Screening of Neurocognitive and Executive Functioning in Children, Adolescents, and Young Adults With Type 1 Diabetes

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National and international treatment guidelines recommend regular psychological screening of children and youth with type 1 diabetes. In this article, the authors argue that neurocognitive screening is another important yet neglected aspect of the care of youth with diabetes. Mild neurocognitive dysfunction is an underrecognized complication of diabetes that can have considerable effects on school performance, activities of daily living, and diabetes self-management. This article offers suggestions for screening and management of neurocognitive dysfunction in pediatric type 1 diabetes patients in various settings, as well as recommendations for future research.

Children, youth, and young adults with type 1 diabetes face many challenges and complications as a result of their disease. One of the less well-recognized problems is an increased incidence of mild to moderate neurocognitive dysfunction: acquired deficits in psychomotor speed, mental efficiency, attention, visual-motor skills, memory, and learning. (See related article by Cato and Hershey on p. 197 of this issue.) In general, these deficits are relatively subtle, with effect sizes reported in the small to moderate range (1). Thus, many individuals who have cognitive dysfunction will have scores on standardized tests that fall within the average range, although the functional impact of small deficits can still be substantial. Children with cognitive dysfunction have an increased likelihood of prob-

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lems at school (2) and difficulties with diabetes management (3,4) that place them at risk for poor glycemic control. Diabetes-related neurocognitive dysfunction therefore has important implications for the lives and long-term outcomes of individuals with diabetes. Just as psychosocial screening is important for standard diabetes care, so too is identifying individuals who are at risk for developing cognitive deficits or are currently experiencing cognitive dysfunction (5).

One way to identify cognitive declines is to monitor youth through comprehensive neuropsychological evaluation (6). Although adopting this strategy could help inform patient care, it would be expensive, require substantial resources, and place a burden on patients and their families that would not be indicated in most cases. A more targeted approach using brief screening for cognitive dysfunction is more feasible. *Screening* refers to a strategy for early identification of problems in a population. Screenings typically are brief, are not diagnostic, and are commonly used to determine whether further assessment is needed. In this article, we use *assessment* to mean a more comprehensive evaluation, the intention of which is to clarify the nature of the identified problem, determine a diagnosis where appropriate, and make recommendations for intervention when needed. Methods of screening for cognitive dysfunction include asking about risk factors or subjective complaints during history-taking, using standardized questionnaires, or actually testing relevant functions (discussed in more detail below).

Screening provides an efficient way to allocate limited or expensive resources to the patients with greatest need, while also fostering early intervention. Identification of cognitive deficits in diabetes patients can help inform development of school-based plans, guide recommendations for diabetes self-management education and support, and, in some cases, lead to changes in the diabetes regimen itself. Unfortunately, there are no established methods for neurocognitive screening of pediatric diabetes patients that have been adapted for use in routine care (e.g., in primary or specialty care clinics). In this article, we briefly discuss the impact of neurocognitive and executive deficits on the health and well-being of children, youth, and young adults with diabetes and then provide detailed recommendations for screening and management of neurocognitive dysfunction in these patients.

Impact of Cognitive Sequelae on School, Diabetes Self-Management, and Health Outcomes

School problems are often the first sign of deterioration in cognitive function. Meta-analyses show a small but significant effect of diabetes on academic achievement, with larger effects evident in children with early-onset disease (1,7). Deficits in memory, attention, and processing speed can subtly affect school performance, yet anecdotal evidence suggests that few school personnel are aware that diabetes can affect these domains. In our experience, declines in school performance in children with diabetes tend to be attributed to psychological or behavioral factors, with little recognition of possible declines in cognition.

Cognitive decline associated with diabetes also may have important implications for diabetes management. The complex treatment of type 1 diabetes is 99% self-management; that is, it is almost entirely dependent on the behavior of the person with type 1 diabetes and his or her family (8). This means that any deficiency in cognition that interferes with cognitive control of behavior and self-regulation has the potential to affect diabetes self-management, especially if parents provide limited supervision. For example, children with memory problems show greater difficulty with blood glucose monitoring (3,4), and learning difficulties can interfere with reading labels and prescriptions, calculating carbohydrates, and adjusting insulin dosages.

