The devastating impact of type 2 diabetes mellitus (DM) on vascular, renal, retinal, and peripheral nerve functions has been well documented. However, there is also evidence that older adults with this disease exhibit impairments in the planning, coordinating, sequencing, and monitoring of cognitive operations, collectively known as executive function. Although poorly understood, disturbances in executive function, particularly within the dimension of time sharing, may contribute to the gait abnormalities and increased risk for falls, functional impairments, and disabilities associated with type 2 DM. However, the relationships between executive function and functional abilities remain poorly understood in this population. Current neuropsychological research regarding the concept of executive function is presented here as a framework upon which to examine the integrity of this critical cognitive entity in adults with type 2 DM. The pathophysiological mechanisms thought to underlie diabetes-related executive dysfunction are explored, and the possible contributions of executive deficits to impairments in gait and function observed in older people with type 2 DM are summarized. Finally, a brief discussion of dual-task assessment and intervention strategies that may facilitate the care and rehabilitation of the growing population of patients with type 2 DM is provided.
Executive Function and Type 2 Diabetes

The public health threat posed by diabetes is unequivocal. It is currently estimated that 1 of every 10 health care dollars spent in the United States is attributable to this disease, and the incidence of type 2 diabetes mellitus (DM), already among the most common major diseases in older adults, is projected to continue to rise because of an aging population, urbanization, and the increasing prevalence of obesity and physical inactivity. Characterized by the improper utilization of insulin and the resulting dysregulation of blood glucose levels, type 2 DM is associated with an array of debilitating clinical sequelae, including visual loss, renal dysfunction, wound formation, limb amputation, neuropathy, and cardiovascular and cerebrovascular diseases. In addition to these traditional complications, type 2 DM also has been identified as a significant risk factor for falls and disability, as well as for cognitive impairments and dementia.

Although still poorly recognized, the impact of type 2 DM on cognition appears to extend across a broad range of functions. Of particular concern are deficits that have been observed in the set of high-level central processes responsible for planning, coordinating, sequencing, and monitoring cognitive operations. Collectively known as executive function, these cognitive entities have substantial functional implications, as explained by Jurado and Rosselli:

In a constantly changing environment, executive abilities allow us to shift our mind-set quickly and adapt to diverse situations while at the same time inhibiting inappropriate behaviors. They enable us to create a plan, initiate its execution, and persevere at the task at hand until its completion. Executive functions mediate the ability to organize our thoughts in a goal-directed way and are therefore essential for success in school and work situations, as well as everyday living.

Consistent with this explanation, executive dysfunction has been linked to impairments in gait and functional abilities, deficits that are more broadly implicated in falls, the loss of independence and, ultimately, institutionalization and mortality.

Although growing evidence suggests that older adults with type 2 DM have impairments in executive processes, the complexity of both executive function and the diabetic disease process makes interpretation of these deficits and their functional consequences difficult. This situation has important implications for rehabilitation, as physical therapists are ideally positioned to identify and address such impairments before they can result in catastrophic functional loss.

Concept and Processes of Executive Function

Despite extensive neuropsychological study, executive function remains notoriously resistant to formal definition. Effectively first identified by Baddeley and Hitch as the “central executive” responsible for overseeing working memory, executive function has evolved to more broadly describe the set of loosely defined control processes responsible for planning, coordinating, sequencing, and monitoring other cognitive operations. These processes enable the performance of goal-directed and future-oriented behavior; therefore, some authors have placed highly functional cognitive activities ranging from attention and visuospatial function to reasoning and planning under the auspices of executive function.

Traditionally, assessment and interpretation of executive abilities have relied on an assumption that performance on 1 or 2 measures reflects overall executive function. However, the fact that executive function must, by definition, be expressed through nonexecutive processes, such as language, visual processing, and memory, has led some neuropsychologists to caution that “a low score on a single executive test does not necessarily mean inefficient or impaired executive functioning.” Rather, they suggest that executive function may be more accurately described in terms of several related but dissociable processes, the more well studied of which are described below. Table 1 shows how these processes may relate to more complex cognitive activities, neuroanatomical areas, and clinical behaviors. Tables 2 and 3 show examples of measures commonly used to examine these executive processes.

