tasks can be solved on the basis of factual knowledge, not inference. Family reports often precisely describe the changes in behavior that have occurred such as lack of empathy, unconcern, and inability to appreciate humor that requires self-reflection.

Summary

Currently available tests of EF typically lack specificity, even when they are sensitive. The few tasks that appear to differentiate processes more specifically lack appropriate normative data. There is a need to develop new tests that target the aforementioned EF domains, establish their validity, including their relation to daily functioning and participation in complex activities in different populations.

INTERVENTIONS FOR EXECUTIVE FUNCTION IN TBI PATIENTS: CONCEPTUAL ISSUES IN DESIGNING INTERVENTIONS

Level of Analysis

Studies must consider the hypothesized mechanism of treatment because this will bear on the appropriate level of analysis at which to assess treatment impact. Some treatments (e.g., pharmacologic interventions, "direct remediation" treatments) may seek to ameliorate the underlying executive process impairments and impact impairment-level outcome measures. Other interventions, however, may seek to train compensatory strategies for overcoming EF impairments (e.g., cuing or reminding devices). In such instances, one may not hypothesize any meaningful change in the executive processes themselves, but may predict improvement in tasks that were secondarily compromised by the executive impairment.

One option is a program of sequential studies that seeks to trace the impact of treatment into progressively more complex domains. In this approach, one might first study treatment effects only at the level most closely linked with the proposed treatment mechanism, because if the treatment is ineffective even here, it is unlikely to be productive to search for larger and more general effects. A second wave of research can be conducted in which subjects with a few other confounding deficits are studied, with activity level outcomes as the treatment target. Finally, a less highly selected group can be studied, potentially combining several treatments aimed at several coexisting impairments, with an assessment of their combined treatment impact (Whyte, 1997, 2002). Alternatively, one can assess multiple levels of treatment outcome simultaneously from the beginning and examine the interrelationships among treatment responses at multiple levels (Whyte et al., 2004). Which approach to take depends largely on practical considerations such as whether it is more difficult to identify appropriate subjects or more difficult to collect large volumes of data on each subject (Whyte & Hart, 2003).

Experimental Design

Crossover designs may be particularly useful in the chronic phase when spontaneous recovery is slow or absent, assuming that the mechanism of treatment can safely be assumed to be reversible upon discontinuation. Such designs necessitate smaller samples than parallel group designs, but require a lengthier involvement of each subject. Crossover designs are more difficult to use in the acute period because the pace of recovery may change substantially between treatment phases. Within-subject designs are also not feasible for practice-based treatments or compensatory strategy interventions, where subjects are unlikely to "unlearn" the intervention after crossover (Woods, Williams, & Tavel, 1989). Parallel group designs are more appropriate in these contexts but will face the challenge of establishing groups with comparable prognosis, requiring either relatively large sample sizes or careful prognostic stratification. Additional study designs such as multiple baselines across behaviors or multiple baselines across subjects may also be appropriate depending on the hypothesized mechanism of treatment effect.

Pharmacological Treatment

There are no medications that currently meet a practice standard for treatment of executive deficits in TBI or, for that matter, any other cognitive impairment in this population. Because of the rich catecholaminergic innervation of the prefrontal cortex (Camps, Cortes, Gueye, Probst, & Palacios, 1989), medications that modulate these neurochemical systems (particularly dopamine) might have treatment potential for executive deficits. Moreover, dopaminergic interventions modulate working memory and EF in animal models (Robbins & Everitt, 1995), in healthy elderly individuals (Kimberg, D'Esposito, & Farah, 1997), and in individuals with TBI (McDowell, Whyte, & D'Esposito, 1997).

Structural and Functional Imaging

Major advances have been made in recent years in understanding recovery after TBI, using both structural and functional imaging techniques in conjunction with behavioral evaluation. Functional brain imaging, including PET and functional magnetic resonance imaging (fMRI) have begun to elucidate mechanisms mediating individual differences in recovery from injuries of similar severity. Functional imaging studies can also be used to indicate how brain reorganization of neural systems underlies functional recovery (Perlstein, Dixit, Carter, Noll, & Cohen, 2003). These imaging techniques could also be used to assess the impact of rehabilitative efforts. Structural measurements such as ventricular size and regional atrophy can identify pathology in the absence of clear focal damage. Diffusion tensor imaging (DTI), which can detect disruption of white matter connections in diffuse TBI (Huisman et al., 2004), is potentially a useful biomarker for severity of tissue injury.

