2010

COGNITIVE DEFICITS AND BLOOD SUGAR CONTROL IN PERSONS WITH DIABETES

Peder Henrik Seglund
Northern Michigan University

COGNITIVE DEFICITS AND BLOOD SUGAR CONTROL IN PERSONS WITH DIABETES

By

Peder Henrik Seglund

THESIS

Submitted to
Northern Michigan University
In partial fulfillment of the requirements
For the degree of

MASTER OF SCIENCE
IN EXPERIMENTAL PSYCHOLOGY

Graduate Studies Office

2010

SIGNATURE APPROVAL FORM

This thesis by Peder Seglund is recommended for approval by the student's Thesis Committee and Department Head in the Department of Psychology and by the Dean of Graduate Studies.

_____

Committee Chair: Sheila L. Burns Date

_____

First Reader: Charles R. Leith Date

_____

Second Reader (if required): Elmer Moisio Date

_____

Department Head: Sheila L. Burns Date

_____

Dean of Graduate Studies: Terrance Seethoff Date

OLSON LIBRARY
NORTHERN MICHIGAN UNIVERSITY

THESIS DATA FORM

In order to catalog your thesis properly and enter a record in the OCLC international bibliographic database, Olson Library must have the following requested information to distinguish you from others with the same or similar names and to provide appropriate subject access for other researchers

Seglund, Peder Henrik

July 3, 1965

ABSTRACT

COGNITIVE DEFICITS AND BLOOD SUGAR CONTROL IN PERSONS WITH DIABETES

By

Peder Henrik Seglund

This thesis assesses verbal and visual/spatial cognitive deficits in people with diabetes as a function of control of the disease process. The purpose was to see if there was a correlation between the severity of the disease and measures of Mild Cognitive Impairment (MCI). Thirty persons with diabetes answered a short questionnaire about their disease and completed three cognitive tests: A Mini-Mental Status Exam, a modified Stroop test, and a modified Mental Rotation test. Several prediction factors were looked at including age, time the participant had the disease, other health issues related to diabetes, A1C level, self-rating of severity, and self-rating of control of diabetes. The A1C score is the only factor that showed a consistent correlation to cognitive function. The outcome suggests that there is a relationship between how well sugar levels are controlled and evidence of MCI.

DEDICATION

This thesis is dedicated to my father Wilfred Seglund who suffered from diabetes.

TABLE OF CONTENTS

LIST OF TABLES

INTRODUCTION

The goal of this thesis was to assess whether or not individuals with diabetes have visual/spatial cognitive deficits related to the control of their disease. There has been considerable work on mild cognitive impairment in people with diabetes (Mohammed et al., 2003; Awad, Gagnon, & Messier, 2004; Roberts et al., 2008). However, the work has been primarily with verbal tests. The interest here was in whether those deficits also extend to visual-spatial skills. This study documened and replicated the verbal-test impairment and extends the assessment to visual-spatial skills.

Diabetes

Diabetes Mellitus is a metabolic disease identified by high blood sugar (glucose) levels that result from problems in insulin secretion. Diabetes is a disease associated with "sweet urine" and excessive muscle loss. Hyperglycemia (high blood glucose) leads to entry of glucose into the urine, which is where the term sweet urine came from (American Diabetes Association, nd). Blood glucose levels are controlled by insulin which is a hormone produced by the pancreas. The blood glucose level elevates after eating food and insulin is then released from the pancreas to bring the glucose level to a normal state. In people with diabetes, the lack of production of insulin leads to hyperglycemia.

Diabetes is a persistent medical condition. Although it can be regulated, there is no cure. It is a disease that must continually be monitored. Diabetes can lead to secondary health issues such as: heart disease, strokes, retinopathy, neuropathy, arthrosclerosis, and kidney failure (Centers for Disease Control, nd). These diseases are

the result of damage to small blood vessels, also known as microvascular disease (Berliner, Vavab, & Fogelman, 1995). This thesis explores the relationship between the control of a person's diabetes and how it affects his/her cognitive function.

Diabetes affects approximately 17 million people in the United States (Centers for Disease Control, nd). Twelve million people in the United States may have diabetes and are not even be aware they have it (Centers for Disease Control, nd). "Diabetes is the third leading cause of death in the United States after heart disease and cancer" (Centers for Disease Control, nd). Diabetes is divided into two diseases which are labeled Type 1 and Type 2 diabetes mellitus. The time of onset and how the body produces or uses insulin distinguish these two diseases (American Diabetes Association, nd).

Type 1 diabetes, sometimes called juvenile diabetes, is usually first diagnosed in young adults. In Type 1 diabetes, the pancreas no longer creates insulin as the body's immune system has damaged the pancreatic cells that make insulin. "Five to ten percent of persons with diabetes are Type 1" (American Diabetes Association, nd).

Type 2 diabetes, sometimes called adult-onset diabetes, is the most prevalent form of diabetes. People can develop Type 2 diabetes at any time in life, even during adolescence. This type usually begins with insulin resistance. Insulin resistance is a condition in which muscle, liver, and fat cells use insulin improperly. The body then produces more insulin to assist glucose to enter cells to then be utilized for fuel. The pancreas tries to keep up with the additional demand by producing more insulin. However, the pancreas eventually loses its capability to produce enough insulin in response to eating (American Diabetes Association, nd).

The inability to produce enough insulin affects mostly the cells of muscle and fat tissues. The result is a condition known as "insulin resistance." This is the main problem in Type 2 diabetes. No insulin is the main problem in Type 1 diabetes. If someone has insulin resistance, the body tries to increase producing insulin to overcome some of the resistance. If production decreases and insulin is not released as actively, then hyperglycemia develops (American Diabetes Association, nd).

Mild Cognitive Impairment

Mild cognitive impairment (MCI) is a brain disorder in which cognition (the processes of thought) is mildly impaired. People with MCI have difficulty memorizing new information, remembering names, remembering the continuance of a communication, and keeping track of objects or items (Roberts et al., 2008). A person with MCI might be able to operate in everyday functions with the assistance of reminders. MCI is not the same as dementia. With dementia, memory loss has progressed to a point that normal self-supporting activities are not possible and the person can no longer maintain his/her own basic needs. Most people with MCI develop an accelerated abatement in their cognition leading to dementia of which Alzheimer's disease is usually the root cause. With diabetes, vascular dementia, not Alzheimer's, would be the problem. MCI can affect many areas of thinking and movement including speech, assiduity, deduction, acumen, reading and/or writing. The most prevalent kind of MCI causes problems with memory (Roberts et al., 2008).

