Executive Functioning, Treatment Adherence, and Glycemic Control in Children With Type 1 Diabetes

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OBJECTIVE — The primary aim of the study was to investigate the relationship among executive functioning, diabetes treatment adherence, and glycemic control.

RESEARCH DESIGN AND METHODS — Two hundred and thirty-five children with type 1 diabetes and their primary caregivers were administered the Diabetes Self-Management Profile to assess treatment adherence. Executive functioning was measured using the Behavior Rating Inventory of Executive Functioning and glycemic control was based on A1C.

RESULTS — Structural equation modeling indicated that a model in which treatment adherence mediated the relationship between executive functioning and glycemic control best fit the data. All paths were significant at $P < 0.01$.

CONCLUSIONS — These results indicate that executive functioning skills (e.g., planning, problem-solving, organization, and working memory) were related to adherence, which was related to diabetes control. Executive functioning may be helpful to assess in ongoing clinical management of type 1 diabetes.

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Type 1 diabetes is a prevalent chronic condition that affects one in every 400–600 youth (1). Effective management of blood glucose levels has been shown to reduce the risk for a wide range of diabetes-related complications (1). However, high rates of treatment nonadherence to the demanding type 1 diabetes treatment regimen and less than optimal glycemic control have been consistently reported (2–5). Maintaining adequate treatment adherence and glycemic control in type 1 diabetes requires the child and family to organize several critical daily management tasks including exercise, dietary intake, blood glucose monitoring, and insulin administration, especially related to carbohydrate intake. Effective completion of these complex tasks requires a range of cognitive skills including organization, planning, problem solving, working memory, and behavioral self-regulation (6) that encompass the broad cognitive domain of executive functioning (7).

The child's overall level of competence in executive functioning (e.g., ability to set goals and organize tasks and flexibility to adapt to treatment regimens) may be an important influence on adherence to treatment in type 1 diabetes and potentially on glycemic control. However, the relationship among executive functioning, treatment adherence, and glycemic control in pediatric type 1 diabetes is not well understood. To our knowledge, only one published study by Bagner et al. (6) has addressed this issue by demonstrating an association between executive functioning, as measured by the Behavior Rating Inventory of Executive Functioning (BRIEF) (7), and treatment adherence in a sample of youth with type 1 diabetes.

However, this study was limited by a number of relevant methodological problems that were addressed in the present study. Bagner et al. (6) studied a very broad age range of participants (ages 8–19), did not test alternative models of the relationship between executive functioning and treatment adherence, and did not include a measure of glycemic control. Age-related differences in executive functioning were not controlled. Moreover, the fact that only one model of association between level of executive functioning and treatment adherence was tested limited the validity of inferences that could be drawn. For example, Bagner et al. (6) suggested that their findings supported the hypothesis that greater executive functioning facilitates adherence. On the other hand, it is also possible that adherence, especially problematic adherence, may lead to poor glycemic control, which, in turn, may have a negative impact on memory and executive functioning (8,9). Because these alternative pathways of influence have very different implications for targeting interventions, it is important to compare them. Finally, Bagner et al. (6) did not describe the relationship of executive functioning and adherence to glycemic control. For this reason, the clinical relevance of their findings was limited.

To address the above methodological problems, the present study was designed to advance scientific knowledge in the following ways: *1*) studying a larger sample and more homogeneous age-group of children (ages 9–11) with type 1 diabetes; *2*) including a measure of glycemic control; and *3*) testing alternative models of the relationship among executive functioning, treatment adherence, and glycemic control. Our first hypothesis was that higher executive functioning would be associated with better treatment adherence, which in turn would relate to better glycemic control. Our second hypothesis was that the relationship between executive functioning and glycemic control

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would depend on (that is, be mediated by) treatment adherence.