Dividing Attention (“Time Sharing”)

A prime example of executive function, the ability to time share or multitask to perform concurrent activities, is particularly relevant to physical therapy and rehabilitation because of its association with abnormalities in gait, falls, and functional limitations. Therefore, dual-task paradigms are often used to examine executive function in terms of time-sharing ability (Tab. 3), and evidence suggests that dual-task training programs may hold promise for improving gait and balance in older adults.

Updating and Monitoring Information (“Updating”)

Similar to working memory, “updating” refers to the process by which incoming information is monitored and processed for relevance to an active task. In this way, older, irrelevant data within the working memory can be actively manipulated and replaced with newer, more relevant information.
Mental Set and Task Shifting (“Shifting”)  
Also known as cognitive flexibility, “shifting” refers to the transfer of attention back and forth between different tasks or mental sets.27 A common feature of frontal lobe damage, the inability to disengage from an irrelevant task to engage in a more relevant task (eg, perseveration), is commonly interpreted as a deficit in shifting.20

Response Inhibition (“Inhibition”)  
The executive process of “inhibition” refers to the deliberate suppression of an automatic response.20 Inhibition provides an adaptive means by which dependence on habit and familiarity may be overcome, as well as a mechanism by which responses already in preparation may be suppressed.28

Visuospatial Function  
Responsible for perception of the surrounding world in 2- and 3-dimensional spaces, visuospatial abilities encompass the encoding of visual information, maintenance of visual imagery, and manipulation of data within memory. In particular, neuropsychological evidence indicates that visuospatial problems requiring complex, multistep solutions extensively involve executive function.29

Table 1. Executive Processes: Related Cognitive Abilities, Anatomical Structures, and Clinical Behaviors Resulting from Impairments

<table>
<thead>
<tr>
<th>Executive Processes</th>
<th>Cognitive Ability</th>
<th>Anatomical Correlate</th>
<th>Clinical Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time sharing, updating, and sequencing</td>
<td>Planning and reasoning</td>
<td>Dorsolateral prefrontal cortex</td>
<td>Disorganization</td>
</tr>
<tr>
<td>Sequencing, updating, shifting, initiation, time sharing, and visuospatial functions</td>
<td>Organization</td>
<td>Superomedial prefrontal cortex</td>
<td>Apathy</td>
</tr>
<tr>
<td>Updating and inhibition</td>
<td>Judgment</td>
<td>Ventromedial and orbitofrontal cortex</td>
<td>Disinhibition</td>
</tr>
<tr>
<td>Time sharing, shifting, updating, and visuospatial functions</td>
<td>Problem solving</td>
<td>Dorsolateral prefrontal cortex</td>
<td>Perseveration</td>
</tr>
</tbody>
</table>


Table 2. Sample Measures of Executive Processes

<table>
<thead>
<tr>
<th>Executive Process</th>
<th>Sample Measure</th>
<th>Task Description</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Updating</td>
<td>N-Back Test</td>
<td>Participant views a continuous string of letters and identifies those that are the same as the letters viewed 2 trials previously (eg, 2-back).</td>
<td>Hull et al11; see also Kirchner57</td>
</tr>
<tr>
<td></td>
<td>Keep-Track Test</td>
<td>Participant views 10 words from 6 semantic categories (eg, animals, colors) and identifies the last word viewed in each of 2 randomly selected categories.</td>
<td>Miyake et al50; see also Yntema58</td>
</tr>
<tr>
<td>Shifting</td>
<td>Trail-Making Test</td>
<td>Participant connects numbered or lettered circles in order (part A) and alternating between numbers and letters (part B).</td>
<td>Homack et al59</td>
</tr>
<tr>
<td></td>
<td>Local-Global Test</td>
<td>Participant views a series of large figures composed of smaller figures (eg, an “A” made up of small “E’s”) and identifies “local” or “global” features based on the color of the figure.</td>
<td>Miyake et al50; see also Navon60</td>
</tr>
<tr>
<td>Inhibition</td>
<td>Stroop Word Color Test</td>
<td>Participant identifies the color of a series of colored “X’s” (condition 1) and a series of incongruously colored words (eg, the word “blue” printed in green ink; condition 2).</td>
<td>Miyake et al50; see also Stroop61</td>
</tr>
<tr>
<td></td>
<td>Hayling Sentence Completion Test</td>
<td>Participant is asked to provide the last word for 2 sets of 15 simple sentences—one set with a word that logically completes the sentence (set A) and 1 set with a word that is nonsensical in the context of the sentence (set B).</td>
<td>Burgess and Shallice62</td>
</tr>
<tr>
<td>Visuospatial function</td>
<td>Rey-Osterrieth Complex Figure Test</td>
<td>Participant is asked to draw an asymmetrical geometric figure as accurately as possible. Recall after 15–60 min also may be tested.</td>
<td>Lezak et al51; see also Rey and Osterieth64</td>
</tr>
</tbody>
</table>
Executive Function and Type 2 DM

