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Clinical Presentation and Memory Function in Youth with Type 1 Diabetes

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Abstract

Objective—While cerebral edema and diabetic ketoacidosis (DKA) in type 1 diabetes (T1DM) have well-described acute effects on cognition, little is known about the impact of clinical presentation on longer-term cognitive outcomes. We hypothesized that clinical factors (degree of hyperglycemia exposure and DKA) at the time of diagnosis would relate to cognition within 3.5 months later in children with T1DM.

Methods—Cognitive testing was performed on children 7–17 years old with T1DM (n=66) within 3.5 months of diagnosis and siblings without T1DM (n=33). Overall intelligence, processing speed and memory (including a sensitive long-delay spatial memory test; Spatial Delayed Response or SDR) were assessed. Medical records were reviewed for hemoglobin A1c (HbA1c), DKA status, and other clinical factors at diagnosis.

Results—Within the group with T1DM, 17 children presented in DKA and 49 did not. After adjusting for age, gender, and socioeconomic status, the subgroup with T1DM and DKA at diagnosis performed worse on the long-delay SDR task compared to sibling controls (p=0.006). In addition, within the group with T1DM higher HbA1c at diagnosis was associated with worse

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performance on the long-delay SDR task ($p=0.027$). Performance on the other cognitive tasks was not different across groups or subgroups.

Conclusions—DKA and degree of hyperglycemia exposure at diagnosis have implications for long delay spatial memory function within 3.5 months of diagnosis. These findings suggest that early detection of T1DM, which decreases risk for prolonged exposure to hyperglycemia and DKA, may avoid negative effects on memory function.

Keywords

Diabetic Ketoacidosis; Diabetes Mellitus; Cognition

Severity of clinical presentation of type 1 diabetes (T1DM) in youth may vary, reflecting differences in duration of hyperglycemia exposure and degrees of beta cell failure (1). A delay in the initiation of insulin therapy may result in the severe and acute life threatening condition of diabetic ketoacidosis (DKA) (2, 3). Approximately 1% of cases of DKA result in cerebral edema, and in severe cases death (4). Despite efforts in increasing awareness of early symptoms of T1DM, the prevalence of DKA at diagnosis remains high (5), particularly in children under age 5, adolescents, individuals lacking health insurance, and those of a lower socioeconomic status (6–8).

Studies on youth with longer duration of T1DM have shown that degree of exposure to hyperglycemia is negatively correlated with verbal intelligence, executive functioning, learning and memory (9–11). Likewise, children with a relatively short duration of T1DM and limited exposure to glycemic extremes beyond what they experienced at diagnosis have lower verbal intelligence and executive function (12). These findings suggest that clinical factors at the time of diagnosis may influence some cognitive outcomes. The effects of DKA on the developing brain and cognition (13–15) have also been studied, but only a few studies assessed DKA at diagnosis and included measures of cognition after the DKA event resolved (14, 16). One study found that children with DKA at diagnosis did not differ from those without DKA on a clinical neuropsychological test battery 6 months after starting insulin treatment (14). However, the study did not include controls without diabetes, and did not assess the effect of degree of hyperglycemia exposure prior to diagnosis on cognition. Thus, the literature has not differentiated whether cognitive outcomes in youth with T1DM are due to the effect of marked hyperglycemia or DKA exposure at diagnosis, the cumulative effect of subsequent exposure to chronic hyperglycemia, or the combined effect of factors at diagnosis and subsequent hyperglycemia exposure.

Understanding the discrete effects of the severity of clinical presentation of T1DM on future cognitive function is important because the factors beyond DKA that influence risk for poor cognitive outcomes in newly diagnosed T1DM are not well understood. Moreover, such information could be useful in explaining conflicting or unresolved data from studies of longer-duration youth with T1DM. Findings linking a more severe clinical presentation to poorer cognitive outcomes could reinforce the importance of early detection of T1DM onset. Thus, the specific purpose of this study was to determine if cognitive function differed in newly diagnosed children with T1DM compared to sibling controls within 3.5 months of diagnosis, and whether cognitive performance in children with T1DM was associated with

the severity of clinical presentation, including the presence of DKA and degree of hyperglycemia exposure prior to diagnosis.