RESEARCH DESIGN AND METHODS

— Participants were 235 children with type 1 diabetes and their caregivers who were followed at pediatric diabetes clinics at three university-affiliated medical centers in the U.S. Institutional review boards at each site approved the study. Data were collected as part of an ongoing, 3-year longitudinal study with the aim of investigating hypothesized psychological processes including parental support and changes in allocation of treatment responsibility that may promote treatment adherence during early adolescence in type 1 diabetes. For the purpose of the present analysis, only baseline data were considered. No prior results from this study have been reported.

Caregivers and children were recruited during a regularly scheduled outpatient clinic visit. Inclusion criteria included diagnosis of type 1 diabetes for at least 1 year, ages 9–11, absence of potential secondary causes of type 1 diabetes diagnosis (e.g., glucocorticoid treatment or cystic fibrosis), English-speaking family, and no known plans to move out of the area within the next 3 years. Exclusion criteria included current involvement in foster care, the presence of severe psychiatric disorders or comorbid chronic conditions (e.g., renal disease) that required burdensome ongoing treatment regimens, or diagnosis of mental retardation.

Eligible participants were identified and contacted by clinic personnel to ask about their interest in the study and then were approached by research staff who explained the study procedures. Of the 361 eligible participants who were approached, 240 (66.5%) consented and participated.

As shown in Table 1, the sample included 108 boys and 127 girls, ages 9.0–12.1 (mean ± SD 10.54 ± 0.95) (4 children were recruited at age 11 but were not seen for baseline visits until after they turned 12 years of age). On average, participants had diabetes for 4.39 ± 2.46 years (range 1–11 years). Based on parental report, three children experienced a severe hypoglycemic episode, resulting in seizures or loss of consciousness in the past 3 months.

Reasons for not participating included being too busy ($n = 54$), having no transportation ($n = 3$), and other ($n = 64$). Signed informed consent was obtained from a parent or legal guardian, and written assent was obtained from 11-year-old children. Five parents did not complete the measure of executive functioning.

Measures

BRIEF. Children's executive functioning was measured using the BRIEF, an 86-item parent report measure that assesses children's executive functioning (e.g., goal setting, organization, working memory, and so on) (7). The BRIEF includes 3-point Likert scale items that indicate the extent to which the child's behavior never occurred, sometimes occurred, or occurred often. The range of possible composite raw total scores is 72 to 216; and the range of possible composite *T* scores is ≤30 to ≥100. For this sample, the range of composite raw total scores was 74 to 198, and the range of composite *T* scores was 31.92 to 82.33.

Reliability of the BRIEF has been established ($\alpha = 0.80–0.98$) for both clinical and normative samples (parent and teacher forms) (7), and validity has been documented with other measures of behavioral and attentional functioning (7). In our sample, internal consistency was 0.98. The composite raw score for the Global Executive Composite (GEC), which is a summed score of all subscales, was used in all analyses. The GEC composite raw score and the standardized GEC *T* score were virtually identical ($r = 0.99$). Raw scores were used in the primary statistical analyses.

Diabetes Self-Management Profile. The Diabetes Self-Management Profile (DSMP) is a 25-item structured interview, which was administered to assess diabetes-related adherence behaviors during the previous 3 months (11). Questions were asked in an open-ended manner and addressed the following domains: insulin administration, blood glucose monitoring, exercise, diet, and hypoglycemia management. A total score was calculated by summing all items to yield an overall adherence score. Higher scores reflected better adherence. The DSMP comprises both dichotomous items (yes or no) and 3- to 5-point Likert scale items that were coded based on how the child or primary caregiver responded to the open-ended questions. The range of possible total scores is 0 to 88. The range of total scores for the primary caregiver in this sample was 42 to 86, and the range of total scores for the child respondents was 39 to 80.

The DSMP total score has demonstrated good internal consistency ($r = 0.76$), moderate cross-informant validity for both parent and child report ($r = 0.26$), and strong interrater agreement ($r = 0.94$) (11). This measure has also demonstrated good predictive validity between parent- and child-reported adherence and self-management behaviors and glycemic control (11). In the present sample, internal consistency was 0.62 for the parent DSMP and 0.59 for the child version.