Although there is no clear consensus about the impact of type 2 DM on executive function in older people, there does appear to be cause for concern about this relationship. Impaired performance on a variety of executive tasks has been reported in older adults with type 2 DM, and a significantly increased risk of executive decline has also been observed in longitudinal investigations of type 2 DM and cognition.

Perhaps the strongest evidence of diabetes-related executive dysfunction stems from an analysis by Yeung et al of a multidimensional executive battery administered to 465 older adults, 41 of whom had type 2 DM. Those with diabetes scored approximately 12% and 14% lower than their peers without diabetes on executive measures of inhibition and shifting, respectively. This detrimental effect of diabetes on executive function remained significant even after the sample was divided into young-old (55–70 years) and old-old (71–90 years) groups, suggesting that the impairments were likely mediated by diabetic status rather than by age.

Others also have reported indications of executive dysfunction in older adults with type 2 DM. One group examined the cognitive profiles of 291 homebound people who were more than 60 years of age, finding that those with type 2 DM (n=115) demonstrated significant deficits—approximately 7%, 17%, and 21%—on executive measures of updating or working memory, reasoning, and shifting, respectively.

These findings are broadly consistent with longitudinal data describing small but significant baseline deficits—of up to 10%—on measures of attention (n=55) and shifting (n=682) in older adults with type 2 DM. These people also had nearly a 2-fold increase in the risk of decline on these measures over 4- and 6-year periods, respectively.

However, associations between type 2 DM and executive dysfunction have not been uniformly demonstrated. For example, a sample of 1,917 elderly people (218 with type 2 DM) revealed no significant executive impairments on a composite measure of updating and inhibition tasks. Likewise, Ruis et al noted no impairments on a series of unspecified executive tasks in a sample of 183 older adults with recently diagnosed type 2 DM. These results corroborate literature reviews describing only inconsistent relationships between type 2 DM and executive dysfunction.

Pathophysiological Mechanisms of Executive Dysfunction in Diabetes

Despite this conflicting evidence, physiological data appear to reinforce the likelihood of executive dysfunction in older adults with type 2 DM.
DM, potentially because of neuroanatomical changes resulting from impaired glycemic control, vascular disease, and insulin resistance. Although there is empirical support for each of these mechanisms, the etiological pathways underlying diabetes-related cognitive and executive impairments likely result from a multifactorial process including these and other factors (Figure).6

Neuroanatomical Changes
Among the notable findings of structural abnormalities associated with diabetes are magnetic resonance imaging observations of diffuse brain atrophy and white matter lesions in people with type 2 DM.39,40 In a study of 164 older adults, those with type 2 DM (n=113) exhibited as much as 23% more cortical atrophy, 12% more subcortical atrophy, and significantly more deep white matter lesions and infarcts than those without type 2 DM.39 Interestingly, the investigators also observed small to moderate (effect size=0.2–0.4), statistically significant deficits in attention, processing speed, and memory in these people.39

Role of Glycemic Control
The hallmark feature of diabetes, impaired glycemic control, has long been suspected to contribute to the development of diabetes-related cognitive dysfunction.6 Supporting this notion are studies describing significant inverse relationships between glycated hemoglobin (HbA1c) and measures of working memory ($r=-.37$) and visuospatial function ($r=-.38$).32 Animal models have indicated that hyperglycemia may induce the formation of advanced glycation end products and reactive oxygen species, the activation of polyl and protein kinase C pathways, increased glucose shunting in the hexosamine pathway, and alterations in neurotransmitter function.6 Although these factors may ultimately lead to neuronal damage, it remains unclear which, if any, participate in the development of executive dysfunction in humans with diabetes.