Research Design and Methods

Participants

Youth between the ages of 7–17 diagnosed with T1DM at St. Louis Children's Hospital were recruited to participate in the study. Healthy siblings within the same age range (without diabetes) of the patients were recruited as controls. The Washington University School of Medicine's Human Research Protection Office approved the protocol for the study and all parents or guardians provided written informed consent and participants provided assent.

Subjects were excluded from participation in the study if they had a history of psychiatric or neurological disorders, hypertension, another chronic disease besides asthma, or if they were on psychoactive medications. Participants were also excluded if they had premature birth (<36 weeks gestation) with complications, or if they had been enrolled in special education classes. Socioeconomic status of the family was calculated based on parents' occupational score on the Hollingshead Four Factor Index of socioeconomic status (17).

Medical History

Medical information related to diagnosis with T1DM was obtained from participants' medical records from their new onset inpatient visit at St. Louis Children's Hospital. These variables were: Tanner pubertal stage, blood glucose level (mg/dL), hemoglobin A1c (HbA1c), bicarbonate (HCO_3 (mmol/L)), blood urea (BUN (mmol/ urea/L)), sodium, and osmolality (osmol/L). Osmolality was calculated using the formula $(2 \times \text{Na}) + (\text{blood glucose}/18) + (\text{BUN}/2.8)$. Puberty was established if a patient was greater than or equal to Tanner stage 2 for breast or testicular development. DKA at diagnosis (DKA+ vs. DKA–) was determined using the Diabetes Control and Complications (DCCT) criteria of a venous pH <7.3, or bicarbonate <15 mmol/L. Severity of DKA was classified as mild (venous pH between 7.20 to 7.29, or bicarbonate between 10–14 mmol/L), moderate (venous pH between 7.10 to 7.19, or bicarbonate between 5–9 mmol/L), or severe (venous pH <7.10, or bicarbonate <5 mmol/L) (18). For youth who did present in DKA, we also recorded their Glasgow Coma Score, anion gap, urine ketone values, and whether they were admitted to the ICU or had an insulin drip. Finally, for all the patients with T1DM, we assessed the HbA1c level obtained at their outpatient follow-up visit (3 to 6 months from diagnosis) closest to the time of their cognitive assessment (within 3.5 months of diagnosis). This allowed us to ensure that the cognitive effects observed were due to the patient's glycemic exposure prior to presentation as opposed to poor glycemic control between diagnosis and follow-up. Handedness was assessed using the Edinburgh Handedness Inventory in all subjects (19).

Between diagnosis and the 3-month testing session, reports of DKA and severe hypoglycemic episodes were obtained through a detailed interview and self-report questionnaire with the participant and parent or guardian. A severe hypoglycemic episode was defined based on the DCCT criteria as a low blood sugar requiring the assistance of

someone else due to seizure, loss of consciousness, disorientation, or the need of a glucagon injection (20). For the purpose of self-report, an episode of DKA was defined as an event where the participant had high blood sugar with ketosis requiring IV fluids.

Cognitive testing—Cognitive testing was performed within 3.5-months of diagnosis for participants with T1DM. In the subjects with T1DM, blood glucose levels were measured before and after cognitive testing. If blood glucose was <70 mg/dL (4 mmol/l) prior to testing, snacks were provided; if it was >300 mg/dL (17 mmol/l) prior to testing, patients were treated with insulin. Testing proceeded once blood glucose levels were within 70–300 mg/dL (4–17 mmol/l). The following cognitive tests were administered to participants:

Intelligence—The General Information and Spatial Relations tests (Woodcock-Johnson III (WJIII)) were administered to assess verbal and spatial intelligence, respectively. In previous studies done in youth with longer duration of T1DM, performance on both subtests has been lower in youth with T1DM and related to hyperglycemia exposure (General Information) (11) and severe hypoglycemia exposure (Spatial Relations) (11). The General Information test requires subjects to answer questions about where objects are found and the general purpose of objects (21). The Spatial Relations test requires participants to manipulate objects visually to complete a shape (21).