Criteria used to diagnose MCI are usually cognitive tests. The tests compare people of same or similar age and education (Rosenberg, Johnston, & Lyketsos, 2006). People with MCI may also be depressed, irritable, anxious, aggressive, and/or apathetic

(Rosenberg et al., 2006). Treatment of one of these other conditions (depression, etc.) may help reduce cognitive issues, but does not completely eradicate the deficits (Rosenberg et al., 2006).

There is no specific assessment that confirms MCI. A physician may try to rule out other things that bring about the symptoms. Tests may include reflex tests, eye movement tests, balance tests, and/or touch sensation assessments. A short mental status exam can be used to diagnose MCI (Folstein, Folstein & McHugh, 1975, as cited by Benson, Slavin, Tran, Petrella & Doraiswamy, 2005). Folstein's Mini-Mental Status Exam includes questions such as naming today's date, the persons location, copy 2 pentagons, follow a three–stage command, remember a list of three words, follow a written direction, count backwards by sevens, and spell the word "world" backwards (Benson et al.,2005). These tests are used to help distinguish typical from atypical cognition due to aging.

Diabetes and Mild Cognitive Impairment

There is an accumulation of research that poorly managed diabetes results in MCI (Mohammed et al., 2003). Their study found that the main reason people with diabetes, age 60 and older, scored low on a cognitive test was because they managed his/her disease improperly. They found a clear difference in cognitive ability between people with diabetes whose disease is under control and those whose disease is not controlled properly (Mohammed et al., 2003).

The participants were put in groups according to their diabetic status. The groups were: poorly controlled diabetes, adequately controlled diabetes, and no diabetes. The participants were tested for blood glucose tolerance and had Hemoglobin A1C

measurements to see what group they were in. The A1C reflects how well glucose levels are controlled over a three month period, while the blood glucose assessment tells glucose level at that point in time.

The study measured the correlation between diabetes and cognitive function in 2583 adults age 60 and older. Eight percent (205) scored lower than a normal control group on a cognitive abilities test. The low score correlated with the participants whose diabetes was currently poorly controlled. The Mohammed et al. (2003) study showed a link between diabetes and dementia. However, how diabetes triggers dementia was not clear. If diabetes is controlled then it is possible that MCI or dementia effects can be diminished. This is important because treatments for dementia are few. "More than 16 million people in the United States have diabetes and about 800,000 new cases are diagnosed each year" (Centers for Disease Control and Prevention, nd).

People with MCI are more apt to have had earlier onset, longer duration, and more poorly controlled diabetes (Roberts et al., 2004). Poor diabetes control may lead to neuron damage (Roberts et al., 2004). Diabetes is also affiliated with heart disease and/or stroke, which may also increase the risk of MCI (Roberts et al., 2008). People with retinopathy are twice as likely to have MCI. Diabetes related damage to blood vessels may cause problems with cognitive function because damage to blood vessels in the brain can cause MCI (Roberts et al, 2008). The findings suggest that the length of time a person has severe diabetes is important. Late onset of diabetes, a lesser duration of time, or maintaining the disease well may not have as great of detrimental effect (Roberts et al., 2008). Forty-two percent of people with diabetes in the US are older than 64 years and

this is projected to increase to fifty-four percent by the year 2025 and fifty-eight percent by 2050 (Centers for Disease Control and Prevention, nd).

Cognitive deficits may be due to hyperglycemia and the production of glycated end products that can harm vascular tissue (Gregg and Brown, 2003). Hyperglycemia may influence blood flow to the brain, neurotransmitters, and/or nutrients essential for brain function. Multiple diabetic insulin reactions may be related to metabolic and vascular disruption that may affect cognition (Gregg and Brown, 2003). There is a sixty percent to one-hundred percent greater risk of decline in cognitive function in people with diabetes compared to people without diabetes (Gregg and Brown, 2003).

The hippocampus is sensitive to atrophy and decreased cognitive functions, such as delayed verbal recall, early in the development of diabetes (Convit, Wolf, Tarshish, & De Leon, 2003). Diabetes may contribute to cognitive decline (Castellani, Lee, Perry, & Smith, 2006). Abnormal brain structure has been reported in Type 2 diabetes and it may especially affect the hippocampus (Gold et al., 2007). People with Type 2 diabetes share memory impairments and a reduction in the volume of the hippocampus similar to Alzheimer's disease (Convit et al., 2003). People with diabetes appear to have an increased risk for developing dementia (Leibson et al., 1997). A reduction of verbal performance and a reduction in declarative memory and speed of processing have been the most consistent problem in people with diabetes (Awad et al., 2004). Type 2 diabetes changes the structure in both white and gray matter of the brain and reduces the volume of both the hippocampus and amygdala (Van Harten, Oosterman, Van Loon, Sheltens & Weinstein, 2006). Diabetic encephalopathy is a term used for these brain complications.

This is a theory introduced several decades ago (Reske-Neilsen, Svendsen & Sofaard, 1965). This thesis tested for cognitive decline associated with diabetes.

The common cognitive assessment tool, the Mini-Mental Status Exam (MMSE), has been used for assessing possible cognitive deficits (Lanska, Schmitt, & Stewart,1993; McKhann, Drachman, & Folstein, 1984). The MMSE has been used previously to assess MCI (Teng, & Chui, 1987; Crum, Anthony, & Bassett, 1993).

The Stroop Color Naming Test (Stroop, 1935) found deficits in attention in participants. The Stroop test assesses a person's ability to ignore verbal information while concentrating on the actual color of ink in which a color word is printed. The Stroop assessment has been utilized to quantify the presence of cognitive function impairments in non-insulin dependent people who have diabetes (Vanhanen & Koivisto, 1997).

Pure visual-spatial assessments are seldom used on people with diabetes. One task, which has been used to look purely at visual-spatial skills, is a mental rotation test (Shepard & Metzler, 1971). This research found that it takes a participant longer to decide if a shape is the same the more the shape is rotated from its original position. They found that the degree of rotation has the greatest effect on the participant's response time (Shepard & Metzler, 1971).

The right cerebral hemisphere, specifically the right parietal area of the brain, is where mental rotation is localized (Johnson, 1990). Perception and mental rotation are in the same areas of the brain (Jones & Anuza, 1982). The rate of spatial processing is correlated with the speed of mental rotation (Hertzog & Rypma, 1991). The different stages of mental rotation are: create an image of the shape, rotate it mentally, make a comparison to other the other shapes it is to be compared to, decide if the shapes are a

match or not, and report the decision (Johnson, 1990). When people are performing mental rotation assessments, Functional Magnetic Resonance Imaging (FMRI) shows there is activity in Brodmann's areas 7A and 7B (parietal lobe), the frontal cortex, and the hand somatosensory cerebral cortex (Cohen, 1996). Changes in these areas may be related to MCI. Mental rotation testing can test whether people with diabetes process visual information more slowly than people without diabetes do.