Children and parents were interviewed separately by trained research staff. All research assistants had at least a bachelor's degree. Several had master's degrees, and one had a Ph.D. Training included a general meeting of investigators and site-specific training that included reading the procedure manual for the DSMP, practicing with another research assistant, observing an experienced research assistant conduct DSMPs, being observed while conducting DSMPs, and then conducting DSMPs independently. Additional quality control procedures involved review of data forms at the central site and troubleshooting problems in administration by the study coordinator at the central site and research assistants at different sites.

Glycemic control. A1C provided an estimate of metabolic control over the previous 2–3 months. Blood samples were obtained by a fingerstick during the visit, and samples from each study site were shipped to one central laboratory for standardization purposes. Samples were analyzed using the TOSOH-G7 method (reference range 4.0–6.0%).

RESULTS

Descriptive analyses

All variables were approximately normally distributed, with the exception of A1C, which was significantly skewed. For this reason, a log transformation was performed for this measure, and all subsequent analyses were conducted on the transformed variable. Average ±SD A1C for the sample was 8.16 ± 1.33 (range 5.7–16.8). The American Diabetes Association recommends an A1C of ≤8.0% for patients aged 6–12 years (1). Thus, the present sample demonstrated fair glycemic control.

For the BRIEF, the average ± SD GEC raw score was 118.98 ± 27.55. The average sex- and age- corrected GEC *T* score (mean ± SD 52.12 ± 11.17) was in the normal range of functioning. For the

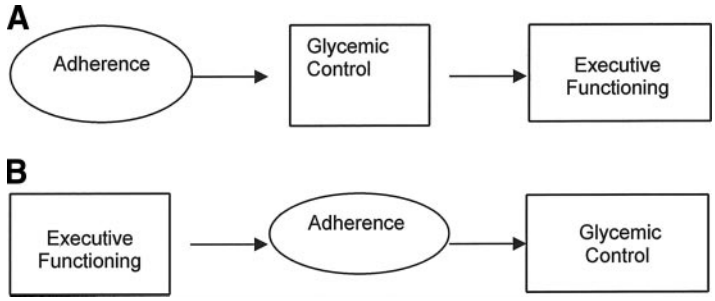

Figure 1—*Hypothesized alternative models of the relationship between executive functioning, treatment adherence, and glycemic control.* A*: Glycemic control mediating the relationship between adherence and executive functioning.* B*: Adherence mediates the relationship between executive functioning and glycemic control.*

DSMP, the adherence score based on parent report (65.16 ± 8.48) was higher than child reported adherence (60.86 ± 8.10; $t = -7.33$, $P < 0.01$).

Statistical analysis

Two alternative hypothesized models that were tested in this study are shown in Fig. 1 (models A and B). In testing model A, bivariate analyses indicated no association between glycemic control and executive functioning. For this reason, this model did not fit the data, indicating that glycemic control did not mediate the relationship between adherence and executive functioning.

In testing model B, bivariate analyses indicated significant correlations between executive functioning with adherence ($r > -0.27$, $P < 0.001$) and between adherence and glycemic control ($r = -0.33$, $P < 0.001$). Structural equation modeling (SEM) was then used to test the adequacy of the statistical fit of model B. Advantages of SEM include specific estimation of error terms and availability of a method to determine the statistical adequacy of model fit (11). In the SEM analysis, the measurement model that included the DSMP parent and child reports as indicators for the latent variable of adherence was tested using AMOS (version 17).

