Neurocognitive Functioning in Children and Adolescents at the Time of Type 1 Diabetes Diagnosis: Associations With Glycemic Control 1 Year After Diagnosis

DOI: 10.2337/dc14-0103

OBJECTIVE
To determine whether impairments in neurocognitive functioning are detectable at type 1 diabetes diagnosis and associated with subsequent glycemic control.

RESEARCH DESIGN AND METHODS
Children/adolescents (N = 147) aged 5–18 years completed neuropsychological testing during their inpatient hospitalization for new-onset type 1 diabetes. Test scores were compared with normative data using one-sample Student t tests. Children with onset before 8 years of age were compared with children aged 9–18 years using ANOVA, and associations between neurocognitive performance at diagnosis and glycemic control 1 year postdiagnosis were examined using regression analyses.

RESULTS
Children with type 1 diabetes performed significantly below expectations on most neurocognitive measures (P values <0.0001), with large decrements from the normative mean evident in psychomotor speed (>1 SD), visuomotor integration (0.7 SD), and phonemic fluency (0.8 SD). High incidence of impairment (scores less than second percentile) was evident on all tasks except digit span. Dominant-hand psychomotor speed was significantly associated with poor glycemic control (A1C ≥9.5% [80 mmol/mol]; P = 0.032) 1 year postdiagnosis, controlling for race/ethnicity, sex, and reading ability. Impaired psychomotor speed was associated with a 0.77% increase in mean A1C (8.4 mmol/mol).

CONCLUSIONS
Deficits were evident in neurocognitive functioning within days of diabetes diagnosis that were associated with diabetes outcomes over 1 year postdiagnosis. Impairment was most apparent in psychomotor speed, consistent with research implicating damage to posterior white matter tracts and associated gray matter regions in type 1 diabetes. Psychomotor impairment may be an early marker for a broader neurobehavioral vulnerability that has implications for long-term diabetes management.
Children and youth with type 1 diabetes are at risk for developing neurocognitive dysfunction, especially in the areas of psychomotor speed, attention/executive functioning, and visuomotor integration (1,2). Most research suggests that deficits emerge over time, perhaps in response to the cumulative effect of glycemic extremes (3–6). However, the idea that cognitive changes emerge gradually has been challenged (7–9). Ryan (9) argued that if diabetes has a cumulative effect on cognition, cognitive test performance should be positively correlated with illness duration. Yet he found comparable deficits in psychomotor speed (the most commonly noted area of deficit) in adolescents and young adults with illness duration ranging from 6 to 25 years. He therefore proposed a diathesis model in which cognitive declines in diabetes are especially likely to occur in more vulnerable patients, at crucial periods, in response to illness-related events (e.g., severe hyperglycemia) known to have an impact on the central nervous system (CNS) (8). This model accounts for the finding that cognitive deficits are more likely in children with early-onset diabetes, and for the accelerated cognitive aging seen in diabetic individuals later in life (7). A third hypothesized crucial period is the time leading up to diabetes diagnosis, during which severe fluctuations in blood glucose and persistent hyperglycemia often occur. Concurrent changes in blood-brain barrier permeability could result in a flood of glucose into the brain, with neurotoxic effects (9).

Unfortunately, there is a paucity of data regarding cognitive functioning during the peri-onset period, and it remains unknown when neurocognitive changes related to type 1 diabetes arise (9–11). In the current study, we report neuropsychological test findings for children and adolescents tested within 3 days of diabetes diagnosis. The purpose of the study was to determine whether neurocognitive impairments are detectable at diagnosis, as predicted by the diathesis hypothesis. We hypothesized that performance on tests of psychomotor speed, visuomotor integration, and attention/executive functioning would be significantly below normative expectations, and that differences would be greater in children with earlier disease onset. We also predicted that diabetic ketoacidosis (DKA), a primary cause of diabetes-related neurological morbidity (12) and a likely proxy for severe peri-onset hyperglycemia, would be associated with poorer performance. Finally, we hypothesized that neuropsychological dysfunction at diagnosis might be a marker for a more general neurobehavioral vulnerability that would be associated with diabetes control 1 year postdiagnosis in older children (preteens/teens) who are likely to have more responsibility for self-management.

