Hostile-Diabetic Men: An Examination of Peripheral Glucose and QEEG Magnitudes Subsequent to Lateralized Fluency-Stressors

Robert Patrick Walters

Dissertation Submitted to the Faculty of Virginia Tech to Fulfill the Partial

Requirements for the Degree of

Doctorate of Philosophy in Psychology

David W. Harrison (Chair)
W. David Crews, Jr.
Bruce H. Friedman
Russell T. Jones
Richard A. Winett

May 28th, 2009

Blacksburg, Virginia

Hostility, Diabetes, Neuropsychology, Glucose, QEEG

Hostile-Diabetic Men: An Examination of Peripheral Glucose and QEEG Magnitudes Subsequent to Lateralized Fluency-Stressors

Robert P. Walters

(Abstract)

Using the *Limited Capacity Model* of hostility (Walters & Harrison, 2006; Williamson & Harrison, 2005; Williamson, Harrison, & Walters, 2007) as a guide, the stress response of individuals with a variable and dysregulated fuel supply to their brain (diabetes) was examined subsequent to lateralized fluency-stress. This theoretical "capacity" model of hostility was applied to a relatively unknown population of high hostile-diabetics. Given the associations between hostility and diabetes, it was argued that a very robust stress response would be evident, as measured as by peripheral glucose and QEEG magnitudes, as a result of modest regulatory capacity subsequent to right frontal lobe stress. Moreover, it was expected that high hostile-diabetics would show diminished performance on neuropsychological indicants of right frontal functions.

Table of Contents

Hostility and Diabetes: Shared Regulatory Systems?

An essential characteristic of hostility is the exaggerated and prolonged response to stress (Smith & Seigman, 1994; Smith Glazer, Ruiz, & Gallo, 2004; Suarez, Kuhn, Schanberg, Williams, & Zimmermann, 1998). This hyper-reactive stress response style has been implicated in the development of cardiovascular disease (Boyle et al. 2004; Brydon, Magid, & Steptoe, 2005; Miller, Smith, Turner, Guijarro, and Hallet, 1996), hypertension (Yan et al. 2003; Zhu et al. 2005), atherosclerosis (Iribarren et al. 2000), and even death (Boyle et al. 2004). In addition to these cardiovascular disease processes, hostility's influence on diabetes is beginning to be elucidated (Chyun et al., 2006; Niaura et al., 2000; Raiikkonen, Keltikangas-Jarvinen, Adlercreutz, & Hautanen, 1996; Raikkonen, Matthews, & Salomon, 2003). Diabetes is potentially devastating as this disease disrupts the fuel supply (glucose) to the body and brain adversely affecting emotional, cognitive, and behavioral functioning (Manschot et al., 2006; Reaven, Thompson, Nahum, & Haskins, 1990), particularly when glucose levels are high (Cox et al., 2005; Sommerfield, Deary, & Frier, 2004). Diabetics are significantly more likely to have structural changes within the brain when compared to those without diabetes (Manschot et al., 2006; Wessels et al., 2006). Moreover, there is some evidence to suggest that these structural changes are lateralized to the right frontal lobe (Hyllienmark, Maltez, Dandenell, Ludvigsson, and Brismar, 2005; Wessels et al., 2006).

Using the *Limited Capacity Model* of hostility (Walters & Harrison, 2006; Williamson & Harrison, 2005; Williamson, Harrison, & Walters, 2007) as a guide, it was argued that hostile men show prolonged and exaggerated responses to stress as a result of a limited stress management capacity attributable to the right frontal lobe. Further, individuals with a variable and dysregulated fuel supply to their brain (diabetes) exhibiting an increased and exaggerated

stress response (hostility) as a result of modest regulatory capacity, should demonstrate an exacerbated stress response within negative affective and sympathetic nervous systems of the right hemisphere. It was proposed that hostile-diabetics should mount a heightened physiological response subsequent to right frontal lobe stress. Moreover, it was expected that diabetics would show diminished performance on neuropsychological indicants of right frontal functions.

In this proposal, a theoretical "capacity" model of hostility was applied to a relatively unknown population of high hostile-diabetics. In addition, this research provided for a heightened level of specificity as previous research has examined cognitive dysfunction with diabetics as a global phenomena (Arvanitakis et al, 2006; Brands et al. 2007; Debling et al. 2006). Specifically, the proposed research examined the left and right frontal lobe capacity of diabetics exposed to lateralized stressors.