SUMMARY AND CONCLUSIONS

Diabetes has been associated with cognitive deficits, which are exacerbated by poorly controlled blood sugar levels. The majority of the studies cited tested individuals on primarily verbal tasks including the MMSE. This thesis assessed the visual/spatial ability and attentional skills of people with diabetes, in addition to MMSE perfomance. It is the hypothesis of this thesis that diabetes has an effect on visual/spatial skills and that, as with verbal memory tests, the severity of the deficit will be related to the degree of control of the disease exhibited by the individual.

METHODS

Northern Michigan University's International Review Board (IRB) approved this project. A copy of the approval form is in Appendix A.

Participants

The Upper Peninsula Diabetes Outreach Network (UPDON) sent participants a letter of introduction inviting them to participate in the study. A copy of this letter is in Appendix B. Additional participants were recruited through diabetes education programs, senior centers, and referrals. The participants signed an informed consent form. A copy of the informed consent sheet is in Appendix C. The participants were asked to fill out an information and demographic questionnaire. A copy of the information sheet is in Appendix D. The participants were grouped into two categories of the control of diabetes by a median split of the A1C score of 7.5. An A1C score of 7.5 was used for the median split to maximize the number of participants in each group. A score of seven or under indicates the disease is currently under control within the last three months. The lower the A1C score the better the control of blood sugar levels. The number and degree of other complications related to diabetes were also recorded. Other demographic data collected were education level, sex, age, and how long the participant had diabetes. The objective was to establish a relationship between the degree of severity of diabetes and the correlation to mild cognitive impairment.

Cognitive Tests

MMSE. The Mini Mental Status Examination is a 30-item test, which takes approximately 15 minutes to administer. The MMSE is a screening tool for detecting changes in cognitive skills. The range of scores is 0 to 30, with increasing scores indicating better performance. A copy of the MMSE is in Appendix E. The MMSE has a reliability coefficient of r = .89 (Benson et al., 2005).

The Stroop Test. The Stroop test demonstrates how the brain operates for mental tasks involving attention and automatic processing and how it relates to the participant's selection and response. The Stroop test is a psychological assessment of how flexible our mind is (Stroop, 1935). The classic Stroop task uses color words ("red") printed in different color inks ("red" printed in "blue" ink). For this research, a modified Stroop test was used. All color words were printed in black ink. They were printed on a solid block of a particular color. The task asked the participant to name the background color while attempting to ignore a written color word in the same block. The task takes advantage of our tendency to read words automatically. If a word is printed or displayed in a box with a different color background; for example, if the word brown is written in a box that has a red background we will say the word brown more readily than we can name the color in which it is displayed. This creates interference. A participant has to inhibit one response, reading the color word, in order to name the background color in which it is printed (Stroop, 1935). Cognition flexibility or attention is measured by the interference produced and the additional time it takes to complete a series of blocks when a color word is present in the same space or block as a different background color which the participant is to name. The scoring came from the difference in the time it took a participant to take the interference test minus the time it took the same participant to

complete a color only test. There were 25 color blocks to be named. A copy is in Appendix F.

Mental Rotation Test. For this study, a modified Vandenberg Mental rotation Test is used (Vandenberg and Kuse, 1978). This test is made up of 20, four-alternative multiple-choice items. The stimuli were two-dimensional shapes developed by Bethell Fox and Shepard (1988). Each item consists of a standard and four alternatives from which the participant must choose two of the four that are the correct response of a rotated diagram. The participant has six minutes to complete the test and it is scored in terms of the number correct adjusted for guessing. This test was developed at NMU for the purpose of having a two-dimensional equivalent to the original Vandenberg test which uses three dimensional items (S. Burns, personal communication, October 1, 2008). The modified test was used here because it is somewhat easier than the original and should have been easier to complete for all participants. Participants were asked to complete the items in order and not to go back to earlier items. The Vandenberg test has become a common substitution for the original reaction time test used by Shepard and Metzler (1971). A copy is in Appendix G.

Procedure

Participants were recruited with the assistance of UPDON and diabetes education programs. Each agency or group, that agreed to participate, was provided basic information about the experiment to potential participants. The information sheet included phone and email information on how to contact the researchers if the person wishes to participate. An appointment was made to meet with the person either at a support group location or in his or her home.

The data collection proceeded in the following order:

a. Obtain informed consent (consent sheet in appendix), and demographic form
b. Administer MMSE, Stroop, or Mental Rotation test in balanced order (rotating order)
c. Debrief and thank participant for his or her participation, and
d. Provide information on how to contact researchers if he/she has further questions.

All data are kept in a secure file. No names were recorded on the data sheets. The only use of names was on the informed consent sheets. Thus, participation was kept confidential and actual data are anonymous.

Design

This study was a correlation design. Interest was in the relationship between diabetes control and A1C levels and performance on the three cognitive tests.

RESULTS

All data were entered into Microsoft Excel and PWS/SPSS which were used to analyze the data.

Sample Demographics.

The final sample of 30 included 14 females (F) and 16 males (M). The overall average age was 67.67 years of age. The average education level was 14.10 years, and the average age of diagnosis was age 51.80 years. The sample population was not random and was taken from a referral group of participants starting with the assistance of UPDON. There were no significant sex differences in age, years of education, age of diagnosis, or A1C levels. Two of the participants did not have an A1C score available. These data are presented in Table 1.

Table 1

Demographic Data for each Sex and Total Sample

Sex		Age	EDYrs	AgeDx	AIC
Fem.	Mean	68.14	13.79	51.43	7.88
	N	14	14	14	13
	Std. Deviation	7.804	2.293	12.978	1.86
Male	Mean	67.25	14.37	52.12	7.67
	N	16	16	16	15
	Std. Deviation	8.606	3.008	7.375	1.27
Total	Mean	67.67	14.10	51.80	7.77
	N	30	30	30	28
	Std. Deviation	8.113	2.670	10.186	1.55

Dependent Variables and Order Effects.

For each task a primary dependent variable was chosen. The primary measurement for the mental rotation test was the Vandenberg score which is based on the number correct adjusted for guessing (Vandenberg and Kuse., 1978). The participants were given a 6-minute time limit to complete twenty mental rotation problems. Scores could range from 0 to 40. The participant had one standard to rotate mentally and the participant was given four possible correct answers of which two were correct and two were not correct.