Problems with executive functioning also can affect adherence and glycemic control (9). *Executive functioning* refers to higher-level cognitive skills that include initiating and stopping behavior, shifting attention from one task to another, planning, prioritizing, and problem-solving. For example, checking blood glucose and administering bolus insulin doses before a meal require interrupting ongoing activities, shifting between tasks, planning ahead, gathering needed data, and implementing a plan to keep blood glucose levels in a healthy range. Youth with type 1 diabetes must have the flexibility to problem-solve and adapt diabetes management tasks when confronted with unexpected events (e.g., a delayed meal in a restaurant) or emergencies such as insulin pump malfunction. Individuals with executive dysfunction may struggle with these organizational aspects of adherence. They also are more likely to act without thinking and take risks that could further affect their diabetes management (10) and health outcomes (11–13). Identifying and addressing deficits in executive functioning may be especially important to prevent declining adherence and increased risk-taking behavior. Individuals with comorbid attention deficit hyperactivity disorder (ADHD) are at especially high risk for executive dysfunction, increased difficulty with diabetes management, and poorer glycemic control (14,15).

Who Should Be Screened for Neurocognitive Dysfunction?

Given that only a subset of children with diabetes will develop cognitive sequelae, a targeted approach of only screening at-risk patients is recommended. Early onset of diabetes (EOD; i.e., age of onset ≤7 years) is perhaps the risk factor most robust-

ly associated with cognitive deficits (1,16). Although the prevalence of neurocognitive dysfunction in diabetes is unknown, one early study found that nearly one-fourth of adolescents with EOD showed clinically significant cognitive impairment compared to only 6% of those with later-onset disease (17). Children diagnosed at earlier ages therefore should receive highest priority for screening.

Individuals who experience severe acute diabetes events also should be prioritized for screening. Diabetic ketoacidosis (DKA) is associated with significantly higher risk for neurocognitive sequelae, especially when it is accompanied by cerebral edema (18) or when it occurs repeatedly (19,20). DKA is quite prevalent at diabetes diagnosis, especially among the youngest children (21,22), and it is associated with brain changes on MRI and subsequent neurocognitive sequelae (23), making it a prime candidate as a diathesis for later cognitive decline (24).

A third group to target are individuals with poor glycemic control. Chronic hyperglycemia is associated with changes in multiple areas of cognitive functioning (16,25–29); it might also be a marker for subtle deficits in cognition that are affecting self-management. Although single episodes of severe hypoglycemia probably do not have an effect on cognition, recurrent episodes are associated with cognitive changes (7,16,29). Patients with significant glycemic variability also might be at greater risk for cognitive dysfunction (30). Importantly, cognitive dysfunction related to acute or chronic dysglycemia appears to be most likely in children with EOD. If resources are limited, one could take a more conservative approach of only screening children with EOD who also have one or more diabetes-related risk factors, such as recurrent DKA, severe hypoglycemic episodes, or poor glycemic control.

When Should Screening Occur?

Screening at Diagnosis

Screening at diagnosis can identify patients who need to be monitored more closely and who may benefit from early intervention. All patients should be screened at diagnosis for preexisting learning and attention problems through a careful history or psychosocial screening (31). Findings can be used to inform development or updating of school plans to minimize the impact of diabetes on school performance. Clinicians also can consider how identified learning or attention problems might affect diabetes self-management and make adjustments to self-management education and support plans accordingly.

Preliminary evidence suggests that risk for cognitive sequelae of diabetes also can be identified through administration of brief neuropsychological tests. In one study of children newly diagnosed with diabetes (32), deficits were found in psychomotor speed that were associated with metabolic control 1 year later, suggesting that impaired motor speed may be an early marker for cognitive changes that can have a long-term effect on diabetes control.