Hostility

The hostility construct is plagued with controversy regarding the purported inclusion or exclusion of anger, aggression (Martin, Watson, & Wan 2000), cynicism, hostile aggression, instrumental aggression (Ramirez & Andreu, 2006), and non-physical aggression (Hillbrand et al. 2005) among others. There has been considerable discussion and debate of the affective, behavioral, and cognitive components of hostility, anger, and aggression (Miller et al., 1996). The intention of this paper is not to add additional confusion to the literature by addressing and explaining the similarities, discrepancies, or the potential areas of overlap among these constructs, especially since there is evidence that these constructs are intercorrelated (Ramirez & Andreu, 2006). Instead, hostility was operationally defined in accordance with Smith & Seigman, (1994) as "…a devaluation of the worth and motives of others, an expectation that others are likely sources of wrong doing, a relational view of being in opposition toward others,

and a desire to inflict harm or see others harmed" (p.26). Within Smith's analysis of hostility, there is a component of "psychophysiological reactivity" reflecting the rationale that hostile individuals have a negative attitude towards others, as well as an increased and exaggerated physiological response to environment stress (Smith, Glazer, Ruiz, & Gallo, 2004).

As a construct, hostility has proven to be stable across the lifespan. Despite the controversy over the inability to partition the environmental from the genetic influences (Moore, 2002), there is evidence for both environmental (Keltikangas-Jarvinen & Heinonen, 2003; Smith, McGonigle, Benjamin, 1998) and genetic effects (Rujescu et al. 2002; Sluyter et al. 2000; Vernon, McCarthy, Johnson, Jang, and Harris, 1999).

From a neuropsychological perspective, it is posited that hostility results from a dysfunctional right hemisphere. Evidence for this model is provided by research on sympathetic dysregulation of blood pressure and heart rate. Additional research has exposed dysfunctional sensory perceptual and memory systems in hostiles including auditory (Demaree & Harrison, 1997; Mollet & Harrison, 2007), visual (Harrison & Gorelczenko, 1990; Herridge, Harrison, Mollet, and Shenal, 2004), and somatosensory systems (Herridge, Harrison, & Demaree, 1997). More recently, our lab has provided evidence through the assessment of motor (Demaree, Higgins, Williamson, Harrison, 2002) and premotor systems (Walters & Harrison, 2006; Williamson & Harrison, 2005; Williamson, et al., 2007). We have, therefore, introduced *The Limited Capacity Model*, asserting that the right frontal lobe is diminished in its capacity to regulate the right posterior systems (sensory perceptual and memory) resulting in elevated sympathetic responses, negative affective perceptions (Walters & Harrison, 2006; Williamson & Harrison, 2005; Williamson, et al. 2007), and diminished acquisition of neutral and positive

information concurrent with a negative bias for the acquisition of new information (Mollet & Harrison, 2007).

Despite the controversy over the origin or development of hostility, hostiles have demonstrated an increased and extended stress response (Suarez et al., 1998). Unfortunately, the consequences of this heightened responsivity include cardiovascular disease (Boyle et al., 2004; Brydon, Magid, & Steptoe, 2005; Miller et al., 1996), hypertension (Yan et al., 2003; Zhang et al., 2005), atherosclerosis (Iribarren et al. 2000), and an increase in metabolic factors (Benton, Kumari, Brain,1982; Donhoe & Benton, 1999; Finney et al., 2002; Hillbrand et al., 2005; McCrimmon et al., 1999; Richards et al., 2000; Virkkunen, 1982; Vogele, 1997).

From a neuropsychological perspective, it is argued that hostility is a negative emotion with an associated exaggerated and prolonged reaction to stress. Evidence for this position is provided by Suarez et al. (1998) in a large scale examination of physiological reactivity in high and low hostile men. Here, 52 Caucasian men classified as either low or high hostile, were randomly assigned to either a non-harassment or harassment conditions. The harassment condition involved an argumentative, challenging, and insulting experimenter and an interpersonal stressor. The high hostile men in the harassment condition demonstrated increased reactivity for systolic blood pressure, heart rate, forearm blood flow, forearm vascular resistance, norepinephrine, testosterone, and cortisol responses relative to the non-harassed high hostiles and the low hostile men. Suarez et al. argued that the hostiles evidenced sympathetic nervous system responsivity through heart rate, blood pressure, and vascular resistance measures, whereas hypothalamic-pituitary-axis (HPA) activity was evidenced through increases in norepinephrine, testosterone, and cortisol.