The dependent variable for the Stroop score was the interference test time minus the color only test time. A larger time difference indicates more interference.

For the MMSE the dependent variable was the number correct out of a possible 30 total using standardized scoring rules. Since each task was presented in three different orders, the potential impact of an order effect was tested using a one-way Analysis of Variance (ANOVA) for each dependent variable as a function of presentation order. These data are presented in Table 2. Because there were no significant order effects, order will not be discussed further.

Table 2

Means and Standard Deviation for Each Task in Each Order

		Mental Rotation Vandenberg Score		Stroop Time between C and C+W		MMSE Score	
		Mean	SD	Mean	SD	Mean	SD
Order	First	21.11	8.95	15.73	4.94	25.09	3.62
	Second	27.56	9.85	22.86.	9.20	26.60	2.99
	Third	21.50	12.88	15.13	9.31	26.89	3.48
Anova							
	F	F(2,27) = 1.019		F(2,27) = 1.019		F(2,27) = .844	
	p(F)	p = .374		P =.374		p = .441	

Diabetic Control

The diabetic control was analyzed through the A1C score, number of severe diabetic reactions, a self rating of severity of the disease, self rating of control of the disease, and number of additional complications related to diabetes mellitus. An A1C score of lower than 7 is considered an indication that the disease is currently well maintained. A score of over 7 is an indication that the disease is not currently well maintained.

Correlation between measures of diabetic control. There was a correlation between self reporting of control to the number of health issues related to diabetes, r(28) =.455, p=.012, and a correlation of self-report of severity to the number of health issues related to diabetes, r(28) =.42, p = .014 (See Table 3). There was no correlation between a participants A1C score and self reporting of control, r(26) = .257, p = .186, or severity r(26) = .210, p = .283. This would suggest that participants are unaware of or do not think they have a control or severity issue with the disease, but may actually have an underlying control or severity issue (See Table 3). There was a strong correlation between participants self-reporting and severity of control, r(28) = .853, p < .001. There were no participants who rated their control or severity as a score of 3 which equals a self report on a scale of 1 minimal, 2 moderate, and 3 severe. There was no correlation between the length of time a participant had the disease and their A1C score r(26) = .203, p = .299. There is a correlation between the number of related health issues and the participants self rating of control, r(28) = .455, p = .012, and the number of health issues and the self rating of severity, r(28) = .442, p =.014. This would suggest that a participant is aware that the other health issues are directly related to the disease.

Table 3

Correlations Between Measures of Diabetic Control

		AIC	HealthIss	SRSever	SRCont	disyrs
AIC	Pearson Correlation	1	.347	.210	.257	.203
	Sig. (2-tailed)		.070	.283	.186	.299
	N		28	28	28	28
HealthIss	Pearson Correlation		1	.442*	.455*	.079
	Sig. (2-tailed)			.014	.012	.676
	N			30	30	30
SRSever	Pearson Correlation			1	.853**	-.227
	Sig. (2-tailed)				.000	.229
	N				30	30
SRCont	Pearson Correlation				1	-.077
	Sig. (2-tailed)					.687
	N					30

. *. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations Between Cognitive Tasks.

There was a correlation between the MMSE and the Stroop time difference $r(28) = .608$, $p < .001$, and the MMSE and Mental Rotation Vandenberg Score $r(28) = .594$, $p = .001$, as well as the Stroop time difference and Metal Rotation Vandenberg Score $r(28) = .467$, $p = .009$ (See Table 4).

Table 4 Correlations Between Cognitive Tasks

		MMSEScor	Timediff	Vand score
MMSEScor	Pearson Correlation	1	-.608**	.594**
	Sig. (2-tailed)		.000	.001
	N		30	30
Timediff	Pearson Correlation		1	-.467**
	Sig. (2-tailed)			.009
	N			30

**. Correlation is significant at the 0.01 level (2-tailed).

. *. Correlation is significant at the 0.05 level (2-tailed).

Relationships Between Control and Mental Tasks.

All 3 mental tasks were significantly related to the A1C scores (see Table 5) This would suggest that participants had both a visual and spatial impairment related to diabetes. As A1C increased, MMSE scores declined, r(26) = -.666, p = .001, interference increased, r (26) = .377, p = .048, and mental rotation performance declined, r(26) = .497, p = .009 (see table 5). There was a correlation between the number of health issues and the MMSE score, r(28) = -.437, p = .016 and the number of health issues and the Stroop time difference, r (28) = .389, p = .034. As health issues increased the MMSE scores declined and the Stroop time difference increased. However, there was no correlation between the number of health issues and the Mental Rotation Score r(28) = -.213, p = .258 (see Table 5). There were no significant relationships between the self-rating of severity or control, or number of years with the disease and the cognitive measures. Thus, the A1C score (and possibly the number of health issues) were the only

predictors of cognitive impairment in this study. This would suggest that if a participant is able to maintain his/her control of diabetes they may be able to stave off any cognitive effects regardless of how long they have had diabetes (see Table 5).

Table 5 Relationships Between Control and Mental Tasks

		MMSEScor	Timediff	Vand Score
AIC	Pearson Correlation	-.666**	.377*	-.487**
	Sig. (2-tailed)	.000	.048	.009
	N	28	28	28
HealthIss	Pearson Correlation	-.437*	.389*	-.213
	Sig. (2-tailed)	.016	.034	.258
	N	30	30	30
SRSever	Pearson Correlation	-.113	.272	.060
	Sig. (2-tailed)	.554	.146	.752
	N	30	30	30
SRCont	Pearson Correlation	-.185	.358	.007
	Sig. (2-tailed)	.326	.052	.973
	N	30	30	30
disyrs	Pearson Correlation	-.131	.012	-.131
	Sig. (2-tailed)	.491	.951	.492
	N	30	30	30

. *. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Mean Scores on Tests of Cognitive Functioning Another way in which to look at these correlations is to look for mean differences between relatively high A1C control

(low A1C score) participants and relatively low A1C control (high A1C score) participants. Table 6 shows the mean scores on the cognitive functioning variables for each A1C group (High Control: A1C < 7.5; Low Control, A1C > 7.5). This analysis used an A1C score of 7.5 or greater to define poor control to keep the sample sizes more equal. It can be seen that the high control (Low A1C scores) group consistently performed significantly better than the low control group. All three cognitive tests demonstrated the cognitive decrements associated with poor sugar control.