Patients who present in DKA at diagnosis are at especially high risk for cognitive dysfunction. Cerebral edema and central nervous system (CNS) changes occur at high rates in DKA but often are not identified clinically (22,23). A recent study by Cameron et al. (23) found deficits in memory and attention associated with cerebral white matter volume reductions in children presenting in DKA at diagnosis, and these deficits persisted for 6 months post-diagnosis, after brain changes on MRI had resolved. Although neuroimaging of most diabetes patients is not feasible, a brief cognitive screening test at diagnosis could inexpensively identify patients who may need to be monitored more closely.

Screening as Part of Routine Follow-Up

Longitudinal studies suggest that some cognitive changes associated with diabetes may only become apparent over time. Northam et al. (33) found no cognitive differences between children with and without diabetes a few months after diagnosis, but small differences emerged after 2 years (33), became more generalized after 6 years (34), and remained stable after 12 years (35). They also found that verbal IQ scores tended to decline over time in individuals with suboptimal glycemic control (36). These findings support the argument for routine (e.g., annual) cognitive screening of children and youth with diabetes who have diabetes-related risk factors such as chronic hyperglycemia.

For patients who are hospitalized for DKA post-diagnosis, we recommend cognitive screening at the next follow-up clinic visit. Screening of attention and memory may be especially important in these patients (29). More generally, screening might be considered for any patient who presents with subjective complaints of a change in cognition (e.g., memory or concentration), behavior (e.g., increased impulsivity or risk-taking), or school functioning, or an unexplained decline in adherence or glycemic control. Table 1 summarizes suggested guidelines for routine cognitive screening of established type 1 diabetes patients.

How to Screen for Neurocognitive and Executive Dysfunction

General Considerations

At present, we know of no published protocols for cognitive screening of pediatric patients with type 1 diabetes. However, protocols have been developed for psychosocial screening of these patients (31,37) and for cognitive screening in other populations, including children and youth with epilepsy (38,39), cancer (40), brain injury (41), and celiac disease (42),

TABLE 1. Preliminary Guidelines for Routine Cognitive Screening of Type 1 Diabetes Patients Using the Cognitive Screening Index

Indication for Screening	When Screening Should Occur
EOD (≤7 years of age)	Annually
DKA (single episode)	3–6 months after episode
Repeated DKA	3–6 months after episodes and annually thereafter
Repeated severe hypoglycemia*	Annually
History of cerebral edema	3–6 months after episode and annually thereafter
Chronic hyperglycemia†	Annually
History of/positive screen for cognitive dysfunction	Annually
Unexplained decline in regimen adherence or glycemic control	During current office visit
Unexplained decline in school functioning	During current office visit

**Severe hypoglycemia is defined as a hypoglycemic event requiring the assistance of another person to take corrective action (46).*
†Chronic hyperglycemia is defined as A1C values outside of ADA-recommended ranges (46).

as well as for older adults with type 2 diabetes (43,44). Review of these guidelines suggests several factors that are important to consider when designing a protocol for cognitive screening, including:

- What level of training or expertise is required of the person conducting the screening and interpreting the results?
- Where will the screening take place (e.g., at home, online, in the clinic waiting room, or in the clinic)?
- How often will the screening occur?
- Can this service be billed to insurance?
- What supplies (e.g., questionnaires or forms) are needed to conduct the screening?
- What technology (if any) is needed to conduct the screening (e.g., computers in clinic)?
- How will the results of the screening be communicated to patients and utilized in practice?

A neuropsychologist with experience in diabetes should be involved in designing the screening protocol and referral process, choosing measures, setting cutoffs for referral, and training medical providers to administer and score measures and be available for additional consultation or referral as needed. Given the need for most patients with type 1 diabetes to receive care in a specialty diabetes clinic, most cognitive screening will likely occur in this setting. Another possibility is for cognitive screening to occur in a primary care setting. Pediatricians are familiar with screening for conditions such as ADHD and learning disorders (45), so it might be a natural extension to add cognitive screening for patients with diabetes. Screenings can be completed by physicians as part of a clinical interview or by allied health professionals (e.g., physician's assistants, nurse practitioners, and diabetes educators) who have been trained in the screening procedure. Cognitive screening also can be incorporated into diabetes self-management education and support programs as part of a regular assessment plan, as recommended by the American Diabetes Association (ADA) (46).