Of particular importance, Suarez et al. (1998) provided clear evidence that high hostile men experience stress at heightened levels, relative to low hostile men. Moreover, this experiment confirmed HPA activation during stress, which was evidenced by cortisol, testosterone, and norepinephrine increases from baseline for the high hostile-harassed condition. Suarez et al. noted that epinephrine did not increase as a result of the stress condition. The authors stated that this finding is somewhat unusual, as epinephrine is thought to be a primary marker of hypothalamic activation (Lovallo, 2005). The potential significance of this research is that Suarez et al. demonstrated that high hostiles are more susceptible to large scale sympathetic nervous system activation and HPA activation. They are among the few successfully providing multiple measures as evidence for this claim. The majority of research on hostility often utilizes one, or perhaps two, measures of stress (i.e using heart rate as a measure of sympathetic activation).

Hostility and the Brain

The frontal lobes have been consistently implicated in the development and expression of hostility. In a review of hostility, aggression, and the frontal lobes, Brower & Price (2000) examined the literature on these topics from 1966 to 2000. A clear association between frontal lobe dysfunction and increased aggressive and antisocial behavior was found. Focal orbito-frontal injury was specifically associated with increased aggression. Supporting this conclusion, Tateno, Jorge, and Robinson (2003) provided data on 89 head injured patients, concluding that patients with frontal lobe injuries were significantly more likely to become aggressive during their recovery relative to non-frontal lobe injured patients. Left and right frontal lobe comparisons for aggression and hostility were not conducted. Unfortunately, the failure to indicate *which* frontal lobe was damaged reflects the flawed notion of a single “frontal lobe

syndrome" that occurs after damage and implies that the two frontal lobes are identical in function. This approach has been criticized by Damasio & Anderson (2003), who write, "The notion that there is a unitary frontal lobe syndrome is not supported by anatomical or neuropsychological evidence" (p.409).

Research from our laboratory has examined functional roles of the left and the right frontal lobes in the regulation of sympathetic tone and negative affect. Examining the brain as a series of systems working together has been labeled a functional cerebral systems approach. This approach has evolved from research by Alexandr Luria (The Working Brain, 1973) who theorized that the brain was organized into specific zones working together in a concerted fashion, with frontal inhibition of both the subcortical and the posterior cerebral systems. Within this framework, hostile men have displayed dysregulation of right posterior cerebral systems as evidenced through an exaggerated sympathetic stress response concurrent with altered right hemispheric auditory (Demaree & Harrison, 1997), visual (Harrison & Gorelczenko, 1990; Herridge et al., 2004), and somatosensory systems (Herridge et al., 1997). Evidence for altered right hemispheric motor (Demaree et al. (2002) and premotor systems (Walters & Harrison, 2006; Williamson & Harrison, 2005; Williamson et al., 2007) support the 'limited capacity model.' Additionally, evidence is provided for the diminished capacity of the right frontal lobe to regulate the posterior systems of the right hemisphere.

Demaree & Harrison (1997) examined the auditory systems in hostile men. Using high and low hostile men, arousal levels were tested with physiological, behavioral, and laterality measures. Participants were administered an auditory dichotic listening test and then underwent a provocative pain stressor, specifically, the application of a cold pressor stimulus. The results indicate that high hostile men had reliably increased blood pressure and heart rate, and that they

correctly identified more word sounds (phonemes) at the left ear following the pain stressor. Heightened levels of sympathetic arousal, as well as the heightened left ear advantage, are indicative of increased right cerebral activation to stress for the high hostile men when compared to the low hostile men. This increase in right cerebral activation in high hostile men occurred with a corresponding increase in sympathetic tone using cardiovascular measures. Diametrically opposite results were found in the low hostiles who showed heightened left cerebral activation as evidenced through a dynamic increase in right ear word sound identification and lowered heart rate and blood pressure to the stressor.

Assessing the functional visual system, Harrison & Gorelczenko (1990) assessed cerebral asymmetry in the visual perception of affect for hostile men and women. Employing a tachistoscope, participants were instructed to identify angry, happy, or neutral faces in either the left or the right visual field. Hostile participants showed faster affect perception and a negative perceptual bias restricted to the left visual field. Herridge, Harrison, Mollet, and Shenal (2004) replicated and extended this research using perceptual accuracy measures within the visual modality while adding a stress component, specifically a cold pressor. Hostile men demonstrated decreased accuracy in the recognition of emotional faces within the left visual field, whereas women demonstrated reduced laterality across the visual fields.