Clinical Memory Tests—The Word Lists subtest (Children's Memory Scale (CMS)) was used as a standard clinical neuropsychological test of episodic learning and memory. Performance on these tasks has been inconsistent in youth with T1DM (11, 12). The Word Lists test (CMS) assesses recall of 14 words over the short (immediate) and long (delayed) term (22). An interference second set of words was also presented after the learning trials, and prior to the immediate recall. After the delayed recall of words, delayed recognition of words also was assessed.

Experimental Memory Test—The Spatial Delayed Response (SDR) Task, a well-validated and sensitive short and long delay spatial memory task (23) was also administered. Poorer long-delay performance on this task has been associated with T1DM and exposure to severe hypoglycemia (11, 24) and is related to the hippocampal-mediated declarative memory system (25, 26). In this task participants were asked to recall the position of one or two dots on a computer screen after a short (5 s) or long (60 s) delay. For each trial, subjects focused on a cross in the center of a computer screen while one or two dots were presented for 150 ms in 1 of 32 locations at a fixed radius from the center. A short or long delay was then imposed during which shapes (squares, diamonds, or triangles) appeared one at a time in random order in the center of the screen, and the participants were required to press a button in response to the diamond shape. Following the delay, a cross was presented and subjects pointed on the screen where they remembered seeing the dot(s). A cursor was moved by the experimenter to record the remembered location. Error was automatically calculated as the distance in mm from the remembered location to the original target location for each trial. In order to control for motor performance and understanding of task demands, the dot the participants were instructed to remember appeared again on the screen and the participants only had to put their finger on the dot (short delay cue present trials). Trial types

were presented randomly: eight trials for each delay condition (5 and 60 s) and four short delay cue-present trials. Average error in mm was calculated for each subject for each trial type.

Response Inhibition and Processing Speed—The Go-No-Go Task measured inhibitory control (27). Subjects were required to press a button as quickly as possible in response to a common target shape (“Go” trials, n=150) in the center of a computer screen and to withhold responses for a non-target shape (“No-Go” trials, n=50). The Speed Task measured simple reaction time (RT) and required subjects to press a button on the computer in response to an image, which occurred on every trial (27). Median RT and the number of false-positive errors were recorded for both tasks. Performance on these tasks is not known to be affected in youth with T1DM, although within adults, hyperglycemia exposure is related to slower processing speed (28).

Methodological and Statistical Analyses

Hemoglobin A1c (HbA1c) was analyzed using an Afinion AS100 Analyzer, bicarbonate and pH were analysed using a Radiometer Gas Machine model 837.

SPSS (IBM Statistics for Macintosh, Version 22.0 Armonk NY: IBM Corp) was used to analyze the data. Groups (T1DM, sibling controls) and subgroups (T1DM with DKA, T1DM without DKA, sibling controls) were compared on demographic and clinical variables using independent samples t-tests assuming equal variance. Analyses were controlled for age, gender, and total occupational score for parents (as an index of socioeconomic status). HbA1c levels at diagnosis and at follow-up clinic visits were compared within the entire T1DM group using a paired t-test and compared between subgroups using a repeated measures general linear model (GLM).

Cognitive variables were compared across groups and subgroups using GLM analyses, adjusting for age, gender, and total occupational score (socioeconomic status). For tasks with multiple conditions (e.g. SDR, Word Lists), repeated measures GLMs were used. Significant main effects or group by condition interactions were followed with univariate analyses and post hoc comparison tests. Hierarchical linear regression was used to evaluate the relationship between HbA1c at diagnosis and cognitive variables between groups. Significance was set at a two tailed p value of less than 0.05.