Table 6

Mean Scores on Tests of Cognitive Functioning

	A1C Control	N	Mean	Std. Deviation	Std. Error Mean	t	p(t)
MMSEScor	High control	17	28.12	2.15	0.52	5.00	0.00
	Low control	13	23.54	2.88	0.80		
Vand Score	High control	17	27.18	7.75	1.88	2.46	0.02
	Low control	13	18.00	12.60	3.50		
Timediff	High control	17	14.95	9.34	2.27	-2.56	0.02
	Low control	13	22.37	5.34	1.48		

DISCUSSION

The purpose of the study was to see if there was a relationship between the severity of the participant's diabetes and the correlation to mild cognitive impairment (MCI). The variable that best reflected disease control was the A1C score. If it was below seven it is classified as currently under control. If it is above seven it is classified as not currently under control.

Previous research looked at diabetes and verbal aspects of cognitive function. This study is took the assessment further by replication of the verbal deficits in the MMSE and the verbal/visual testing with the Stroop test, and added the Mental Rotation test which is purely spacial/visual. The addition of the Mental Rotation test may provide a more complete picture of cognitive deficits related to diabetes.

The participants were evaluated on their A1C score, a self-diagnosis of control and severity, the length of time they had diabetes, type of diabetes (1 or 2), and other demographics such as education, age, and sex. The data suggest the A1C score is the most reliable indicator of any correlation to MCI. The results suggest there is a correlation between a high A1C score and MCI. In this study the length of time a participant had diabetes was not correlated to MCI. The order in which the cognitive tests were given, the age of the participant, the self-rating of severity, and the self-rating of control did not indicate a consistent relationship of diabetes to MCI.

A summary of the participant's performance on the cognitive tests indicates those participants with a higher than seven A1C score did not fair as well as those whose score was under seven. The participants, who had an A1C of seven or more, scored lower on the MMSE, had a higher time score on the interference portion of the Stroop test, and a lower Vandenberg score on the Mental Rotation test. All three tests showed deficits

associated with poor sugar control. Thus, the data suggested a correlation between the control of the disease rated by the A1C score, and MCI. The study supported the hypothesis that the deficits previously demonstrated on highly verbal assessments (MMSE) and attentional assessments (Stroop), were also apparent on a purely visual assessment (Mental Rotation).

The data also suggest that if persons with diabetes can maintain their disease and keep their A1C score under seven, they may have a greater chance of not getting or delaying MCI due to the disease. This is important because there is no cure for MCI and it is a progressive disease. If fewer people are being treated for the cognitive complications of diabetes, fewer resources will have to be applied to the cognitive care and well being of these individuals. This study found self-reports of disease status to be less reliable than the A1C blood sugar measure and not consistently related to cognitive performance.

The data of the study must be assessed under the following limitations: The participants were a non-random sample population and we were not able to track the participants over a period of time. A sample larger than 30 participants may have allowed more confidence in the replicability of these results. The participants were relatively high functioning individuals (MMSE scores). The participants were volunteers from UPDON, diabetic resource centers, and senior centers who were willing to participate, that is, they were a self-selected group. But note: the restriction in range for this group should work to reduce the size of the correlations that were obtained.

REFERENCES

American Diabetes Association. (n.d.). http://www.diabetes.org/diabetes-basics.

Awad, N., Gagnon, M., & Messier, C. (2004). The relationship between impaired glucose tolerance, Type 2 diabetes, and cognitive function. *Journal of Clinical and Experimental Neuropsychology*: *Official Journal of the International Neuropsychological Society*, 26, 1044-1080.

Benson, A., Slavin, M., Tran, T., Petrella, J., & Doraiswamy, P. (2005). Mini-Mental Status Examination, Screening for Early Alzheimer's Disease. *Journal of Clinical Psychiatry,* 2005;7(2):62-69.

Berliner, A., Vavab, V., & Fogelman, R. (1995). Atherosclerosis: Basic mechanisms. Oxidation, Inflammation, and Genetics; *American Heart Association*, 1995; 91: 2488-2496.

Bethel-Fox, C.E., & Shepard, R. (1988). Mental Rotation: Effects of stimulus complexity and familiarity. *Journal of Experimental Psychology: Human Perception and Performance,* 14(1): 12-23.

Castellani, R.J., Lee, H.G., Perry, G., & Smith, M.A. (2006). Antioxidant protection and neurodegenerative disease: The role of amyloid-beta and tau. *American Journal Alzheimer's Disease and other Dementia,* 2006;21:126-30.

Centers for Disease Control and Prevention, (2008). http://www.cdc.gov/diabetes.

Cohen, M. (1996). Changes in cortical activity during mental rotation. A mapping study using Functional Magnetic Resonance Imaging. http://airto.bmap.ucla.edu/BMCweb/BMC_BIOS/MarkCohen/Papers/Rotate.pdf.

Convit, A., Wolf, O.T., Tarshish, C., & De Leon, M.J. (2003). Reduced glucose tolerance is associated with poor memory performance and hippocampal atrophy among normal elderly. *Proc National Academy of Science USA 2003*; 100:2019-22.

Crum, R.M., Anthony, J.C., & Bassett, S.S. (1993). Population-based norms for the Mini-Mental Status Examination by age and educational level. *JAMA,* 269:2386–2391, 1993.

Gregg, E.W., & Brown, A. (2003). Hyperglycemia and Cognition. *Clinical Diabetes,* 21: 113-118.2003.

Gold, S., Dziobek, I., Sweat, V., Tirsi, A., Rogers, K., Bruehl, H., . . . Convit, A. (2007). Hippocampal damage and memory impairments as possible early brain complications of type 2 diabetes. *Diabetologia,* 50: 711-719.

Jones, B., & Anuza, T. (1982). Effects of sex, handedness, stimulus and visual field on mental rotation. *Cortex,* 18, 501-514.

Johnson, A. (1990). Speed of mental rotation as a function of problem solving strategies. *Perceptual and Motor Skills*, 71, 803-806.

Hertzog, C., & Rypma B. (1993). Age differences in components of mental rotation task performance. *Bulletin of the Psychonomic Society*, 29(3), 209-212.

Lanska, D.J., Schmitt, F.A., & Stewart, J.M. (1993). Telephone-Assessed Mental State. *Dementia,* 4:117–119, 1993.

Leibson, C.L., Rocca, W.A., Hanson, V.A., Cha, R., Kokmen, E., O'Brien, P.C., & Polumbo, P.J. (1997). Risk of dementia among persons with diabetes mellitus: A population based cohort study. *American Journal Epidemiol*, 145. 3.