Hostile men have demonstrated asymmetry for skin conductance as a primary measure of sympathetic arousal (Herridge et al., 1997). High hostiles have evidenced increased skin conductance at the left hemibody, as well as a reduced habituation rate at the left hemibody when compared to the right hemibody subsequent to posing facial configurations consistent with anger (corregator muscle contraction). Low hostiles evidenced prolonged habituation rates at the right hemibody suggestive of relative left cerebral activation in this group.

Extending this line of research to the motor systems, Demaree et al. (2002) examined grip strength in right handed high and low hostile men. Each group was equivalent on handedness scores with a right hemibody preference across sensory and motor domains. Hand dynamometer measurements were used to assess grip strength, which is a measure of lateralized motor functioning. It was expected that high hostile men would demonstrate increased "antigravity" strength as measured using hand grip strength due to right frontal lobe dysfunction. Specifically, the prediction that upper motor neuron deficits at the right frontal region would result in heightened flexor "grip" at the left hand was confirmed. Moreover, heightened facial motor tone was found in hostiles, specifically left hemifacial asymmetry was demonstrated in hostiles using facial electrophysiological recordings (Rhodes & Harrison, 2007).

Recently, Williamson & Harrison (2005) investigated the left and right prefrontal regions in this group evaluating cardiovascular reactivity to lateralized prefrontal stressors. The Controlled Oral Word Association Test (COWAT) and Ruff Figural Fluency Test (RFFT) were used as verbal and nonverbal frontal lobe stressors, respectively. Previous research has demonstrated the COWAT to be sensitive to left frontal functioning (Benton & de Hamsher, 1976), whereas the RFFT is sensitive to right frontal functioning (Demakis & Harrison, 1997). Foster, Williamson, and Harrison (2004) found those with poor performance on the RFFT had reliability increased delta wave magnitudes over the right frontal regions. Williamson & Harrison (2005) administered these lateralized fluency measures to the high and low hostile men. The verbal and nonverbal stressor tests produced diametrically opposite effects on systolic blood pressure in high hostile men. Specifically, systolic blood pressure increased subsequent to the nonverbal stressor [right frontal (RFFT)], whereas systolic blood pressure decreased subsequent to the verbal stressor [left frontal (COWAT)]. For the low hostile group, the verbal stressor

increased systolic blood pressure, whereas the nonverbal stressor (RFFT) yielded no significant changes for systolic blood pressure. This research has implications for cardiovascular regulation in hostile men, as Williamson & Harrison (2005) conclude that the frontal regions were unable to regulate blood pressure with the concurrent demand of the stressor task citing a 'capacity model.' This research is in accord with and extends previous research on the anterior-posterior model of hostility, specifically supporting relative right posterior activation and relative right frontal dysfunction (reduced capacity) for high hostile men.

Williamson et al. (2007) continued this line of research. Here, the influence of hostility on cardiovascular regulation, verbal fluency, nonverbal fluency, and dichotic listening was assessed. Twenty-four high and low hostile men underwent physiological measurements of SBP, DBP, and HR before and after verbal and figural fluency tasks, which were used as stressors. It was predicted that high hostile men would produce results indicative of diminished right frontal capacity when compared with low hostile men as reflected through cardiovascular activation subsequent to the nonverbal but not the verbal stressor. As predicted, high hostile men produced a reliable increase in blood pressure when compared to baseline and to low hostile men and produced significantly more perseverative errors than did low hostile men on this nonverbal fluency task. In addition, dichotic listening performance was evaluated across unfocused, focus left, and focus right conditions. Differences in dichotic listening performance were expected as a function of the fluency tasks. It was predicted that high hostile men would evidence a priming effect in that a left-ear bias would be found subsequent to the nonverbal fluency task but not the verbal fluency task. Support for this prediction was found. However, the low hostile men also displayed a priming effect at the left ear during the nonverbal fluency condition. Results are

discussed within the context of the functional cerebral systems regulating negative emotion and sympathetic cardiovascular function.