RESEARCH DESIGN AND METHODS

Participants
Charts were reviewed for 147 children/adolescents aged 5–18 years (mean = 10.4 ± 3.2 years) who completed a short neuropsychological screening during their inpatient hospitalization for new-onset type 1 diabetes, as part of a pilot clinical program intended to identify patients in need of further neuropsychological evaluation. Participants were patients at a large urban children’s hospital in the southwestern U.S. Children were included in the study if they completed at least one test measure and had at least five postdiagnosis A1C values in their medical chart. All data were abstracted from chart review.

Among 88 children aged 5–8 years who were asked to participate in the clinical screening, 53 (60.2%) completed at least one neuropsychological measure, and of these, 50 had five or more A1C values in their chart. Among 174 eligible patients aged 9–18 years, 108 (62.1%) completed at least one measure and 97 had enough A1C values to be included. The most common reason for decline was fatigue. No one complained of residual visual problems from insulin deficiency.

Procedure
The study was approved by the institutional review board of record. Neuropsychological testing was completed by trained predoctoral psychology residents as part of a larger risk-screening program for newly diagnosed type 1 diabetic patients that has been described elsewhere (13). Legal caregivers provided informed consent for the clinical evaluation, and the children provided assent. Each child was told that she/he could opt out of any test due to discomfort, difficulty seeing materials, or fatigue. Participants were tested in their inpatient room, usually in their hospital bed with materials placed on a free-standing tray. Nursing staff was informed that an assessment was occurring and a sign was posted to limit disturbances, although testing was sometimes disrupted by staff coming into the room, and we did not always have time to complete the test battery before the medical team needed to see the patient. Some children did not attempt one or more motor tasks due to bandaged fingers or an IV (most often affecting the nondominant hand). As a result of these factors, not all participants completed every measure.

Neuropsychological Tests
Measures were five well-known neuropsychological tests with demonstrated validity and reliability for pediatric populations (14,15). The Grooved Pegboard (GP) (16) measures eye-hand coordination and fine-motor speed/dexterity. It requires participants (aged 9 years and up) to place 25 pegs into a pegboard, first with the dominant hand (GPD) and then the nondominant hand (GPN). The primary outcome is time to complete the board with each hand. On the Beery-Buktenica Developmental Test of Visual-Motor Integration (VMI) (17), participants copy a series of line drawings of increasing complexity. The Trail Making Test (TMT) (18) has subjects first connect a series of numbered circles as quickly as possible (TMT-A) and then connect numbers and letters in alternating sequence (TMT-B). TMT-A provides a measure of visual attention/visual search, whereas TMT-B adds a component of set switching/executive control. The Verbal Fluency Test (FAS) (19) is a test of phonemic fluency and verbal executive functioning that asks participants to name as many words as possible in one minute that start with a specified letter, excluding proper names and numbers. There are three 1-min trials, one for each letter, and the raw score is the correct number of words summed across trials. We also examined two tasks of the Wechsler Digit Span (DS) subtest (20,21). Digit span forward (DSF) requires participants to repeat strings of numbers of increasing length and provides a measure of focused attention. Digit span backward (DSB) has children repeat number strings backward and provides a measure of working memory. DSF and DSB have the same format on both the child and adult versions of the test, except that different digits are used.
Older participants (aged 9+ years) completed the five measures above. Participants aged 5–8 years were administered the 10-peg “Kiddie” version of the GP (Kiddie-GP [16]) and the VMI. The first four tests (GP, VMI, TMT, and FAS) have a mean of 100 and SD of 10; DSF and DSB have a mean of 10 and SD of 3. Results were compared with published norms (15,17,20–23).

The reading subtest of the Wide Range Achievement Test-4 (WRAT-4) (R.M. Knights, unpublished data) (24) is a measure of word recognition used in this study to control for premorbid differences in IQ and education. Reading performance remains relatively intact in the face of cognitive insult and is considered a reasonable proxy for premorbid functioning (25).

**Glycemic Control**

Glycemic control was assessed using A1C assays obtained as part of clinical care over the year following diabetes diagnosis using the DCA 2000+ Analyzer point-of-care assessment (Siemens Healthcare Diagnostics, Deerfield, IL). In our center, A1C values are routinely obtained 1 month postdiagnosis, and then approximately once every 3 months. To create composites of average glycemic control and variability, we used the mean and SD of the second through fifth A1C values obtained postdiagnosis. We omitted the first postdiagnosis A1C, reasoning that it might still be elevated due to peri-onset hyperglycemia and thus not validly reflect postdiagnosis diabetes management. Indeed, preliminary analysis revealed that the first A1C was significantly higher than the mean of the next four A1Cs (8.9% [74 mmol/mol] vs. 7.8% [62 mmol/mol]; \( t = 4.710, P < 0.001 \)). We defined poor glycemic control as A1C ≥9.5% (80 mmol/mol), according to the convention established in the multisite SEARCH for Diabetes in Youth study (26), and a reduction of ≥0.5% was considered clinically meaningful (27). Incidence of DKA (and ketosis without acidosis) at presentation was extracted through medical chart review.