Role of Vascular Disease
Diabetes is known to be associated with a greater risk of cardiovascular and cerebrovascular diseases,3 and it has been suggested that vascular dysfunction may contribute to executive disturbance.6 This notion is consistent with findings that the interaction of diabetes and hypertension is related to cortical brain atrophy40 and may confer as much as a 2-fold increase in the risk of dementia.41 In addition, neuropathic and angiopathic changes have been observed in the cranial nerves and spinal cord of the diabetic nervous system.6 How these abnormalities arise is not clear; however, there is speculation that the combination of reduced cerebral blood flow and activation of the thromboxane A2 receptor may disrupt cerebral vasodilation. The resulting ischemia may be exacerbated by hyperglycemia, providing an environment in which damaging agents such as lactate or glutamate can accumulate and cause neural injury.6

Role of Insulin Resistance
It is known that insulin has important neurotrophic roles and interacts with receptors throughout the brain, including regions thought to be critical to executive abilities.12 How insulin resistance may relate to executive dysfunction, however, remains a matter of speculation. Recent evidence suggests that insulin resistance may promote the development or inhibit the degradation of the
Executive Function and Type 2 Diabetes

\(\beta\)-amyloid plaques characteristic of Alzheimer disease.\(^5\) Relationships have also been observed among inflammatory markers, type 2 diabetes, and Alzheimer disease, and it has been suggested that as-yet-unknown cellular pathways link these variables.\(^6\)

**Executive Function, Diabetes, and Gait**

Initially thought to require little cognitive control, the neuropsychological influences mediating gait are now increasingly being recognized. This recognition is likely due to a growing appreciation for the fact that locomotion requires not only the generation and control of motor commands but also an awareness of purpose and an ability to process multiple incoming stimuli to adapt to dynamic environments.\(^43\) The integration, sequencing, and monitoring of these various cognitive, motor, and behavioral demands are often attributed to executive function.\(^44\)

Illustrating the impact of diabetes on the critical relationships between executive function and gait in a large sample of older adults, Brach et al\(^45\) found that those with diabetes \((n=119)\) ambulated at speeds 8% lower than those without diabetes, with an 8% shorter step length, 14% wider and 4% longer stance, and 6% longer double-support time. Each of these differences was statistically significant, as was the amount (~6%) of the association between diabetes and walking speed explained by executive tasks assessing attention and shifting. When combined with a global cognitive task and a measure of depression, these measures attenuated the relationship between diabetes and gait speed by more than 50% after controlling for age, sex, and race.\(^45\)

Although the gait deviations observed in older adults with diabetes appear to resemble those associated with executive dysfunction, these abnormalities are most frequently attributed to diabetic peripheral neuropathy. However, there is evidence that people with diabetes but no evidence of neuropathy walk at speeds as much as 48% lower than people without diabetes, with a significantly wider stance and increased lower-extremity flexion/extension and lateral joint movement (or “errors”). These joint errors appear to be due, in part, to tremors occurring at frequencies implicating a central neurological origin.\(^46\)

Furthermore, it appears that gait abnormalities associated with diabetes can be exacerbated in situations requiring higher levels of executive involvement, such as those involving time sharing between simultaneous dual tasks. For example, Paul et al\(^47\) found that performing a serial mental subtraction task or carrying a tray of water-filled cups while walking significantly slowed gait speed—by up to 27%—in 15 older adults with diabetes and no signs of peripheral neuropathy. In addition, these tasks decreased step length by up to 20% and increased double-support time by as much as 17%. That these changes were not significantly different from those elicited in a similar group of people with diabetic peripheral neuropathy seems to emphasize a central limitation in the executive ability needed to divide attention between the tasks rather than a peripheral limitation in the somatosensory pathways affected by diabetic neuropathy.

**Executive Function, Diabetes, and Functional Abilities**

It is clear that severe damage to brain areas implicated in executive function can produce impairments across a wide spectrum of functional abilities. However, even subtle disturbances that occur in the absence of overt neurological damage are of significant concern, as they are powerful predictors of functional loss.\(^48\)

Although very few studies have investigated whether executive dysfunction may contribute to the disproportionately large degree of physical impairment and disability known to exist in elderly people with diabetes, there is some evidence for such a contribution.

For example, Kuo et al\(^29\) analyzed measures of cognition and physical function and the status of activities of daily living (ADL) in 2,802 community-dwelling older adults (358 with diabetes) and reported a significantly greater rate of decline in performance on an executive measure of attention in people with diabetes than in people without diabetes. This decline was matched by a significantly increased rate of decline in performance on the physical function component of the Medical Outcomes Study 36-Item Health Survey (SF-36) questionnaire and a measure of ADL function assessing meal preparation, housework, financial and health care management, telephone use, shopping, and traveling.