In an attempt to replicate and to extend Williamson & Harrison (2005), Walters and Harrison (2006) examined the stress response via glucose regulation and cardiovascular measures in 12 high and 12 low hostile men with concurrent left frontal lobe (Control Oral Word Association Test [verbal]) or right frontal lobe (Ruff Figural Fluency Test [nonverbal]) stress. Specifically, the glucose levels of high hostile men were significantly higher subsequent to the nonverbal stressor when compared to levels regulating from the verbal stressor. For the low hostile group, glucose levels (mg/dl) remained stable, or unchanged, for both types of stress. Additionally, the high hostile men made significantly more preseverative errors on the nonverbal stressor when compared to the low hostile men. These results were interpreted within a right hemispheric model of hostility. Additionally, it was suggested that the high hostile men were unable to concurrently regulate their glucose levels while completing a right frontal lobe task potentially as a result of diminished right frontal lobe capacity.

The limited *capacity model* is an extension of Kinsbourne's functional cerebral space model (Kinsbourne, 1980; Kinsbourne & Hicks, 1978; Reuter-Lorenz, Kinsbourne, & Moscovitch, 1990). The premise behind this theory is as holds, "When the human operator, while fully engaged in an attention-demanding task, is required simultaneously to perform a second such task, he typically loses efficiency on the main task" (Kinsbourne & Hicks, 1978, p.345.) Williamson & Harrison, (2005), Walters & Harrison (2006) and Williamson et al. (2007) applied this concept to an emotionally dysregulated population, specifically hostiles, and concluded that due to a limited capacity of the frontal regions, hostile participants are unable to experience frontal lobe stress and to maintain their baseline sympathetic arousal states concurrently.

The literature on hostility also supports a right hemispheric model of hostility for healthy individuals as evidenced using Positron Emission Tomography (PET) (Kimbral et a. 1999; Weisz et al. 2001), combined serotonin depletion and functional Magnetic Resonance Imaging (fMRI)(Rubia et al. 2005), and electroencephalogram measures (EEG) (Hewing, Hagemann, Seifert, Naumann, & Bartussek, 2004). Moreover, the literature supports the right hemispheric model of hostility on both a functional and structural level.

Following an anger induction in 16 healthy adults, Kimbrell et al. (1999) used PET to measure regional cerebral blood flow changes as a function of the emotional response. Subsequent to the anger induction, the participants displayed significant increases for the right thalamic and the right temporal regions, whereas there was significant deactivation for the right frontal regions. Kimbrell et al. concluded that transient levels of anger provide unique regional brain activity, which includes a relative deactivation of the right frontal lobe.

Further support for the right hemispheric involvement in the regulation of cardiovascular processes has been found by Weisz et al. (2001). Baroreceptor stimulation (through a neck suction device) led to significantly increased rCBF in the anterior, inferior part of the lateral prefrontal cortex only in the right hemisphere, thereby implicating the right frontal lobe in sympathetic activity in normal men. Weisz et al. concluded that the right hemisphere plays a larger role than the left hemisphere in baroreceptor regulation. Although this research is not specific to hostility, it demonstrates the regulatory role of the right frontal lobe in sympathetic activation.

On a neurochemical level of analysis, Rubia et al. (2005) administered an amino acid cocktail to deplete tryptophan (precursor to serotonin) before subjects underwent an fMRI. The rational for the depletion of serotonin was that it was intended to provide evidence for the

lateralization of serotonin regulation, and to further examine serotonin's role in aggression and hostility. In a double-blind sham controlled design, subjects consumed either the tryptophan depletion cocktail, or a sham amino acid cocktail, and then completed a 'go/no go' task while undergoing fMRI. Subjects consuming the tryptophan depletion cocktail demonstrated right orbital and right inferior prefrontal deactivation, whereas right middle temporal and left temporal regions were activated during the frontal lobe task. Although not stated explicitly by the authors, the deactivation of the right prefrontal region subsequent to the serotonin depletion specifically implicates this region for the involvement of hostility.

Using EEG, Hewing et al. (2004) examined anger scores and left and right frontal lobe activation during baseline. The results indicated that subjects with elevated 'anger-out' and lowered 'anger-control' scores displayed increased left frontal activation relative to right frontal lobe deactivation during baseline conditions. Although the authors proposed a left frontal lobe activation model of anger, their data support the right hemispheric model of hostility as the heightened anger scores were associated with decreased right frontal lobe activity.

Given this evidence, a right hemispheric model of hostility is proposed in which the right frontal lobe is unable to regulate the exaggerated and prolonged stress response in high hostiles. Moreover, the over activation of this stress response reflects a limited capacity within the right frontal lobe to regulate sympathetic tone. In addition to the limited capacity, it is argued that high hostiles are more likely to have a hypersensitive sympathetic response as the result of interpreting ambiguous situations as negative and having an interpersonal style that elicits aggression from others (Miller et al., 1996). Unfortunately, this activation pattern has health related consequences, and these consequences have considerable overlap with diabetes.