McKhann, G., Drachman, D., & Folstein, M. (1984). Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology,* 34:939–944, 198401-308.

Mohammed, Y., Qureshi, M., Siddiqui, S., Kirimani, S., Xavier, J., Safdar, S., & Suri, A. (2003) Diabetes and Dementia in the Elderly. *Prevention Magazine,* 3:118 -119, 2005.

Reske-Neilsen, E., Svendsen, K., & Sofaard, H. (1965). Cerebral emboli as a result of "mute" juvenile endocarditis. *Acta Pathol Microbial Scandinavia,* 1965;63:321-32.

Roberts, R.O., Geda, Y.E., Knopman, D.S., Christianson, T.J., Pankratz, V.S., Boeve, B.F., . . . Peterson, R.C. (2008). Association of Duration and Severity of Diabetes Mellitus with Mild Cognitive Impairment. *Archives of Neurology*, 2008; 65(8): 1066.

Rosenberg, P.B., Johnston, D., & Lyketsos, C.G. (2006). Diabetes and Dementia. *American Journal of Psychiatry,* 163:1884-1890, November 2006. DOI: 10.1176/appi.ajp.163.11.1884.

Shepard, R., & Metzler, J. (1971). Mental rotation of three-dimensional objects. *Science,* 1971. 171(972):701-703.

Stroop, J. (1935). Studies of Interference in Serial Verbal Reactions. *Journal of Experimental Psychology,* 18, 643-662.

Teng, E.L., & Chui, H.C. (1987). The Modified Mini-Mental State (3MS) Examination. *Journal of Clinical Psychiatry,* 48:314–318.

Vandenberg, S., & Kuse, A. (1978). Mental Rotations, a Group Test of Three-Dimensional Spatial Visualization. *Perceptual and Motor Skills*, 1978, 47, 599-604.

Vanhanen, M., & Koivisto, K. (1997). Stroop and Cognitive Function. *NeuroReport*, (1997, April 14) Volume 8, Issue 6, P 1527-1530.

Van Harten, J., Oosterman, P., Van Loon, N., Sheltens, R., & Weinstein, H. (2006). Brain lesions on MRI in elderly patients with Type 2 diabetes mellitus. *European Neurology,* 57, 70.

APPENDICES

A: IRB Approval

B: Letter of Introduction

C: Informed Consent Form

D: Participant Information

E: MMSE

F: Stroop Test

G: Vandenberg Mental Rotation Test

APPENDIX A

IRB APPROVAL

Northern Michigan University

Continuing Education
1401 Presque Isle Avenue
Marquette, MI 49855-5301

April 1, 2010

TO: Peder Seglund
Psychology

FROM: Cynthia A. Prosen, Ph.D.
Dean of Graduate Studies & Research

RE: Human Subjects Proposal # HS10-341

"Cognitive Deficits and Blood Sugar Control in Persons with Diabetes"

The Internal Review Board (IRB) has reviewed your proposal and has given it final approval. To maintain permission from the Federal government to use human subjects in research, certain reporting processes are required. As the principal investigator, you are required to:

A. Include the statement "Approved by IRB: Project # (listed above) on all research materials you distribute, as well as on any correspondence concerning this project.

B. Provide the Internal Review Board letters from the agency(ies) where the research will take place within 14 days of the receipt of this letter. Letters from agencies should be submitted if the research is being done in (a) a hospital, in which case you will need a letter from the hospital administrator; (b) a school district, in which case you will need a letter from the superintendent, as well as the principal of the school where the research will be done; or (c) a facility that has its own Institutional Review Board, in which case you will need a letter from the chair of that board.

C. Report to the Internal Review Board any deviations from the methods and procedures outlined in your original protocol. If you find that modifications of methods or procedures are necessary, please report these to the Human Subjects Research Review Committee before proceeding with data collection.

D. Submit progress reports on your project every 12 months. You should report how many subjects have participated in the project and verify that you are following the methods and procedures outlined in your approved protocol.

E. Report to the Internal Review Board that your project has been completed. You are required to provide a short progress report to the Internal Review Board in which you provide information about your subjects, procedures to ensure confidentiality/anonymity of subjects, and the final disposition of records obtained as part of the research (see Section II.C.7.c).

F. Submit renewal of your project to the Internal Review Board if the project extends beyond three years from the date of approval.

It is your responsibility to seek renewal if you wish to continue with a three-year permit. At that time, you will complete (D) or (E), depending on the status of your project.

kjm

E-mail: conteduc@nmu.edu ■ Web site: www.nmu.edu/ce

APPENDIX B

LETTER OF INTRODUCTION

JANUARY, 2010

Dear Potential Research Participant,

I am a graduate student in the Department of Psychology at Northern Michigan University. We are looking for individuals to participate in a study of the relationship between diabetes severity, blood-sugar control**,** and cognitive functioning. We know that the diabetes disease process may have effects on cognitive functioning, especially if blood-sugar is not well con trolled. The research on cognitive functioning has been primarily concerned with verbal functioning and our interest is in visual-spatial functions and attention.

If you are interested in participating, we will ask for a little background information about your diabetes and then ask you to take three short cognitive tests. Participation is voluntary and you may discontinue your participation at any time without penalty or giving us a reason.

I have attached a copy of the diabetes history we will ask about and the informed consent sheet for the investigation.

We will not contact you directly unless you return this note with contact information to the Upper Peninsula Diabetes Outreach Network (UPDON) office in which your received it. The work has been approved by UPDON.

Please read the attached sheets and if you are willing to participate, provide your contact information.

If you have further questions, you may contact me, your UPDON office, or Sheila Burns at Northern Michigan University.

Thank you for reading this information and considering this opportunity.

Sincerely,

Peder Seglund
PHONE. 248-210-8703
MA candidate
Department of Psychology
Northern Michigan University

Supervisor: Sheila L. Burns, Ph.D.
906-227-2935

APPENDIX C

INFORMED CONSENT FORM

I have asked you to participate in research which is part of my Master's thesis at Northern Michigan University. I am working in agreement with the Upper Peninsula Diabetes Outreach Network.

This experiment is intended to test your cognitive performance determining the relationship between diabetes and mild cognitive impairment. We are looking at the effects diabetes has on cognition (the process of thought). The experiment will take approximately 45 minutes. Upon completion, you will have the chance to ask the experimenter any questions you may have about the experiment itself.