Results

Subjects

The study sample consisted of 66 youth with T1DM and 33 sibling controls without T1DM between ages 7 and 17 years at enrollment. 27 participants with T1DM had 1 sibling control without diabetes, 1 participant with T1DM had 2 sibling controls without diabetes, and the rest had no sibling controls enrolled. Four of the controls did not have a sibling with T1DM in the study due to dropout or meeting exclusion criteria. Age, gender, and socioeconomic status did not differ between groups (Table 1). After diagnosis and during the length of the study, subjects with T1DM were treated with an intensive basal-bolus insulin regimen with 4 injections per day.

Within those with T1DM, HbA1c did not differ between those that were or not in puberty ($t=-0.38$, $df=60$, $p=0.71$). In addition, 17 subjects with T1DM presented in DKA at diagnosis (DKA+) and 49 did not (DKA-). Age, gender, and socioeconomic status (total occupational score) did not differ between DKA+, DKA- and controls (Table 1). Within those that presented in DKA, 10 had mild DKA, 5 had moderate DKA, and 2 had severe DKA by DCCT criteria. All patients with DKA were on an insulin drip except for 6 of the patients that presented in mild DKA. Given the limited number of subjects with greater than mild DKA, statistical analyses could not be performed across severity categories. Between diagnosis and the 3-month testing session, no participants reported episodes of severe hypoglycemia. No participants reported having any additional DKA episodes. No children in the study had clinical evidence of cerebral edema at time of DKA.

Subgroups (DKA+ vs. DKA-) did not differ in osmolality ($t=0.04$, $df=64$, $p=0.97$), HbA1c level at diagnosis ($t=-1.01$, $df=64$, $p=0.32$), HbA1c level at follow-up ($t=-1.23$, $df=57$, $p=0.22$), or change in HbA1c level between diagnosis and follow-up ($t=-0.76$, $df=57$, $p=0.45$), although as expected, with the initiation of insulin treatment, both subgroups exhibited decreased HbA1c levels over time (DKA+, $t=13.82$, $df=13$, $p<0.001$; DKA-, $t=14.67$, $df=44$, $p<0.001$), (Table 1). DKA Subgroups (DKA+ vs. DKA-) differed in bicarbonate level ($t=11.26$, $df=64$, $p<0.001$) and anion gap ($t=-7.14$, $df=62$, $p<0.001$). Subgroups differed in the proportion of subjects in puberty, with more pubertal subjects in the DKA+ group, and more pre-pubertal subjects in the DKA- group ($X^2=5.14$, $df=1$, $p=0.023$). Some participants had missing cognitive test data due to computer issues, lack of time, refusal, or for other reasons (General Information, $n=1$; Spatial Relations, $n=1$; Speed Task, $n=5$; Go-No-Go, $n=6$; Word Lists, $n=5$; SDR, $n=7$).

Cognitive performance across group (Type 1 Diabetes vs. Control) (Table 1)

Groups did not differ on General Information ($F(4, 93)=1.18$, $p=0.28$, $d=0.23$), Spatial Relations ($F(4, 92)=1.04$, $p=0.31$, $d=0.21$), median Speed RT ($F(4, 89)=0.28$, $p=0.60$, $d=0.11$) median Go-No-Go RT ($F(4, 88)=0.003$, $p=0.96$, $d<0.001$), and Go-No-Go false positive errors ($F(4, 88)=0.08$, $p=0.77$, $d=0.06$). Performance across time points (immediate and delayed condition) on the Word Lists recall task did not vary by group ($F(1, 89)=0.19$, $p=0.70$, $d=0.07$). For the SDR task, there was no effect of subgroup on performance across time points (cue present, 5 s, 60 s) on the 1 dot task ($F(2, 86)=2.23$, $p=0.11$, $d=0.45$). However, performance across time points did vary between groups on the 2 dot SDR task ($F(2,86)=6.06$, $p=0.003$, $d=0.75$) (Figure 1). Post-hoc comparisons revealed that the group with T1DM had greater error on the 60 s delay compared to the control group ($F(1,87)=4.72$, $p=0.033$, $d=0.46$) (Table 1) (Figure 1).