INTERVENTIONS FOR EF DEFICITS IN ADULTS AFTER TBI: CURRENT PRACTICE AND SCIENCE

Impairments of EF can represent a distinct challenge to the rehabilitation process. In many cases, remedial interventions for acquired cognitive impairments emphasize the acquisition of specific compensations in controlled situations. Responsibility for the selection and application of compensatory strategies may initially rely on the therapist, with the assumption that the patient will be capable of implementing these compensations independently with adequate practice. In contrast, disturbances of EF are most likely to be evident when the patient is required to assume responsibility for the application of compensatory strategies (Shallice & Burgess, 1991) or to cope with novel situations (Godefrey & Rousseaux, 1997). Disturbances of EF often coexist with impaired self-awareness, representing an additional challenge to rehabilitation.

Recognizing the interplay of executive cognitive, behavioral self-regulatory activation, and metacognitive processes, as well as the lack of specific assessment techniques for parsing these processes, clinicians widely endorse global functional assessments and "holistic" rehabilitation. For instance, functional assessment in clinical populations has focused on complexes of behaviors (such as pragmatic communication skills, other social skills, and adaptive behaviors) using self-report or rating scales, such as the Awareness Questionnaire (Sherer, Bergloff, Boake, High, & Levin, 1998), the Patient Competency Rating Form (Prigatano & Altman, 1990), the Neurobehavioral Rating Scale (Levin et al., 1987), and the Mayo-Portland Adaptability Inventory (Malec, 2004). Such assessment has focused on functional behaviors with the premise that these behaviors are the final common pathway for a variety of EF dysfunctions.

In rehabilitation, these behavioral complexes are targets of interventions that are equally general and multimodal. Such holistic rehabilitation efforts are directed at simultaneously addressing the complex of cognitive, metacognitive, behavioral, and emotional dysfunctions that may result from disruption of the proposed anatomic/behavioral systems. Only a small number of studies have examined the efficacy of rehabilitation interventions that target specific aspects of executive functioning.

The review of specific studies of interventions for EF deficits is organized according to our previous distinction among the domains of executive cognitive functions, behavioral and emotional self-regulatory functions, activation self-regulatory functions, and metacognitive processes. Although these distinctions may correspond to specific anatomic substrates, these anatomic–behavioral relationships have typically not been specified in the rehabilitation literature.

Interventions for Problem-solving Deficits

Three prospective, randomized controlled trials of interventions directed at problem-solving deficits have been conducted. Von Cramon, Matthes-Von Cramon, and Mai (1991) trained patients to reduce the complexity of a multistage problem by breaking it down into manageable subgoals. Training was provided to 37 subjects (including some subjects with cerebral insult other than TBI), who were identified as poor problem solvers on formal tests of planning and response regulation. Twenty participants received an intervention directed at remediation of EF deficits, whereas 17 participants received an alternative intervention consisting of memory retraining. The experimental intervention included training in problem orientation, problem definition and formulation, generation of alternatives, decision making, and solution verification. When compared with memory training, the participants who received the problem-solving training demonstrated significant gains on measures of planning ability and improvement on behavioral ratings of EF, such as awareness of cognitive deficits, goal-directed ideas, and problem-solving.

Levine et al. (2000) developed a formalized, staged intervention for executive dysfunction, referred to as goal-management training (GMT), based on Duncan, Emslie, Williams, Johnson, and Freer's (1996) theory of goal neglect and similar to the algorithm employed by Von Cramon et al. (1991). Training to evaluate the current problem state ("What am I doing?") was followed by specification of the relevant goals (the "main task"), and partitioning of the problem-solving process into subgoals (the "steps"). Participants were then assisted with the learning and retention of goals and subgoals ("Do I know the steps?") and finally taught to self-monitor the results of their actions with the intended goal state ("Am I doing what I planned to do?"), and in the event of a mismatch the entire process was repeated.