Fit indexes were used to assess model fit. An acceptable fit was defined as follows: if the likelihood ratio χ^2 test of model fit was nonsignificant. Both the comparative fit index (CFI) and the Bentler and Bonnett Normed Fit Index (NFI) were >0.90, and the root mean square error of approximation (RMSEA) was <0.08 (12). Using these criteria, all indexes indicated adequate fit for the overall measurement model (likelihood ratio χ^2 [df = 2] = 5.34, $P = 0.07$; CFI = 0.96; NFI = 0.94; RMSEA = 0.08). The structural model (i.e., treatment adherence mediating the relationship between executive functioning and glycemic control) was then tested. Figure 2 shows the standardized path coefficients. The results indicated that all paths were significant at $P < 0.01$. Examination of the fit indexes showed that the overall fit of the model was good; all fit indexes surpassed the threshold for adequate fit (likelihood ratio χ^2 [df = 2] = 4.04, $P = 0.13$; CFI = 0.97; NFI = 0.96; RMSEA = 0.07). Examination of modification indexes revealed that adding no other paths improved model fit.

CONCLUSIONS

The primary findings of the present study were the following: *1*) the level of the child's executive functioning was associated with treatment adherence and self-management such that high levels of executive functioning related to better adherence; *2*) the child's adherence to the diabetes treatment regimen related to glycemic control such that better control was associated with better adherence; and *3*) the child's glycemic control depended on (i.e., was mediated by) treatment adherence. To our knowledge, this is the first empirical demonstration of the interrelationships among executive functioning, treatment adherence, and glycemic control in a sample of children with type 1 diabetes.

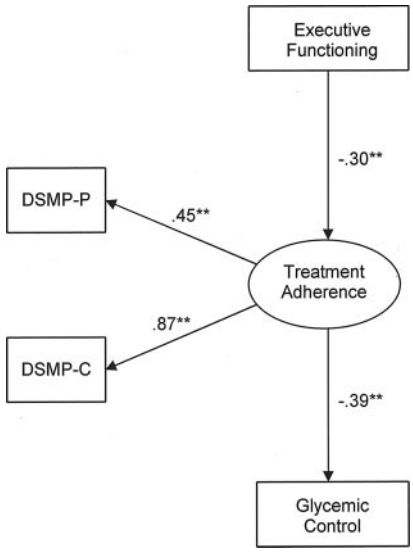

Figure 2—*Structural model with treatment adherence mediating the relationship between executive functioning and glycemic control. Standardized path coefficients are shown. DSMP-P, Diabetes Self-Management Profile, parent interview; DSMP-C, Diabetes Self-Management Profile, child interview.* **P < *0.01.*

These findings underscore the potential importance of individual differences in executive functioning (e.g., goal setting, behavioral regulation, and working memory) in promoting adherence and glycemic control in children with type 1 diabetes. Children with competencies in executive functioning were more likely to demonstrate better adherence in their diabetes regimen, which in turn related to glycemic control.

Several issues, including sample selection and generalizability, should be considered in interpreting our findings. The generalizability of the findings is limited by the fact that this sample included a majority of Caucasian patients who were also not at high risk for deficits in executive functioning based on their age at diagnosis or frequency of hypoglycemic episodes (8,9). For this reason, it is possible that the findings would have been even more powerful in a sample of children and adolescents with type 1 diabetes with a broader range of ethnic diversity, educational levels, and executive functioning competence.

Future studies will be necessary to determine whether our findings generalize to a more diverse sample of families, children with higher rates of hypoglycemia, or older adolescents who might be expected to demonstrate greater problems in executive functioning (12). Executive functioning competence might be expected to have a stronger relationship to adherence in older adolescents who have greater levels of responsibility for diabetes management than the younger children who participated in this study. On the other hand, parental executive functioning may be especially influential in the management of younger (preschool and school-aged) children with type 1 diabetes and should be studied in future research.