Cognitive performance within subjects with T1DM

A higher HbA1c at diagnosis was significantly associated with greater error on the 2 dot SDR 60 s condition ($F(3, 55)=9.12$, $p=0.027$, $\beta=0.24$, R^2 change=0.35) (Figure 3) (Table 1). After controlling for DKA presence the effect of HbA1c on the error in the 2 dot 60 s condition was borderline significant ($4, 54)=8.97$, $p=0.052$, $\beta=0.21$, R^2 change =0.38. No association was found between HCO₃, pH, osmolality and anion gap, with any of the cognitive testing.

Cognitive performance across subgroups (DKA+, DKA-, Controls)

Subgroups did not differ on General Information ($F(5,92)=0.71$, $p=0.50$, $d=0.25$), Spatial Relations ($F(5, 91)=0.53$, $p=0.59$, $d=0.21$), median Speed RT ($F(5, 88)=0.14$, $p=0.87$, $d=0.11$), median Go-No-Go RT ($F(5, 87)=0.008$, $p=0.99$, $d<0.001$) and Go-No-Go false positive errors ($F(5, 87)=0.40$, $p=0.67$, $d=0.19$). The performance across time points (between immediate and delayed condition) on the Word Lists recall did not vary by subgroup ($F(2, 88)=0.08$, $p=0.92$, $d=0.09$). For the 1 dot SDR task, there was no effect of subgroup on performance across time points (cue present, 5 s, 60 s) on the 1 dot task ($F(2, 86)=2.57$, $p=0.08$, $d=0.49$). However, performance across time points did vary by subgroup on the 2 dot SDR task ($F(4,172)=4.41$, $p=0.002$, $d=0.64$) (Figure 2). Post hoc comparisons were conducted to determine which delay condition of the 2 dot SDR and which subgroups were driving the overall effect. The post hoc comparison showed that subgroups performed differently on the 2 dot 60 s delay ($F(5, 86)=4.80$, $p=0.011$, $d=0.67$). Compared to the control group, the group without DKA did not have greater error on the 60 s delay ($F(4, 71)=2.31$, $p=0.13$, $d=0.36$). Compared to the group without DKA, there was borderline evidence that the group with DKA had greater error on the 60 s delay ($F(4, 55)=3.88$, $p=0.054$, $d=0.53$) (Figure 2). However, compared to the control group, the group with DKA had greater error on the 60 s delay ($F(5, 42)=8.52$, $p=0.006$, $d=0.88$).

Conclusions

This study shows that the presence of DKA at diagnosis and greater hyperglycemia exposure prior to diagnosis in youth with T1DM can influence long delay spatial memory performance months after these exposures have occurred. The selectivity of the cognitive effects to a sensitive, well-validated memory task has been observed in other cross-sectional analyses of youth with a longer duration of T1DM (11, 24), which highlights the selective cognitive impact of this disease.

Few studies have investigated the impact of severity of clinical presentation at diagnosis on long-term cognitive function (14) in children with T1DM. DKA or HbA1c at time of diagnosis are rarely accounted for in these types of studies. One previous study found that youth presenting with DKA at diagnosis had poorer performance on a verbal delayed memory task and a mental state task within 48 hours of diagnosis compared to those presenting without DKA at diagnosis (14). However, no differences were found at follow-up (5 days and after) across DKA subgroups. In addition, there was no control group without T1DM and no baseline clinical data (e.g. HbA1c at diagnosis, osmolality, PH, HCO₃, anion gap and pubertal status) was obtained on their subjects. In our study, we observed that patients in the subgroup with T1DM and DKA performed worse compared to healthy controls on the long delay condition of the 2 Dot SDR task within 3.5 months of diagnosis. Moreover, this finding was not attributable to the severity of DKA but rather to DKA state per se. DKA, a severe complication of T1DM, is known to affect the structure and function of the brain (4, 13, 29, 30), which could adversely affect cognition. Children with DKA at diagnosis have been shown to have both white and gray matter alterations in the frontal, temporal, and parietal regions that did not resolve 6 months after diagnosis (14). In addition, a study by Ghetti et al. found that children who experienced DKA at any age or stage of

diagnosis had lower memory performance compared to those who never had DKA (13), and consistent with our findings, changes in memory function were present even when DKA did not result in clinically apparent cerebral edema. However, the study was unable to differentiate between the effects of the clinical presentation at diagnosis of T1DM and the effects after diagnosis of exposure to hyperglycemia and DKA.