The GMT consisted of a single session in which participants were instructed to apply the problem-solving algorithm to two functional tasks (proofreading and room layout) that involved keeping goals in mind, analysis of subgoals, and monitoring outcomes. Patients in the motor skills training condition practiced reading and tracing mirror-reversed text and designs; a trainer provided general instruction and encouragement, but the treatment procedure did not include any processes related to GMT. Treatment effectiveness was assessed on several paper-and-pencil tasks that resembled the training tasks and were intended to simulate the kind of unstructured everyday situations that might elicit goal-management deficits. Participants who received the GMT demonstrated significant reduction in errors and prolonged time to task completion (which was interpreted as an indication of their increased care and attention to the tasks) on two of the three outcome measures. The entire treatment in this study consisted of 1 hr of intervention, which may be adequate to suggest the putative efficacy of GMT but provides little evidence of its clinical effectiveness.

Rath, Simon, Langenbahn, Sherr, and Diller (2003) evaluated the effectiveness of an "innovative" group treatment focused on the treatment of problem-solving deficits ($n = 27$), compared with a "conventional" neuropsychological group treatment ($n = 19$), for patients with TBI. The participants were selected from a large outpatient neuropsychological rehabilitation program as being "higher functioning" but with documented, persistent impairments in social/vocational functioning, an average of 4 years postinjury. Both groups received 2 to 3 hr of small group intervention per week for 24 weeks. The conventional treatment consisted of group exercises intended to improve cognitive skills and support for coping with emotional reactions and changes after injury. The problem-solving intervention focused on the development of emotional self-regulation strategies as the basis for maintaining an effective problem orientation, along with a ''clear thinking'' component that included cognitive-behavioral training in problem-solving skills, a systematic process for analyzing real-life problems, and role-play of real-life examples of problem situations. Both groups showed significant improvement of their memory functioning after treatment. Only the problem-solving group treatment resulted in significant beneficial effects on measures of executive cognitive functioning, self-appraisal of clear thinking and emotional self-regulation, and objective observer ratings of interpersonal problem-solving behaviors in naturalistic simulations. These gains were maintained at 6 months after treatment, but did not translate into significant improvements on a measure of community integration.

Rath et al.'s (2003) inclusion of a treatment component directed specifically at patients' developing improved emotional self-regulation in the context of the cognitive intervention is innovative and particularly relevant to the clinical treatment of patients with EF deficits after TBI. Moreover, the study included behavioral observations of participants' actual interpersonal behaviors in naturalistic situations. Given the lack of an established relationship between psychometric measures of executive cognitive functioning and everyday behaviors, and the well-known potential for dissociation between verbal self-appraisal and actual behavior after frontal lobe damage, the use of real-life behavioral observations to assess treatment outcomes is well advised.

Fox, Martella, and Marchand-Martella (1989) conducted a small observational study of remediation for ''real-life'' problem-solving skills. The treatment consisted of cuing and feedback to develop effective problem solutions, using verbal analogs of problem situations in four general areas of everyday life relevant to community placement and adjustment (e.g., community awareness and transportation, using medications, and responding to emergency situations). Training was provided to three participants with TBI within a residential rehabilitation facility; three subjects within the same facility served as untreated controls. Throughout the course of training, appropriate verbal responses to analogous problem situations showed significant increases. The participants who received the treatment also demonstrated generalization to simulated interactions conducted in the natural environment, whereas the untreated subjects showed essentially unchanged performance. This use of ecologically relevant problems and situational simulations in this area of cognitive remediation appears promising.

Interventions for Working Memory Deficits

Impairments of higher level cognitive functions include difficulties with the effective allocation of attention and the organization of multiple task demands. Impairments in the ''central executive'' component of working memory, identified by poor dual-task performance, have been shown to be related to behavioral indices of executive dysfunction (Baddeley et al., 1997). There is also evidence that interventions derived from, and directed at, the central executive component of working memory can be effective in remediating the subjective and objective attention difficulties in patients with mild TBI (Cicerone, 2002).

One study in post-acute TBI patients based on Baddeley et al.'s (1997) model of the central executive demonstrated a beneficial effect of a single 2.5-mg dose of bromocriptine, a D2 agonist, on efficiency of the central executive but not on the corresponding working memory buffers, in a dual task paradigm (McDowell, Whyte, & D'Esposito, 1998). That is, dual task performance improved without improvement in the two tasks when performed alone.