For the research, you will be asked to provide some basic demographic information, a brief history of your experiences with diabetes, and to take three short cognitive tests. Demographic questions, include such as your age and marital status. Information about your diabetes history include when you were diagnosed, severity of your diabetes, your level of control of the disease, and the score on your most recent A1C test. This information is important because it will help us to understand our results.

All data we collect will remain anonymous with no names on the data sheets or in the data analysis. We only take names on a separate sheet to indicate participation and your name is not associated in any way with your performance data. Thus, the data themselves are anonymous. Your participation is confidential. Your name will not be released, without your written permission to anyone.

POTENTIAL RISKS:

The tests should not cause you any discomfort unless you grow tired of answering questions or worry about your performance. If the testing makes you uncomfortable, the researcher and/or one of the nurses in the office can speak to you about the testing.

If you feel uncomfortable, in any way, about the task, you may discontinue at any time without penalty. If you change your mind about participating, do not worry, just indicate you would like to stop and we will.

POTENTIAL BENEFITS:

The benefits to you will not be direct, unless you enjoy the session. The indirect benefits are helping us to better understand the effects on cognitive functioning of diabetes and related diseases. This is one of many studies being done to further understand how diabetes has subtle effects on behavior.

COSTS:

There are no costs to you beyond your time.

We appreciate your contribution to this study of diabetes. Remember, you are under no obligation to participate. The goal of the study is research. We hope to gain a greater understanding of the diabetes disease process.

This project has been reviewed and approved by the Northern Michigan University Institutional Review Board for research with human subjects, the Upper Peninsula Diabetes Outreach Network association, and the Department of Psychology at Northern Michigan University.

If you have any questions about the work you may contact either of the individuals listed below.

NMU Dean of Research	Head, NMU Department of Psychology
Cinthia Prosen, Ph.D. 601 Cohodas 1401 Presque Isle Avenue Marquette, MI 49855 906-227-2300	Sheila L. Burns, Ph.D. 346 Gries hall 1401 Presque Isle Avenue Marquette, MI 49855 906-227-2935

This research is supervised by Dr. Sheila Burns, Department of Psychology, Northern Michigan University. 906-227-2935. Primary investigator is Peder Seglund, NMU, phone……..

Providing your name and signing below indicates you have been given a brief description of our study, you understand you can discontinue the experiment at any time without penalty, you understand your name will not be connected in any way to your performance on the task, and you are willing to participate in the research and to provide the basic information about your diabetes as indicated in the introduction letter.

Thank you for your time.

Print Name_____

Sign Name_____Date_____

APPENDIX D

PARTICIPANT INFORMATION

Sex: M F

Age on day of testing: _____-

Education (Circle one)

Some high school High school graduate or GED

Some College Associates degree

Bachelors degree Masters Degree

PhD or professional degree

Other including training/education/certificates_____

When were you first diagnosed with diabetes? _____

What kind of diabetes do you have? _____

Age when you were diagnosed?_____

Approximate date of diagnosis_____

Have you had any serious low blood sugar reactions? Y N

How many average per week_____ Per month? _____

A1C diabetes severity score (if available or known) _____

Self-rating of severity of diabetes: 1 = Minimal 2 = Moderate 3 = Severe

Self-rating of general level of blood-sugar control 1 = Minimal 2 = Moderate 3 = Severe

Other health issues related to diabetes (circle all that apply): Heart attack, stroke, eye problems (retinopathy), Neuropathy (numbness, nerve damage), kidney disease, depression, sleep impairment.

Do you smoke? Y N

What do you use to control your diabetes (circle all that apply) Insulin, medications – type_____, meal planning, exercises, other_____

APPENDIX E

MMSE COPY

Mini-Mental Status Examination

The Mini-Mental Status Examination offers a quick and simple way to quantify cognitive function and screen for cognitive loss. It tests the individual's orientation, attention, calculation, recall, language and motor skills.

Each section of the test involves a related series of questions or commands. The individual receives one point for each correct answer.

To give the examination, seat the individual in a quiet, well-lit room. Ask him/her to listen carefully and to answer each question as accurately as he/she can.

Don't time the test but score it right away. To score, add the number of correct responses. The individual can receive a maximum score of 30 points.

A score below 20 usually indicates cognitive impairment.

The Mini-Mental Status Examination

Name: _____ DOB: _____

Years of School;_____ Date of Exam: _____

Orientation to Time

Correct Incorrect

What is today's date?

What is the month?

What is the year?

What is the day of the week today?

What season is it?

Total:_____

Orientation to Place

hose home is this?

What room is this?

What city are we in?

What county are we in?

What state are we in?

Total:____

Immediate Recall

Ask if you may test his/her memory. Then say “ball”, “flag”, “tree” clearly and slowly, about 1 second for each. After you have said all 3 words, ask him/her to repeat them – the first repetition determines the score (0-3):
Ball
Flag
Tree
Total: ____

Attention

A) Ask the individual to begin with 100 and count backwards by 7. Stop after 5 subtractions. Score the correct subtractions.

93
86
79
72
65
Total:_____

B) Ask the individual to spell the word ”WORLD” backwards. The score is the number of letters in correct position.

D
L
R
O
W
Total:_____

Delayed Verbal Recall

Ask the individual to recall the 3 words you previously asked him/her to remember.
Ball
Flag
Tree
Total: _____

Naming

Show the individual a wristwatch and ask him/her what it is. Repeat for pencil.
Watch
Pencil

Repetition

Ask the individual to repeat the following:
“No if, ands, or buts”

3-Stage Command

Give the individual a plain piece of paper and say, “Take the paper in your hand, fold it in half, and put it on the floor.”

Takes

Folds

Puts

Reading

Hold up the card reading: “Close your eyes” so the individual can see it clearly.

Ask him/her to read it and do what it says. Score correctly only if the individual actually closes his/her eyes.

Writing

Give the individual a piece of paper and ask him/her to write a sentence. It is to be written spontaneously. It must contain a subject and verb and be sensible.

Copying

Give the individual a piece of paper and ask him/her to copy a design of two intersecting shapes. One point is awarded for correctly copying the shapes. All angles on both figures must be present, and the figures must have one overlapping angle.

Total Score:_____

APPENDIX F

STROOP TEST

At least three different timed readings will be used: All timing done with a stopwatch to nearest millisecond.