**Risk Factors**

Risk factors for poor glycemic outcomes were assessed using the Risk Index for Poor Glycemic Control (RI-PGC) (28), a validated nine-item caregiver interview completed as part of the clinical screening. The RI-PGC assesses demographic risk (underinsurance, caregiver unemployment, large family size, and single-parent status) and psychosocial risk (child mood/depression, social problems, and behavior problems; parent stress/anxiety; and family conflict). Items are summed to provide a single numerical risk score.

**Data Analysis**

Descriptive statistics were used to compare diabetes outcomes between age, sex, and racial/ethnic groups using a series of univariate analyses of variance for continuous outcomes and logistic regression for binary outcomes. Participants were categorized into three age-groups: early childhood (aged 5–8 years), preteen (aged 9–11 years), and teen (aged 12–18 years). We chose the age range for the youngest group to correspond with the age range of the Kiddie-GP.

One-sample Student t tests were computed to compare standard scores/scaled scores against expected values for each neuropsychological test (100 for GP, TMT, FAS, and VMI; 10 for DS) and to compare the percentage of participants showing impairment on each measure (standard score <70; scaled score <4) against the expected value of 2.2% (based on prevalence of impairment within the normal distribution curve). Performance on the Kiddie-GP was analyzed separately, as we reasoned that the 10- and 25-peg versions are not exactly comparable (e.g., fatigue may be less likely to impact performance on the shorter version, resulting in artificially elevated scores).

To test the relationship between neuropsychological functioning and diabetes outcomes (preteens/teens only), we constructed linear regression models for continuous outcomes (A1C, mean and averaged SD) and logistic regression models for poor glycemic control (mean A1C ≥9.5% [80 mmol/mol]). For each analysis, participants were included only if they had completed the relevant measure. As the reasons for missing data were unrelated to the potential value of the variable, treating missingness in this way reduced power but would not bias parameter estimates. In each model, we first entered race/ethnicity and the RI-PGC score to control for demographic and psychosocial factors known to influence glycemic outcomes (28), and word reading to control for premorbid cognitive functioning. The neuropsychological measure was entered on the final step in each model. As we were interested in the relationship between neuropsychological impairment and diabetes outcomes, we also examined test results as categorical predictors (impaired/not impaired) in a second set of analyses.

All analyses were conducted using PASW Statistics version 21 for Windows (IBM SPSS Inc., Chicago, IL). A P value \( \leq 0.05 \) was considered statistically significant.

**RESULTS**

**Demographic Factors**

Participant characteristics are shown in Table 1. Black children/youth had significantly higher mean A1C (P < 0.001) and incidence of poor glycemic control (P = 0.003) than other racial/ethnic groups. Males and females did not significantly differ in glycemic control. RI-PGC score was significantly correlated with mean A1C (r = 0.416, P < 0.0001), A1C variability (r = 0.300, P < 0.003), and poor glycemic control (r = 0.386, P = 0.0001).

**Neurocognitive Measures**

There was a main effect of race/ethnicity on TMT-B (P = 0.04), although no significant group differences emerged in paired comparisons. There were no other significant associations between demographic factors and either diabetes outcomes or neuropsychological measures. None of the neurocognitive tests was significantly associated with DKA (or ketosis without acidosis) at diagnosis. Blood glucose levels at time of testing (available for a subset of patients; n = 69) were not significantly correlated with any test measure.

Compared with normative expectations, children/youth with type 1 diabetes performed significantly worse on GPD, GPN, VMI, and FAS (P < 0.0001 in all cases), with large decrements evident on all four measures (Fig. 1). A small but significant effect was also evident in DSB (P = 0.022). High incidence of impairment was evident on all neuropsychological tasks completed by older participants (aged 9–18 years) except DSF/DSB (Fig. 2). Performance on the reading subtest was consistent with normative expectations (mean 103.7, SD 14.7).