Since not all children present in DKA at diagnosis, our study also aimed to determine the cognitive effects of greater exposure to hyperglycemia prior to diagnosis of T1DM. We found that a higher HbA1c at diagnosis was associated with poorer long delay spatial memory at the time of assessment. The rigorous design of our study, including sibling controls and lack of confounders such as hypoglycemia and recurrent DKA over time, expands the literature by suggesting that an elevated HbA1c or a single DKA episode at diagnosis may have effects on memory function within 3.5 months of diagnosis.

DKA and hyperglycemia may affect brain structure or function through several potential mechanisms. Hyperglycemia is associated with oxidative stress, which could result in cellular dysfunction (31). DKA can cause acute osmotic changes in the brain (32) that may result in cerebral edema. Even though regionally specific effects are not well understood, one recent study showed that severe DKA in rats was likely associated with reactive gliosis (based on glial fibrillary acidic protein (GFAP) staining), which preferentially affected the hippocampus more so than other regions (30). That study reported hippocampal effects both during DKA, and 4, 24, and 72 hours post insulin and saline treatment. Given that poor performance on the long delay condition of the 2 dot SDR task relates to the functioning of the hippocampus and surrounding cortex in both animals (25) and humans (26), it would be reasonable to examine in follow-up the structure and function of the hippocampus in children who experienced DKA or had a very elevated HbA1c at diagnosis to determine if there are underlying structural changes that explain performance differences on the 2 dot SDR Task.

Despite its novelty, this study has several limitations. The relatively small number of subjects in the DKA severity subgroups limits our power to assess the cognitive effects of DKA severity. Due to the retrospective nature of this study (e.g. no cognitive testing prior to T1DM diagnosis) we cannot rule out that the cognitive differences between groups and subgroups observed in our study were present prior to diagnosis. In addition, although the long-delay 2 dot SDR task is a sensitive memory measure within youth with T1DM (11, 24), it is unknown whether these differences have any implications for clinical, academic or occupational outcomes. Finally, an additional limitation in the study could be that the results observed in the long-delay 2 dot SDR task were due to type 1 error, although other studies have reported similar cognitive findings using the same test in youth with T1DM (11, 24).

Our findings have clinical implications, suggesting that early detection of T1DM may limit potential cognitive impairments by decreasing the degree of hyperglycemia exposure prior to diagnosis and avoiding DKA. Moreover, it has been noted that cognitive function at diagnosis may be predictive of long-term glycemic control, emphasizing the importance of early detection (16). Educational interventions targeting pediatricians and the public could increase awareness of signs and symptoms of T1DM, which may result in improved

cognitive functioning later in life (33). However, long-term prospective studies of newly diagnosed T1DM individuals are necessary to determine the impact of diabetes and its clinical presentation on cognition, brain development, and everyday functioning.

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Figure 1.

A) 2 dot SDR performance across groups with T1DM and healthy controls. Within three and a half months after diagnosis, groups performed differently across delays on the 2 dot SDR task ($p=.003$). *The group with T1DM had greater error on the 60 s delay of the 2 dot SDR task compared to controls ($p=.033$). B) 2 dot SDR performance across subgroups without DKA, with DKA, and healthy controls. Within three and a half months after diagnosis, subgroups performed differently across delays on the 2 dot SDR task ($p=.011$). *The subgroup with DKA at diagnosis had greater error on the 60 s delay of the 2 dot SDR task compared to the control group ($p=.006$).

Figure 2. Within the group with T1DM, a higher HbA1c at diagnosis was associated with greater error on the 2 dot, 60 s condition of the SDR task controlling for age, gender and socioeconomic status ($p=.027$).