Table 1—*Demographic characteristics of participants*

	% (*n*)	Mean ± SD
Child age (years)	—	10.5 ± 1.0
Primary caregiver age (years)	—	40.6 ± 6.0
Child sex		
Male	46.0 (108)	
Female	54.0 (127)	
Relationship of primary caregiver		
Biological mother	94.9 (223)	
Biological father	2.6 (6)	
Other	2.6 (6)	
Child ethnicity		
Non-Hispanic, Caucasian	76.2 (179)	
Non-Hispanic, African American	4.3 (10)	
Non-Hispanic, other	6.8 (16)	
Hispanic, Caucasian	10.6 (25)	
Hispanic, other	2.1 (5)	
Primary caregiver education (years)	—	14.5 ± 2.3
Duration of diabetes (years)	—	4.4 ± 2.4
Insulin regimen		
Insulin pump	56.2 (132)	
Multiple daily injections	43.8 (103)	

Based on our cross-sectional design, we cannot conclude that executive functioning influenced adherence or that adherence influenced control. Moreover, our study described the relationship of executive functioning competence to adherence and glycemic control rather than the relationship of clinically significant deficits in executive functioning to nonadherence or glycemic control. It is also possible that the relationships among executive functioning, adherence, and control may differ in clinically relevant subgroups of patients (e.g., those with very poor versus those with good control). For this reason, the direction of effects found here and our inferences concerning causal influence will be tested in our ongoing prospective study. It would also be informative to study the potential impact of executive functioning on children's competence in managing information from new technologies such as continuous blood glucose monitoring.

Our findings have several relevant potential clinical implications. For example, they suggest that measuring executive functioning competence in ongoing management of type 1 diabetes may be helpful in understanding protective factors associated with better diabetes management and adherence. On the other hand, children with clinically significant deficits in executive functioning may also benefit from interventions that focus on providing family support to improve their organizational, planning, and problem-solving skills (13).

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References

1. American Diabetes Association. Standards of medical care for patients with diabetes mellitus. Diabetes Care 2003;26:S33–S50
2. Miller-Johnson S, Emery RE, Marvin RS, Clarke W, Lovinger R, Martin M. Parent-child relationships and the management of insulin-dependent diabetes mellitus. Consult Clin Psychol 1994;62:603–610
3. Morris AD, Boyle DI, McMahon AD, Greene SA, MacDonald TM, Newton RW. Adherence to insulin treatment, glycaemic control, and ketoacidosis in insulin-dependent diabetes mellitus. The DARTS/MEMO Collaboration Diabetes Audit and Research in Tayside Scotland Medicines Monitoring Unit. Lancet 1997;350:1505–1510
4. Wysocki T, Greco P, Buckloh LM. Childhood diabetes in psychological context. In Roberts MC, ed. *Handbook of Pediatric Psychology*. 3rd ed. New York, Guilford, 2003, p. 304–320
5. Helgeson VS, Siminerio L, Escobar O, Becker D. Predictors of metabolic control among adolescents with diabetes: a 4-year longitudinal study. J Pediatr Psychol 2007;34:254–270
6. Bagner DM, Williams LB, Geffken GR, Silverstein JH, Storch EA. Type 1 diabetes in youth: the relationship between adherence and executive functioning. Child Health Care 2007;36:169–179
7. Gioia GA, Isquith PK, Guy SC, Kenworthy L. Behavior rating inventory of executive function. Child Neuropsychol 2000;6:235–238
8. Gaudieri PA, Chen R, Greer TF, Holmes CS. Cognitive function in children with type 1 diabetes: A meta-analysis. Diabetes Care 2000;31:1892–1897
9. Ryan CM. Memory and metabolic control in children. Diabetes Care 1999;22:1239–1241
10. Harris MA, Wysocki T, Sadler M, Wilkinson K, Harvey LM, Buckloh LM, Mauras N, White NH. Validation of a structured interview for the assessment of diabetes self-management. Diabetes Care 2000;23:1301–1304
11. Kline RB. *Principles and Practice of Structural Equation Modeling*. New York, Guilford Press, 2004
12. Dahl RE. Adolescent brain development: a period of vulnerabilities and opportunities. Keynote address. Ann NY Acad Sci 2004;1021:1–22
13. Wysocki T, Harris MA, Greco P, Bubb J, Danda CE, Harvey LM, McDonell K, Taylor A, White NH. Randomized, controlled trial of behavior therapy for families of adolescents with insulin-dependent diabetes mellitus. J Pediatr Psychol 2000;25:23–33