Interventions for Behavioral and Emotional Regulation

These interventions emphasized the need for patients to anticipate and monitor the outcomes of their behavior. In most cases, the goal of remediation was not the training of task-specific performance, but the training and internalization of regulatory cognitive processes. Several studies have relied on external cuing or environmental restructuring to modify specific behaviors. Lengfelder and Gollwitzer (2001) noted that the automatic control of habitual behavior remains relatively intact after frontal lobe damage. They argued that patients with frontal lobe dysfunction might therefore benefit from linking situational cues to goal-directed behavior through the use of ''implementation intentions'' (e.g., ''if situation *y* arises, I will perform the goal-directed behavior *z*'') that do not require conscious deliberation. Among 34 patients with frontal or nonfrontal brain injuries, implementation intentions were found to improve the efficiency of reactions on a dual task. The effectiveness of the intervention was not related to whether patients had frontal or nonfrontal lesions, but was related to the presence of impaired planning and self-regulation. Manly, Hawkins, Evans, Woldt, and Robertson (2002) developed an intervention that was again based on the Duncan et al. (1996) theory of goal neglect. Ten participants with TBI were required to perform a complex task comprising multiple elements, with or without provision of an external auditory stimulus intended to interrupt their activity and cue them to consider their overall goal. Without the external cues, participants performed more poorly than healthy controls, in large part due to their perseveration on one aspect of the task and failure to allocate sufficient time to the multiple task components. Significant improvement and normalization of task performance was obtained with provision of the external cue, suggesting that environmental cuing could facilitate behavioral regulation during complex task performance. Burke, Zencius, and Weslowski (1991) described the effective use of external compensatory strategies to support patients' performance of relevant functional tasks (e.g., checklists for cuing and monitoring completion of job steps). Alderman, Fry, and Youngson (1995) utilized a program of prompts and rewards to enable a patient to exert control over inappropriate behaviors through increased self-monitoring. This was effective in reducing the frequency of inappropriate behaviors within both the treatment and community environments.

Few studies have explicitly addressed the remediation of impairments in emotional regulation after TBI. Medd and Tate (2000) conducted a prospective controlled trial to examine the effectiveness of a cognitive–behavioral program of anger management for 16 participants with acquired brain injury. Participants in the treatment condition received a stress-inoculation procedure modified to include information relevant to individuals with acquired brain injury. Modifications included training in the relationship between brain injury and subsequent anger management difficulties. Participants in the no-treatment control group monitored their anger for 8 weeks. The participants receiving anger-management training showed a significant decrease in the negative, outward expression of anger, although there was no change in participants' self-reported awareness of problems with emotional control as a result of treatment.

There is evidence to suggest that disturbances of emotional regulation after orbitofrontal injury may be particularly refractory to treatment. Although training under a routinized, external structure has been shown to be effective in changing behaviors specific to the situations in which they had been trained, this improvement was not apparent in novel situations and the patients continued to exhibit disturbances in their emotional and social behavior (Cicerone & Tanenbaum, 1997).

Interventions for Activation

Sohlberg, Sprunk, and Metzelaar (1988) treated a patient with traumatic frontal-lobe damage who exhibited decreased initiation and range of affect. The therapist provided the patient with intermittent external cues (such as placing an index card in front of the subject with an instruction to initiate conversation) that placed little demand on internal self-monitoring, to increase verbal initiation and response acknowledgments. Both behaviors increased during application of the external cuing procedure; the patient's verbal initiation decreased when the external cuing procedure was withdrawn, although the level remained above baseline.

To our knowledge, there have been no other studies, and certainly no randomized control studies, of cognitive remediation related to disturbances of behavioral drive or activation.

One pharmacologic trial evaluated dopamine agonist therapy for deficits in clinical motivation in 11 patients with TBI or subarachnoid hemorrhage (SAH), 2 months to 5 years after injury. Bromocriptine was administered starting at 2.5 mg/day, increased by 2.5 mg/day per week to a maximum of 10 mg/day. Clinical ratings of spontaneity and responsiveness to incentives, but not mood, improved with drug treatment for all patients (Powell, Collin, & Sutton, 1996).