Diabetes

According to the American Diabetes Association (ADA) (ADA, 2005), diabetes is a disease in which the body does not produce, or properly use insulin. Insulin is the needed hormone to convert food (glucose) into energy. Around 20.8 million children and adults in the United States have diabetes equating to around 7% of the population. There are two primary forms of diabetes, including type I (early onset) and type II (late onset). In addition to type I and type II diabetes, the ADA (2005) recognizes gestational diabetes, in which pregnant mothers develop hyperglycemia, and pre-diabetes. An individual warrants a pre-diabetes diagnosis if they have slightly elevated glucose levels after a random plasma glucose test, or fasting plasma glucose test, but the levels are not high enough for a diabetes diagnosis. Pre-diabetes is thought to be heavily influenced by diet and exercise, and does not necessarily develop into type II diabetes.

Type I and type II diabetes have significantly different causal factors, symptoms, and treatment. However, there is also a considerable amount of overlap between the two disorders, such as the presence of ketones, obesity, and insulin resistance (Ramchandani, 2004). According to the ADA (2005), the principal distinction between type I and type II diabetes is that in type I diabetes the immune system mistakenly destroys the beta cells in the pancreas, which is the site of insulin production. As of yet, there is no known cause of this autoimmune response, although genetics, autoantibodies, viruses, cow's milk, and oxygen free radicals have been implicated. The symptoms of type I diabetes usually occur at very young age, most often before age 20. In addition to hyperglycemia, these symptoms include frequent urination, unusual hunger and/or thirst, weight loss, blurred vision, and increases of ketones in the blood. The treatment of this

disease often requires daily insulin injections and is usually not related to the individual's weight.

As described by the ADA (2005), type II diabetics are able to produce insulin via the pancreas. However, either not enough insulin is produced or the insulin that is produced is not used efficiently, or both. The latter is referred to as insulin resistance. No singular cause of type II diabetes has been identified, although genetics, age, obesity, hypertension, cholesterol, and lifestyle issues are all factors. Here, an individual's diet, exercise patterns, and weight play a direct role in the development of this disease. Of these factors, physical activity and body mass index have been cited as the most crucial (Hu et al. 2004; Hu, Rico-Sanz, Lakka, Tuomilehto, 2006). Type II also sets itself apart from type I diabetes in the age of diagnosis, which is most often given in adulthood, with half of all new diagnoses given after age 55. Due to these environmental factors, type II diabetes was the focus of this study. Diabetes's primary characteristic is that it is a disruption in fuel (glucose) to the body and especially the brain. Glucose is the integral fuel source for the brain and its role in vital brain functioning as well as it's role in disease is only beginning to be elucidated (Biessels, Bravenboer, and Gispen, 2004). To further this notion, the human body gives the brain preferential treatment in the utilization of glucose. For example, despite only consisting of 2% of an individual's total mass, the brain consumes almost 50% of the available glucose (Fehm, Kern, & Peters, 2006). Moreover, Dwyer (2002) stated that glucose is involved in nearly all of the brain's activities to include all cognitive abilities and nearly all cellular processes. "Because the brain is dependent on a continuous supply of glucose as its principal source of energy, changes in blood glucose concentration rapidly affect cerebral function" (Sommerfield et al., 2004, p. 2335), and irregularities in glucose

levels have implications for cognitive functioning, cognitive decline (dementia), structural and functional neuropsychological changes, and emotional functioning.

Diabetes: Global Cognitive Dysfunction

Early research by Reaven et al. (1990) compared performance on a series of cognitive tests between older (mean years of age = 68) diabetics and non-diabetics. Relative to the non-diabetics, the diabetics demonstrated decreased scores on "complex" verbal learning, reasoning, and psychomotor performance. These differences were not evident for "simple" verbal, reasoning, and psychomotor tasks. More recently, Debling et al. (2006) used a brief telephone interview to assess cognitive function and found significant differences between adult diabetics and non-diabetics. Here, cognitive performance was measured by a brief telephone interview that consisted of several questions concerning long-term memory, prospective memory, orientation in time and space, and verbal fluency. Sinclair, Girling, and Bayer (2000) found significant differences in cognitive function between diabetic and non-diabetic patients using the Mini-Mental Status Exam (MMSE) and the Draw-a-Clock Test. Also using the MMSE, Fontbonne, Berr, Ducimetiere, and Alperovitch (2001) tracked cognitive impairment over time in diabetics. Relative to the non-diabetics, the diabetics evidenced poorer outcomes on this global measure of cognitive impairment.