These findings appeared to be largely consistent with those reported for a sample of homebound people 60 years of age and older.\(^7\) In that study, people with type 2 DM exhibited significant impairments—of up to 21%—in executive tasks of shifting, working memory, and visuospatial function, as well as a 10% reduction in ADL function on a measure assessing walking, eating, dressing, bathing, toileting, and food preparation. Although the authors reported that the poorer ADL function scores were related to the observed executive deficits, they did not elaborate on this finding.\(^7\)

**Clinical Implications**

As keen observers of both cognitive functioning and physical function-
Executive Function and Type 2 Diabetes

ing, physical therapists are ideally positioned to recognize and address cognitive and motor impairments such as those that appear to be associated with type 2 DM. Given the enormous prevalence of type 2 DM in the elderly population and the known consequences of executive dysfunction in terms of falls and functional limitations, the involvement of physical therapists may be critically important—especially as multidisciplinary input from neuropsychologists, speech-language pathologists, and occupational therapists is not always readily available.

Although several instruments are available for assessing executive function and its component processes, the most clinically relevant of these, from a physical therapy standpoint, seem to be dual-task assessments of the ability to time share. Specifically, the disruptions in task performance that are typically observed under dual-task conditions are thought to arise from an insufficient executive capacity to share attention between the demands of the tasks. These “dual-task costs” are easily calculated with the following formula: [(dual-task performance – single-task performance)/single-task performance] × 100. Dual-task costs represent the percent difference between single-task and dual-task conditions (e.g., a 5% decline in walking speed) and allow comparisons across people, groups, or time. Among the clinical measures that make use of dual-task costs to assess cognitive and motor time sharing are the Walking and Remembering Test, cognitive and manual task variations of the Timed “Up & Go” Test, and the Walking While Talking Test. Table 3 provides brief descriptions of these measures.

Although dual-task assessments have yet to be widely used in people with diabetes, most evidence appears to suggest that these measures can provide physical therapists with valuable quantitative data regarding an individual’s executive ability to safely coordinate and perform simultaneous tasks. In particular, the Walking and Remembering Test described by McCulloch et al. addresses many of the limitations generally associated with dual-task assessments (for a review, see McCulloch). Further research and collaboration with workers in the field of neuropsychology are needed to establish the validity and reliability of such assessments for older adults with diabetes. However, it seems likely that the use of these tools will only enhance the recognition of cognitive and motor deficits in this population and may help identify people at risk for falls and other functional impairments.

In addition to facilitating clinical assessments, the executive process of time sharing appears to be an attractive target for the deployment of intervention strategies aimed at improving functional ability, cognitive ability, or both. Preliminary evidence indicates that dual-task training interventions may have a beneficial impact on function. For example, 26 found that a randomized, controlled 4-week training intervention combining balance activities with numeral recall and animal naming tasks improved dual-task gait speed by as much as 0.18 m/s (effect size = 0.46–0.57) in older adults with balance impairments. Similar results were reported in randomized, controlled studies examining dual-task interventions in older adults with dementia. Notably, the lack of significant improvements in dual-task abilities observed in the control groups in these studies indicated that single-task training alone may not improve dual-task abilities. As dual-task activities more closely mimic normal function than do single-task activities, physical therapists may be well advised to consider incorporating such activities into their treatment plans.

Conclusions

Although it is difficult to fully elucidate their impact, it seems likely that disease-related changes in executive function adversely affect daily functional abilities in older adults with type 2 DM. Physical therapists should be prepared to recognize possible impairments in executive function in older people with diabetes and should understand that these changes may directly or indirectly affect even the most basic daily activities.

Although not commonly applied in people with DM, the evaluation of dual-task performance appears to represent a promising means of both assessing and improving the highly functional executive process of time sharing. Future research and collaboration with workers in the field of neuropsychology must establish the validity, predictive ability, efficacy, and generalizability of this strategy. Ultimately, such research will yield a clearer understanding of diabetes-related executive and cognitive impairments and facilitate the development of clinical tools that physical therapists can use to detect and address the consequences of diabetes.

All authors provided concept/idea/project design. Mr Rucker and Dr Kluding provided writing. Mr Rucker provided data collection, data analysis, and project management. Dr McDowd and Dr Kluding provided consultation (including review of manuscript before submission).


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Executive Function and Type 2 Diabetes