Contrary to predictions, children with diabetes onset in the first 8 years of life did not show greater evidence of neuropsychological impairment. In fact,
scores were lowest and impairment highest in the teen group, although none of the age-group differences reached significance (Table 2). Neuropsychological test performance was also uncorrelated with diabetes outcomes within the early childhood group (P values > 0.15), and there were no differences between the preteens and teens on any measure (P values > 0.3).

In the older children (aged 9–18 years), mean GPD was significantly correlated with poor glycemic control ($r = -0.298, P = 0.005$), with a trend evident for mean A1C ($r = -0.200, P = 0.064$). Impairment on GPD was associated with mean A1C ($r = 0.253, P = 0.018$) and poor glycemic control ($r = 0.333, P = 0.002$).

Mean DSB was associated with mean A1C ($r = -0.223, P = 0.039$) and glycemic variability ($r = -0.296, P = 0.005$), whereas impaired DSB was associated with mean A1C ($r = 0.257, P = 0.017$) and approached significance for poor glycemic control ($r = 0.199, P = 0.066$). Word reading was significantly correlated with mean A1C ($r = -0.280, P = 0.009$), A1C variability ($r = -0.240, P = 0.025$), and poor glycemic control ($r = -0.212, P = 0.049$).

### Multivariate Analyses

The model predicting poor glycemic control from mean GPD was significant ($\chi^2 = 25.74, P = 0.0002$). Black race/ethnicity ($\beta = 2.186, P = 0.031$), RI-PGC score ($\beta = 0.711, P = 0.011$), and mean GPD ($\beta = -0.044, P = 0.034$) remained significant in the final model, which explained 50.9% of the variance. The model predicting poor glycemic control from impaired GPD was also significant ($\chi^2 = 24.86, P = 0.0004$), explaining 49.4% of the variance. RI-PGC score ($\beta = 0.734, P = 0.007$) and impaired GPD ($\beta = 1.821, P = 0.045$) were significant in the final model, with black race/ethnicity approaching significance ($\beta = 1.938, P = 0.052$). Impaired GPD was associated with a 6.2-fold increase in risk for poor glycemic control. Reading did not remain significant in either model. Associations between GPD and mean A1C were no longer statistically significant when controlling for race/ethnicity, psychosocial risk, and reading ability, although the association with impaired GPD approached significance.
significance ($P = 0.081$). Impairment in DSB ($n = 3$) also remained a significant predictor of mean A1C in multivariate analysis ($\beta = 2.41, P = 0.04$). Mean DSB was no longer a significant predictor of glycemic control when controlling for other variables.

To rule out an effect of depressive symptoms on performance, we completed post hoc analyses examining self-report on the Short Mood and Feelings Questionnaire (29), a validated screener for depressive symptoms that had been administered as part of the larger clinical screening (13). Youth who met the clinical cutoff for depressive symptoms showed worse performance on TMT-B (mean 86.9 vs. 99.9; $P = 0.024$) and FAS (77.4 vs. 89.7; $P = 0.026$), but not on other measures ($P$ values $>0.3$).

**CONCLUSIONS**

Deficits in neurocognitive functioning were evident in children and adolescents within days of type 1 diabetes diagnosis. Participants performed $\approx 0.8$ SDs below normative expectations in bilateral psychomotor speed (GP) and 0.7–0.8 SDs below expected performance in visuomotor integration (VMI) and phonemic fluency (FAS). Incidence of impairment was much higher than normative expectations on all tasks except DSF/DSB. For example, $>20\%$ of youth were impaired in dominant hand fine-motor control, and $>30\%$ were impaired with their nondominant hand. These findings provide provisional support for Ryan’s (7–9) hypothesis that the peri-onset period may be a time of significant cognitive vulnerability.

Importantly, deficits were not evident on all measures. Performance on measures of attention/executive functioning (TMT-A, TMT-B, DSF, and DSB) was largely consistent with normative expectations, as was reading ability (WRAT-4), suggesting that the below-average performance in other areas was not likely due to malaise or fatigue. Depressive symptoms at diagnosis were associated with performance on TMT-B and FAS, but not on other measures. Thus, it seems unlikely that depressive symptoms accounted for the observed motor slowing.