It should be noted that contrary to the above findings, not all researchers have found differences between diabetic and non-diabetics using cognitive measures. For example, Kanaya, Barrett-Connor, Gildengorin, and Yaffe (2004) compared performance on the Mini-Mental State Examination and the Trail-Making Test which did not differ by baseline glucose status.

An unfortunate consequence of diabetes is the detrimental affect on cognitive ability with the acceleration, or exacerbation, of the dementia process. For example, it has been documented

that adults with diabetes are at 1.5-2.6 fold increase for developing dementia later in life (Biessels, Staekenborg, Brunner, Brayne, and Scheltens, 2006). Arvanitakis, Wilson, & Bennett (2006) conducted a meta-analytic review of all research involving diabetes and global cognitive impairments, specifically dementia, over the past 15 years. These authors conclude that diabetes has an adverse impact on dementia, although the precise mechanisms are not fully understood. In a review of the role of the specific risk factors for type 2 diabetes, cognitive impairment, and dementia, van den Berg, Kessels, Kappelle, de Hann, and Biessels (2007) concluded that hypertension, atherosclerotic vascular disease, type 2 diabetes-specific conditions (hyperglycemia and hypoglycemia), medication, and depression among others, places diabetics at a heightened risk for developing diabetes, although a causal pathway has yet to be identified. In addition, these authors noted that these risk factors may illustrate indirect disease pathways. Despite the lack of a direct mechanism, the effect of diabetes on cognitive decline is devastating.

Furthering this relationship, Debling et al. (2006) examined the relationship among diabetes, cognitive function, and cognitive decline in an older population (ages 70 and higher). Here, there were statistically significant differences between diabetics and non-diabetics on a series of cognitive tasks that included the Telephone Interview of Cognitive Status (TICS) and the East Boston Memory Test (EBMT). These measures assess for global cognitive impairment, and due to the age of the participants, poor performance places them at a very high risk for developing dementia. The authors noted that these tests themselves did not specifically assess for dementia but did specify a very high correlation (r=.97) with the common dementia screening measures such as the Mini Status Mental Exam (MMSE). The results also reflect that the diabetics that did not treat their diabetes had the lowest scores on these measures. Debling et al.

concluded that diabetes adversely affects cognitive ability and ultimately can impede an older adult's ability to care for themselves, as is the case with dementia.

Diabetes: Specific Cognitive Dysfunction

The use of the term 'cognitive dysfunction' is argued to be too vague and implies a global disruption in brain processes. An objection to this approach has been broached by Brands et al. (2007) who raised the issue that the inconsistent results concerning cognitive dysfunction requires further assessment as it has yet to be determined if diabetes causes a global decline in all cognitive domains, "or that the observed cognitive changes follow a certain pattern in which limitations in one area" (p.289) of cognition are found. Attempting to respond to this dilemma, Brands et al. examined cognitive functioning, measures of well being including the assessment of depression, and magnetic resonance imaging (MRI) in patients with type II diabetes and in those without diabetes. Here, cognitive functioning was assessed with a number of neuropsychological tests that were organized according to the five "cognitive domains" of abstract reasoning, memory, information processing speed, attention and executive functioning, and visoconstruction. The diabetics had significantly worse performance for attention and executive functioning, information processing speed, and memory. In addition, the diabetics performed significantly lower than the non-diabetics on the measures of verbal fluency and depression. There were also neuroanatomical differences between groups as the diabetics had significantly more deep white matter abnormalities, and both cortical (hemisphere not listed) and subcortical atrophy (specific locations not given).

It should be noted that several researchers have argued that a slowing in processing speed may be the culprit behind the majority of cognitive dysfunction experienced by diabetics. For example, a review by Messier (2005) identified the primary factors negatively impacting

cognitive function in diabetics as poor performance on processing speed and verbal memory. Similarly, a review by Brands, Biessels, de Haan, Kappelle, and Kessels (2005) also documented the slowing of mental speed and flexibility in diabetics relative to non-diabetics. In addition, Watari et al. (2006) found depressed diabetics to have significantly slower processing speed and executive functioning relative to diabetics without depression and non-diabetics. It was concluded that the diabetic process interrupts the "neural circuitry underlying cognitive and mood changes" (p.787). Despite these findings on the slowing of cognitive processes, these authors do not provide a causal mechanism, and it is argued that processing speed remains a non-specific global measure of impairment.