Cognitive Screening Methods

There is currently no gold standard for cognitive screening of young patients with diabetes. Several different types of measures may be used, each with its own benefits and considerations. When choosing screening methods, it is important to balance the measure's sensitivity (ability to detect problems) with its specificity (ability to discriminate between patients who do and do not have the condition being screened). Setting a low bar for referral will ensure that few patients with cognitive dysfunction are missed, but at the cost of referring patients who do not need additional evaluation or services. Conversely, setting a high bar will help to ensure that identified patients are more likely to have cognitive dysfunction, but at the cost of missing more subtle cases. We therefore suggest taking a stepwise approach to cognitive screening, starting with briefer and more sensitive measures, and working toward more comprehensive measures with higher specificity for patients who screen positive.

First, providers can identify patients at greater risk for neurocognitive sequelae based on their diabetes history and by querying for difficulties in regimen adherence that might implicate possible cognitive deficits (e.g., increased problems with remembering to check blood glucose levels) and querying for declines in school performance. Identified patients or their caregivers (or both) then can be asked directly about cognitive functioning in different domains. Although no validated measures currently exist for cognitive screening in

this population, we have previously suggested using the brief Cognitive Screening Index (47), which we have found clinically useful and are currently in the process of validating. Specifically, the provider would ask whether the patient has been having any difficulty with:

- Comprehension or understanding
- Learning new information
- Remembering things he or she has already learned
- Remembering to do things he or she is supposed to do
- Thinking or working more slowly than others his or her age or completing work on time
- Putting thoughts into words or saying things that do not make sense
- Paying attention or staying focused
- Concentrating or feeling as if he or she is in a fog
- Fine-motor skills (e.g., handwriting, tying, or fastening clothes) (47).

For any "yes" response, follow-up questions can be asked with regard to the severity of the problem (e.g., is it a mild, moderate, or major concern?) and whether it is a change from previous functioning. Currently, there is no empirically derived cutoff for referral; as a provisional approach, we suggest referring for further assessment any patient for whom such problems are a major concern or represent a notable change in functioning.

Conducting a brief interview may be the easiest way of implementing a cognitive screen, as it does not take much extra time, does not cost money to administer, and does not require any special equipment. However, even with the guidelines suggested above, it may be difficult to tell when a problem is significant enough to warrant a referral, and patients may be over- or under-referred as a result. Moreover, comorbid concerns that can affect cognitive performance (e.g., symptoms of depression) might result in elevated false-positive rates.

A more conservative approach would be to follow-up affirmative responses with a standardized questionnaire that can further guide clinical decision-making. For example, the Vanderbilt ADHD Diagnostic Rating Scales (available free online at www.brightfutures.org) provide a reliable and valid way to measure daily attention problems and are likely familiar to many health care providers (HCPs). Other validated questionnaires for different domains of cognitive functioning exist in the research literature or are commercially available, but they are likely to be difficult to use and interpret without additional training.

Standardized cognitive testing is the screening procedure that generally has the best reliability and predictive validity for identifying cognitive dysfunction. Although comprehensive neuropsychological assessment will not be feasible in most cases, diabetes clinicians can be trained to administer a brief cognitive test as a screening instrument, provided that *1*) clinicians receive formal training in administering the selected test and *2*) test findings are only used to inform referral decisions. For example, Benedict et al. (48) demonstrated the value of a brief test of processing speed for screening for cognitive impairment in adults with multiple sclerosis. Nursing staff were taught to administer the measure with a high degree of reliability, and empirically derived cutoffs identified cognitive impairment with good accuracy (49). No comparable tests have been identified as gold-standard instruments for cognitive screening in type 1 diabetes, although there is evidence that the Grooved Pegboard Test (50) may be particularly sensitive to diabetes-related cognitive dysfunction (32,51–53).