Instead, the findings suggest that the visual-motor system may be especially vulnerable to early effects of type 1 diabetes. This interpretation is especially compelling given that psychomotor impairment is the most consistently reported long-term cognitive effect of type 1 diabetes. The sensitivity of the visual-motor system at diabetes diagnosis is consistent with a growing body of neuroimaging research implicating posterior white matter tracts and

![Figure 2](#) — Percentage impairment on neuropsychological measures at diabetes diagnosis. Impairment is defined as standard score $<70$ or scaled score $<4$. Expected rate of impairment for each measure is $2.2\%$, as defined by the area under the normal curve. Error bars show 95% CI. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

<table>
<thead>
<tr>
<th>Table 2 — Test findings by age-group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test measure</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>WRAT-4 reading</td>
</tr>
<tr>
<td>VMI</td>
</tr>
<tr>
<td>GP</td>
</tr>
<tr>
<td>GPN-Kiddie†</td>
</tr>
<tr>
<td>GPD</td>
</tr>
<tr>
<td>GPN</td>
</tr>
<tr>
<td>FAS</td>
</tr>
<tr>
<td>TMT- A</td>
</tr>
<tr>
<td>TMT- B</td>
</tr>
<tr>
<td>DSF</td>
</tr>
<tr>
<td>DSB</td>
</tr>
</tbody>
</table>

Values under the age columns are standard scores (mean 100, SD 15) or scaled scores (mean 10, SD 3). Data are mean (SD). No age-group differences were significant. †Kiddie version, 10 pegs only (vs. 25 for standard version).
associated gray matter regions (particularly cuneus/precuneus) as areas of vulnerability in type 1 diabetes (30–32). These regions form part of the neural system responsible for integrating visual inputs with motor outputs, and in adults with type 1 diabetes, structural pathology in these regions is directly correlated to performance on GP (30,31). Arbelaez et al. (33) noted that these brain areas account for impaired GPD performance on GP (30,31). Arbelaez et al. (33) noted that these brain areas form part of the “default network” (34), a system engaged during internally focused cognition that has high resting glucose metabolism and may be especially vulnerable to glucose variability.

The second major finding is that neuropsychological deficits at diagnosis were associated with diabetes outcomes a year later. Impairment in GPD was associated with a 0.77% increase in mean A1C (8.4 mmol/mol), a clinically significant finding (27). The three individuals with impaired working memory (DSB) had an even larger increase in A1C (2.41%; 25.8 mmol/mol), consistent with research indicating effects of executive functioning on diabetes self-management (35). However, this finding will need to be replicated in a larger group before any firm conclusions can be drawn.

It should be noted that previous studies (e.g., Northam et al. [3]) have not found evidence of neurocognitive dysfunction around the time of diabetes diagnosis. This may be due to study differences in measures, outcomes, and/or timeframe. We know of no other studies that completed neuropsychological testing within days of diagnosis. Given this timeframe, it is possible that our findings reflect transient effects rather than more permanent changes in the CNS. Contrary to predictions, we found no association between DKA at diagnosis and neurocognitive performance, although we cannot rule out effects of other transient metabolic changes. However, even transient effects could be considered potential indicators of CNS vulnerability. Neurophysiological changes at the time of diagnosis have been shown to persist under certain circumstances or for some patients. For example, Verrotti et al. (36) documented delayed visual pathway nerve conduction within 1 week of diabetes diagnosis, which could account for impaired GPD performance. Mean visual response latencies normalized after 6 months of strict glycemic control, but strong correlations between latencies and A1C remained evident, suggesting impairment may persist in patients with poor glycemic control. Tsaliokian et al. (37) reported electroencephalographic abnormalities in children newly diagnosed with diabetes that resolved within days for the majority but persisted for months or longer in a subset of patients. These findings suggest that some individuals may be particularly susceptible to the effects of glycemic extremes on neurocognitive function, consistent with a large body of research in developmental neuroscience indicating individual differences in neurobiological vulnerability to adverse events.

Thus, although it is possible that the neurocognitive impairments observed in our study might resolve with euglycemia, deficits at diagnosis could still be considered a potential marker of CNS vulnerability to metabolic perturbations (both acute and chronic). This would lead to the testable prediction that changes in cerebral white or gray matter and declines in neurocognitive functioning would be more likely in children who show initial impairment and go on to have poor metabolic control. It is also possible that neurocognitive impairments might resolve in some but not all patients.