INTERVENTIONS FOR METACOGNITIVE PROCESSES

Planning, Inhibition, and Self-monitoring

Interventions in this area have typically been conceptualized in terms of fostering the internalization of strategies for effective self-monitoring and self-regulation. Cicerone and Wood (1987) used a self-instructional training procedure to treat a patient with traumatic frontal-lobe damage who exhibited executive dysfunction four years post injury. The training procedure included three stages of self-verbalization, progressing from overt verbalization through faded verbal self-instruction to covert verbal mediation of appropriate responses. The three stages of self-instructional training were provided over an 8-week period, followed by 12 weeks of treatment to promote the application of self-regulation strategies in the patient's everyday functioning. Over the initial course of self-instructional training, there was a dramatic reduction in task-related errors as well as more gradual reduction and eventual cessation of off-task behaviors. Generalization to the patient's functional, real-life behaviors was observed only with the additional instruction and practice in the application and self-monitoring of the verbal mediation strategy to his or her everyday behaviors. Cicerone and Giacino (1992) replicated this intervention with six patients, using a multiple-baseline across-subjects design. The participants were all at least 1 year since the onset of their injury or illness, all had evidence of damage to the frontal lobes and were selected for the intervention because they exhibited impaired planning and self-monitoring on the basis of family observations and therapist reports, as well as evidence of impaired performance on at least one of three neuropsychological measures of executive cognitive functioning. Five of the six patients showed marked reduction of task-related errors and perseverative responses, suggesting that the effectiveness of training was related to the patients' improved ability to inhibit inappropriate responses.

Ownsworth, McFarland, and Young (2000) evaluated a group intervention directed at improving participants' self-regulation abilities and self-awareness. Participants receiving the treatment consisted of 21 patients with acquired brain injury (16 with TBI). Sixteen patients had documented frontal lobe damage and all exhibited severe cognitive impairments and poor self-awareness when evaluated an average of 8.6 years after injury. The intervention incorporated elements of problem-solving training, role-plays, and training in compensatory strategies over a 16-week period. Following treatment, participants exhibited reliable clinical improvement on measures reflecting their knowledge and use of self-regulatory strategies and the self-rated effectiveness of strategies in their daily functioning, and these gains were maintained after six months.

The study by Ownsworth et al. (2000) noted that improvements in self-regulatory strategies was associated with increased awareness of deficit and anticipatory awareness of situations wherein the patients might experience difficulty. Two additional studies of patients with TBI suggest that having subjects predict their task performance and providing them with tangible feedback may reduce discrepancies between their predicted and actual performance (Rebmann & Hannon, 1995; Youngjohn & Altman, 1989). In both of these latter studies, the primary effect of the intervention was related to modification of patients' predictions rather than a change in actual task performance, suggesting an impact on their self-monitoring and self-appraisal. However, evidence also suggests that interventions can produce improvements in behavioral functioning without accompanying increases in participants' awareness of deficit (Medd & Tate, 2000).

KEY ISSUES AND QUESTIONS RELATING TO TREATMENT FOR EXECUTIVE DYSFUNCTION IN TBI PATIENTS

There is a need to better specify the patient samples and nature of impairments being addressed. Relevant patient characteristics might include the presence and location of focal cerebral lesions, nature and severity of executive dysfunction, and the presence of comorbid cognitive impairments. There is also a need for continued development of appropriate outcome measures and efforts to ensure that interventions translate into meaningful changes in real-world functioning.

Executive function has assumed too broad a connotation for the adult developed brain. Within this broad term, a more precise classification of the four domains (executive cognitive, behavioral self-regulatory, activation-regulatory, and metacognitive) based on documented anatomical/behavioral distinctions is possible with the recommendation that these domains should be assessed in TBI patients. Pressing questions for future research include the following:

1. Can sensitive and specific measurement techniques be developed that define the impairment of executive cognitive, behavioral self-regulatory, activation-regulatory, and metacognitive processes? How are these behavioral measurements related to functional activities and societal participation?
2. Is rehabilitation that targets impairments in specific EF domains effective in changing both the specified impairments and associated activities and participation?
3. Alternatively, is holistic or multimodal rehabilitation more effective than specifically targeted rehabilitation interventions in improving activities and participation?
4. Is an approach combining the targeted and multimodal approaches the most effective?
5. How can structural and functional brain imaging be used to elucidate the mechanisms mediating changes in EF performance resulting from cognitive rehabilitation? Could imaging techniques be useful in selecting patients who will benefit from specific cognitive and pharmacologic interventions?

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