Cognitive tests might be especially valuable at the time of diabetes diagnosis, before subjective complaints or longer-term risk factors (e.g., chronic hyperglycemia) become evident. Most patients are hospitalized at diagnosis, and many hospitals have psychologists on staff with some training in test administration. In addition to the Grooved Pegboard Test, a version of the Digit Span Test with forward and backward spans is familiar to many clinicians (e.g., as part of the Wechsler Intelligence Scales for children and adults [54,55]) and can provide a quick assessment of attention and working memory. Using these measures to screen for acute cognitive dysfunction at diagnosis is feasible and acceptable to families (32), and evidence is growing that the findings may be predictive of subsequent outcomes (23,32).

Computer-based tests provide another means to screen cognitive abilities in the office. The feasibility of a computerized cognitive screening program has been demonstrated for a pediatric epilepsy population (39) and for patients with concussion (56), although these tools have not yet been applied to individuals with diabetes. Computer tests automate administration and scoring, although some unique resources may be required (e.g., a computer and a quiet room with no distractions), and computer assessments can be expensive. Providers should also be wary of computer programs that generate canned "interpretations." Although computerized tests provide data that can help guide referral decisions, they should not be used by themselves to identify cognitive decline.

What to Do With Positive Screens

The purpose of screening is "to gain enough information to ascertain the best next steps" (38), which may include more extensive assessment, school planning, and/or intervention. Positive screens should never be interpreted as evidence of a confirmed cognitive decline or change in the CNS. Instead, positive findings should be presented to patients and families as an indication of a current difficulty that might benefit from further evaluation or increased support at school

or home. Providers should keep in mind that evidence of cognitive dysfunction might reflect a patient's performance on that day alone, might be temporary, or might have different causes that do not necessarily implicate a CNS-based cognitive change (possibilities include stress, fatigue, anxiety, mood, or patient disinterest during assessment).

Determining true cognitive dysfunction requires data of different types (e.g., testing of multiple cognitive domains and standardized behavioral questionnaires), obtained from multiple settings (e.g., clinic, school, and home) and sources (e.g., patient, parent, and teacher), and considered in the context of the patient's medical, developmental, and psychosocial history. This type of comprehensive assessment typically is best performed by a neuropsychologist. A neuropsychological evaluation can identify specific cognitive strengths and weaknesses and help with differential diagnosis between neurocognitive changes and conditions such as depression or ADHD. Evaluation can also help distinguish between acute cognitive effects of glycemic extremes and more chronic changes in cognition. Perhaps most importantly, a neuropsychologist can help patients, families, HCPs, and school personnel understand how diabetes can affect cognitive and behavioral functioning so that individuals will be more likely to get the support they need.

Positive screens do not necessarily require a comprehensive neuropsychological workup as the next step. In cases in which the extent or severity of concerns is unclear, a neuropsychologist or appropriately trained pediatric health psychologist could provide an initial consultation to determine whether more formal neurocognitive testing is indicated. In regions where a neuropsychologist is unavailable, it may be necessary to rely on more limited assessments completed by pediatric health psychologists or school psychologists with some knowledge of diabetes. It is important that providers investigate resources in their area and develop a network of referral sources to enable them to help their patients who screen positive find appropriate care. Appropriately trained psychologists and neuropsychologists can be identified through local pediatric hospitals or by looking through the online directory of the American Board of Professional Psychology (http://www.abpp.org).

School recommendations are an important part of most pediatric neuropsychological evaluations, although a neuropsychological evaluation is not necessary to initiate a school-based plan. The most common mechanism for school accommodations for students with diabetes is a 504 Plan, usually under the classification of Other Health Impairment. Section 504 of the Rehabilitation Act is a U.S. federal law ensuring that individuals with disabilities receive equal educational opportunities at any school that receives federal funding. In addition to typical 504 accommodations such as environmental supports within the classroom and extended time for tests, diabetes-specific recommendations are also important. An example would be allowing a youth with diabetes to check blood glucose before (or during) a school exam, and, if it is out of range, allowing her to take the test with extra time or on another day. ADA has developed a valuable online resource for 504 Plans for children and youth with diabetes that includes model 504 Plans in English and Spanish (57).