Our finding that fine-motor impairment at diagnosis predicts subsequent glycemic control provides provisional support for the view that the impairment represents an early marker for a broader neurobehavioral vulnerability. Of course, it is unlikely that motor functioning by itself would have a direct impact on diabetes outcomes, but it is possible that motor deficits are a leading indicator of more generalized vulnerability to damage of cerebral white matter. Under conditions of poor glycemic control, white matter deficits may progress to the degree that attention and working memory also become affected and compromise diabetes management. Consistent with this possibility are data from longitudinal investigations showing a gradual emergence of deficits in attention/executive functioning within the first 2 years following diagnosis (3). A related possibility is that motor deficits may be a marker for damage to (or the vulnerability of) the posterior portion of the default network. Although the exact functions of this network remain speculative, it may be involved in creating and reviewing mental scenarios that “provide a means to prepare for upcoming, self-relevant events before they happen” (34). Impairment in this ability, if present, would have clear implications for managing a complex chronic illness like diabetes. Alternatively, acute motor slowing and chronically higher A1C might both reflect the downstream effects of an underlying predisposition to metabolic dysregulation. Further longitudinal research would help disentangle these possibilities.

Contrary to predictions, children with earlier onset of type 1 diabetes in our study did not have weaker neuropsychological performance. This may in part have been an artifact of using the Kiddie-GP, which appeared to lack the sensitivity of its longer counterpart. We also may have used too high an age limit to provide an adequate test of the early-onset effect, although post hoc analyses showed no relation between age and neurocognitive performance within the younger group.

This study has a number of limitations. Most important is the lack of an experimental control group. As testing was done as part of a clinical service and extracted retrospectively, there were no available controls aside from normative samples. A control group would have helped rule out the potential effects of testing in the inpatient setting, which differs from standardized procedures. Interruptions were relatively common, and as a result, not every participant completed every measure. However, none of the tests had significantly more missing data than any other, arguing against an effect of order in which the tests were given, and in no case did testing have to be discontinued due to a patient feeling unwell. Thus, there did not appear to be any systematic pattern to missingness. Nonetheless, interpretation of the findings is constrained by the fact that data from somewhat different groupings of participants contributed to each analysis. We also cannot completely rule out the impact of incomplete recovery from presenting symptoms on test performance, but as noted above, we believe we minimized this likelihood by careful exclusion of patients who felt unwell or had physical symptoms that may have affected their performance. Another limitation is the lack of neuropsychological test
data predating diabetes onset. It is possible that lower-performing participants had poor functioning prediabetes, which would argue against a peri-onset effect. However, we believe this is unlikely given the average performance in reading, which provides a reasonable estimate of premorbid abilities (25), and the high incidence of impairment we observed, which we would be unlikely to find by chance (e.g., $P < 0.0001$ for GPD). Finally, conclusions must be tempered by the relatively small sample size.

In summary, this study provides the first demonstration that type 1 diabetes–associated neurocognitive impairment can be detected at the time of diagnosis, supporting the possibility that deficits arise secondary to peri-onset effects. Whether these effects are transient markers of vulnerability or represent more persistent changes in CNS awaits further study. The findings have clinical as well as theoretical implications. Screening children for neurocognitive dysfunction at diagnosis can potentially inform preventive interventions, such as implementing academic accommodations to minimize impact on school functioning (38). Neuropsychological deficits at diagnosis might also be a marker for neurological morbidity. Correlating neuropsychological testing at diagnosis with neuroimaging would offer a powerful way to determine whether deficient neuropsychological performance represents underlying neurological pathology. Moreover, if it can be demonstrated that neurocognitive performance at diagnosis does correlate with neurocognitive findings, this would provide support for using a brief, noninvasive, and inexpensive neuropsychological test such as GP as a screening tool to determine whether more expensive neuroimaging might be indicated. This may prove especially important for detecting subclinical edema, which is believed to go unrecognized in many children with new-onset type 1 diabetes (39). Our experience in this study demonstrates that neuropsychological screening at the time of diabetes diagnosis is feasible even for young children.

Author Contributions. D.D.S. designed the study, monitored data collection, wrote the statistical analysis plan, cleaned and analyzed the data, and drafted and revised the manuscript. M.E.A. and B.J.A. contributed to writing and revising the manuscript. D.D.S. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Prior Presentation. Preliminary findings from this study were presented at the 41st Annual Meeting of the International Neuropsychological Society, Waikoloa, HI, 6–9 February 2013.

References
30. Franc DT, Kold CT, Mueller BA, Muetzel RL, Lim KO, Seaquist ER. High connectivity between reduced cortical thickness and disrupted white matter tracts in long-standing type 1 diabetes. Diabetes 2011;60:315–319

Acknowledgments. The authors would like to thank the children who participated in this study and their families.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.
that correlate with reduced neurocognitive function. Diabetes 2008;57:3083–3089