Table 1**Clinical Characteristics**

Mean (SD) demographic and clinical information of participants.

	Con trols	Type 1 diabetes	No DKA	DKA
N	33	66	49	17
Age	11.9 (2.7)	11.9 (2.6)	12.1 (2.6)	11.5 (2.8)
Gender, Male/ Female	17/16	38/28	29/20	9/8
BMI %	62.3 (33.9)	64.9 (29.5)	62.3 (31.0)	72.2 (24.3)
Tanner, Tanner 1/ Tanner 2–5		24/38	14/32	10/6
Total Occupational Score	25.4 (9.9)	25.9 (10.1)	26.7 (10.3)	23.4 (9.3)
# of months from diagnosis to test	N.A.	2.2 (0.6)	2.2 (0.6)	2.2 (0.6)
HbA1c at diagnosis	N.A.	11.9% (2.1) (107 mmol/mol)	11.7% (2.2) (104 mmol/mol)	12.3% (1.8) (111 mmol/mol)
HbA1c at follow-up	N.A.	6.6%(0.9) (49 mmol/mol)	6.6% (0.9) (49 mmol/mol)	6.9% (1.0) (52 mmol/mol)
Mean serum osmolarity	N.A.	298.9 (9.6)	298.9 (8.0)	298.8 (13.4)
Bicarbonate	N.A.	19.72 (6.88)	23.00 (3.7)	10.28 (4.8)
Anion Gap	N.A.	N.A.	12.74 (4.5)	22.76 (6.0)

Table 2**Cognitive Testing Score**

Mean (SEM) scores for cognitive tests. Cognitive test scores are adjusted for age, gender, socioeconomic status (total occupational score), and sibling status.

	Controls	Type 1 diabetes	No DKA	DKA
General Information, raw score	28.9 (1.1)	28.1 (0.7)	28.4 (0.8)	27.6 (1.2)
Spatial Relations, raw score	68.5 (1.0)	67.4 (0.9)	67.0 (1.1)	66.7 (1.4)
Word Immediate Recall, words recalled	9.6 (0.5)	8.9 (0.3)	9.1 (0.3)	8.3 (0.4)
Word Delayed Recall, words recalled	9.2 (0.5)	8.7 (0.3)	8.9 (0.4)	8.1 (0.5)
1 dot SDR, cue present error, (mm)	1.2 (0.1)	1.3 (0.1)	1.3 (0.1)	1.1 (0.2)
1 dot SDR, 5 s delay error, (mm)	20.9 (2.0)	16.8 (1.0)	17.0 (1.2)	16.1 (1.2)
1 dot SDR, 60 s delay error (mm)	33.5 (3.0)	31.3 (2.3)	28.7 (2.2)	39.8 (6.3)
2 dot SDR, cue present error (mm)	1.2 (0.1)	1.9 (0.5)	2.1 (0.6)	1.5 (0.2)
2 dot SDR, 5 s delay error (mm)	24.9 (1.9)	22.1 (0.8)	22.0 (1.1)	22.4 (1.3)
2 dot SDR, 60 s delay error (mm)	32.7 (2.3)	38.1 (2.1) ^{a, b}	35.1 (2.2)	46.2 (5.0) ^c
Speed Median RT (ms)	295.4 (7.0)	291.7 (6.5)	289.8 (7.6)	297.3 (13.2)
GNG median RT (ms)	405.9 (10.3)	403.4 (7.0)	401.4 (7.7)	409.9 (16.2)
GNG false positives (percent)	30.9% (3.4)	31.7% (2.4)	31.4% (2.8)	32.6% (4.9)

SDR= spatial delayed response, RT=Reaction Time, GNG= Go No Go.

Higher scores indicate greater error on task performance.

^aControl group comparison, $p < .050$;

^bSubgroup comparison to subjects without DKA and controls, $p < .050$;

^cEffect of HbA1c at diagnosis, $p < .050$.