HCPs also may consider the implications of cognitive dysfunction for diabetes self-management and provide additional guidance to families or make changes to the medical regimen as needed. For example, a youth who is experiencing difficulties with memory may need reminders from parents to engage in self-management tasks or might benefit from technology supports such as using a smartphone with a reminder application (or "app"). It is important for diabetes care providers to stay current on new apps and other diabetes-related technologies that could scaffold a patient with mild cognitive dysfunction. Similarly, problems with working memory and math could make it difficult for a patient to calculate carbohydrates and make accurate adjustments to insulin dosing. Potential supports could include help from a family member, use of a bolus calculator, or use of pre-filled insulin pens and placement on a fixed-dose regimen.

Patients with identified executive dysfunction might be at particularly high risk for problematic adherence. They may act more impulsively, have difficulty with making and following through on plans, and take more risks with their diabetes care (10). For these patients, HCPs might recommend heightened parental monitoring (58) and schedule more frequent clinic visits. Referral to a pediatric health psychologist might also be beneficial, with a focus on helping improve family teamwork around diabetes care (58,59).

Conclusion

Routine cognitive screening for children, adolescents, and young adults with type 1 diabetes is a relatively new idea, but one that should be strongly considered given the mounting evidence for CNS changes and cognitive deficits in these patients and the possible effects of cognitive dysfunction on school functioning, diabetes management, and health outcomes. Early identification of subtle cognitive dysfunction can help HCPs make changes in the level of support a patient needs to reduce the likelihood of suboptimal adherence or even make changes to the medical regimen to better accommodate the patient's unique needs. As a result, cognitive screening has the potential to improve patient care and health outcomes. Recommended steps for screening are summarized in Table 2.

TABLE 2. Summary Recommendations for Routine Cognitive Screening in Clinical Practice

Before the visit

- Identify a network of referral sources for neuropsychological consultation and evaluation
- Identify patients at higher risk of cognitive dysfunction based on diabetes history

During the visit

- Consider cognitive factors in patients with declines in adherence or glycemic control
- Inquire about changes in school functioning
- Administer Cognitive Screening Index or screening test (if appropriately trained) to identified patients and/or their caregivers

After the visit

- Refer milder concerns to a pediatric health psychologist or neuropsychologist for further consultation
- Refer major concerns or clear changes in functioning for neuropsychological evaluation

Valid and reliable tools exist for cognitive assessment, but at present, there are no validated and standardized cognitive screening tools for use specifically with this population. This is an area of significant need. We have offered a brief set of questions and a stepwise protocol for clinical decision-making, but without validated screening tools with established sensitivity and specificity, there is no way to know whether patients will be under- or over-referred for neuropsychological evaluation. Measure validation is an important area for future research.

Despite its potential benefits, many HCPs may remain wary of integrating cognitive screening into routine care (even for at-risk patients) because it falls outside of their usual scope of practice and takes additional time during visits that are already too short (60). Screening may become more feasible in the near future, however, as a result of changes occurring in the U.S. health care system.

Under the impetus of the Patient Protection and Affordable Care Act, there is a move toward integrating behavioral health services into primary care settings (61); similar efforts may also affect specialty care clinics. In this model, behavioral health providers, including health psychologists and neuropsychologists, are integrated into routine patient care to provide consultation that is typically brief, problem-focused, and focused on prevention. Co-located or consulting neuropsychologists could help with screening and follow-up assessments of patients with identified concerns. Bundled payments could be used to cover the costs of screening. Although not yet expanded to include neuropsychology, initial reports of integrated behavioral health care suggest that the model is cost-effective and results in an improved patient experience and patient health, the "triple aim" of the current health care reform (62).

Cognitive dysfunction in youth with type 1 diabetes has important implications for diabetes self-management, school performance, and other aspects of patients' lives, yet it often goes unrecognized and unaddressed, reducing quality of life for many patients. Thus, there is a strong case to be made for screening patients at higher risk of neurocognitive dysfunction. However, much work remains to be done to determine the most effective, accurate, reliable, and cost-effective ways to screen for cognitive dysfunction in patients with chronic illness, to coordinate screening and follow-up across different HCPs, and to integrate screening seamlessly into clinical operations in various settings.

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Duality of Interest

No potential conflicts of interest relevant to this article were reported.

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