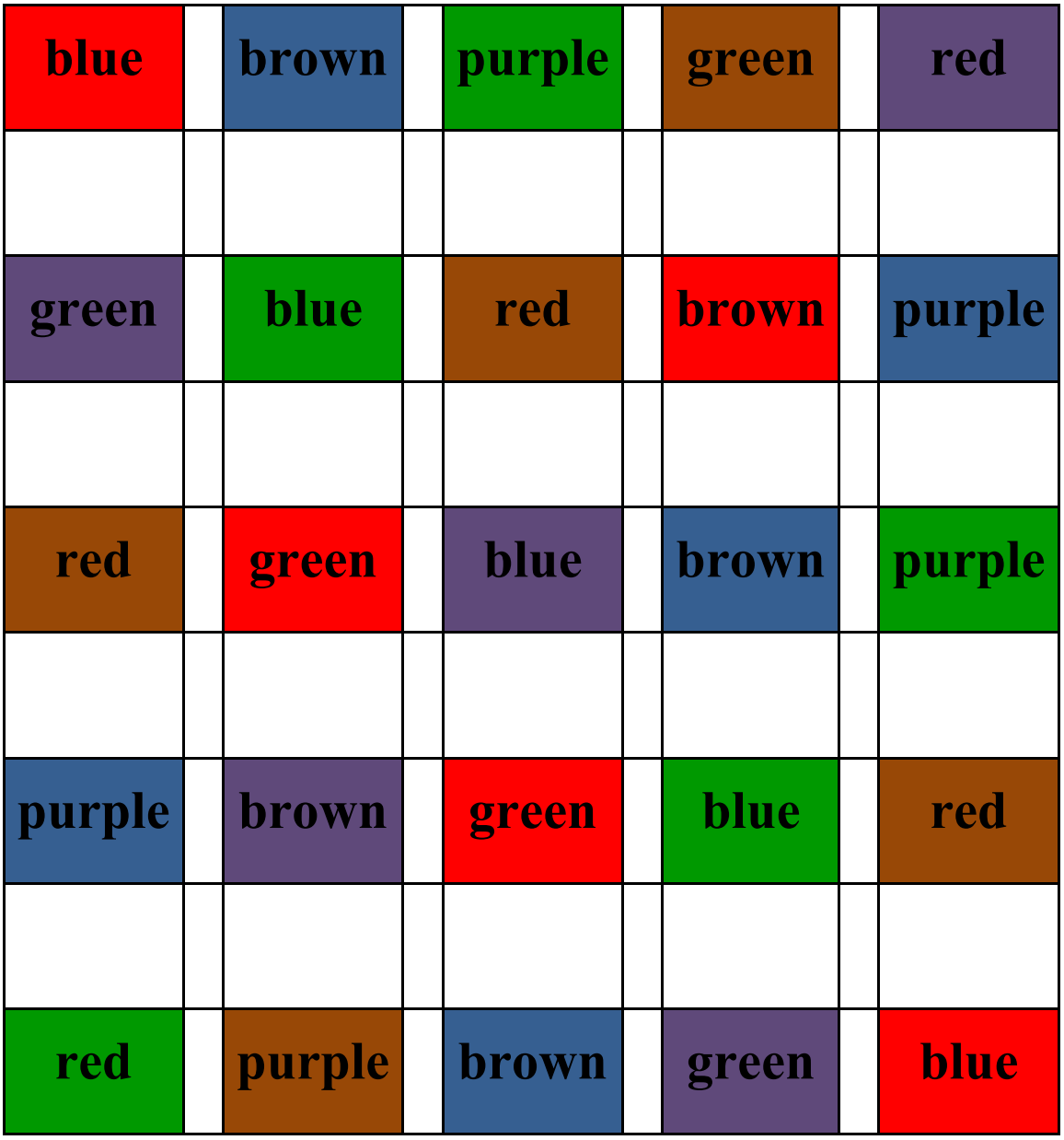
Time to read 25 color words written in black, with no color on background.

Time to name 25 color blocks with no written color words.

Time to name ink color on twenty five miss-matched ink-color word pairings.

Most significant time is difference between naming color blocks and naming ink colors. This difference is the measure of interference. Sheet below is with color and miss-matched color words.

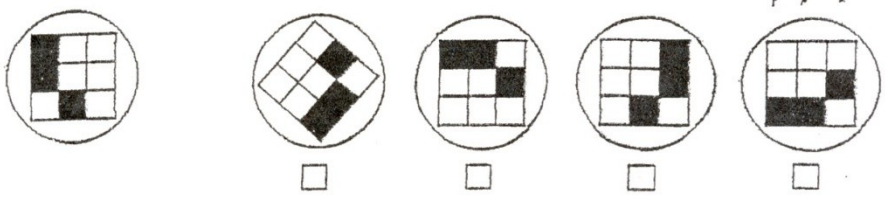
Actual test sheets were printed on glossy 8.5 x 11 inch paper.

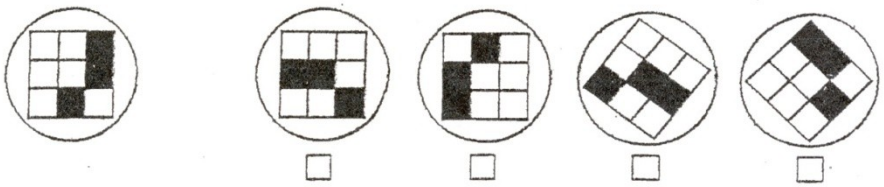

blue brown purple green red
green blue red brown purple
red green blue brown purple
purple brown green blue red
red purple brown green blue

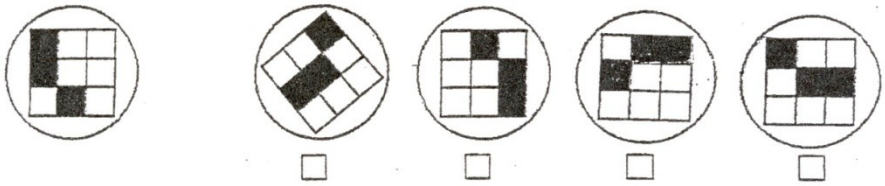
APPENDIX G

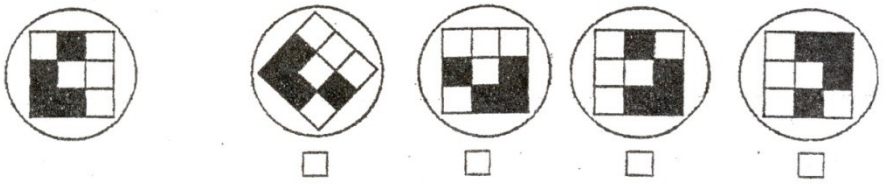
MENTAL ROTATION TEST

Example Page: Subject chooses two from right which will rotate to match example on left.

6. 

7. 

8. 

9. 

10.