As the literature on diabetes has advanced, there has been some effort to assess specific cognitive systems that may be detrimentally affected by diabetes. Using adults without dementia, Arvanitakis et al. (2006) examined over 800 diabetic men and women without dementia and administered a variety of neuropsychological tests that were merged into five categories: Episodic memory (Word List recall, Recall of a Story from Wechsler Memory-R), semantic memory (Verbal Fluency Test, Boston Naming Test, and Reading Test), working memory (Digit Span Forward and Backward, Digit Ordering) perceptual speed (Symbol Digits, Number Comparison, Stroop Neuropsychological Test), visuospatial ability (The Judgment of a Line Orientation, Standard Progressive Matrices) and a summary measure of global cognition. Of these five domains, the diabetic group performed significantly worse for the domains of semantic memory and perceptual speed. Unfortunately, the researchers did not provide the data from the individual tests. They do not provide a causal mechanism and they do not discuss the potential for lateralization of their findings.

Qiu et al. (2006) have also attempted to increase the specificity of the research on diabetes. These authors administered the Wechsler Adult Intelligence Scale (WAIS) III Block Design, Digit Span, Word Learning, Logical Memory, Trails A and B, and Verbal Fluency to 291 homebound, older adults with and without diabetes. Significant differences were found between the diabetic group and the non-diabetic group on Block Design, Trails B, Digit Span, and Word Learning. In addition, there were statistically significant trends for differences among groups for verbal fluency ($p=.08$). Given these findings, Qiu et al. concluded that the diabetic performance is characteristic of a "frontal-subcortical syndrome." In addition, there is "significant impairment in executive as well as visuospatial abilities but less in memory or language functions"(p.500). Of significance here, is the identification of specific brain regions that are implicated in diabetes. Interestingly, the authors did not dichotomize the findings in terms of left or right hemispheric functioning, although the results could be interpreted with reference to lateralization.

Diabetes: Cognitive Dysfunction a Function of Glucose Level

While the majority of research on cognitive dysfunction and diabetes consists of between groups differences present at baseline, there are also within group differences for diabetics during euglycemia (normal blood glucose) and hyperglycemia (increased blood glucose). Cox et al. (2005) followed 232 patients with Type I and Type II diabetes over 40 weeks. The patients were given hand held computers. Using these devices, they completed a total of 70 trials of verbal fluency, subtraction, and reaction time tasks over the 40 weeks. In addition, the participants used the devices to enter their blood glucose levels. When the diabetics were experiencing a hyperglycemic episode, they demonstrated slowing on of each of the cognitive tests and increases in the number of mental subtraction errors.

Similarly, Sommerfield et al. (2004) evaluated cognitive performance in individuals with diabetes. Here, 20 diabetics completed a wide variety of neuropsychological tests under euglycemic and hyperglycemic conditions. The glucose levels were manipulated and then maintained with a hyperinsulinemic glucose clamp. The tests and conditions were counterbalanced. During the hyperglycemic episodes, the participants had significant decreases in the speed of processing, working memory, and attention. During this time, the participants also reported less energetic arousal, increased sadness, and anxiety.

Awad, Gagnon, and Messier (2004) examined research published before 2004 that examined cognitive performance in diabetics that compared performance on cognitive tasks for diabetics that treated their diabetes and for diabetics that did not treat their diabetes. The authors concluded that cognitive performance as assessed with a variety of measures improves as a function of glycemic improvement. Specifically, performance increased for the diabetics treating their diabetes (glucose returns to normal range) relative to the diabetics experiencing more frequent hyperglycemic episodes resulting from not treating their diabetes.

The distinction of measuring glucose across time within a single subject is a significant consideration in that one's glucose level is always fluctuating. This variability of glucose is the key feature of diabetes. The current project continued this advancement by examining glucose changes across time within subjects, and assessed glucose change as a function of stress.

Diabetes: Structural and Functional Dysfunction

Recently, Manschot et al. (2006) examined both the functional abilities and the structural or anatomical differences between diabetics and non-diabetics. Here, the participants completed a neuropsychological assessment battery and underwent Magnetic Resonance Imaging (MRI) to assess white matter lesions, subcortical atrophy, and infarcts. Compared to the non-diabetics, the

diabetics evidenced significant impairment for attention, executive function, information processing speed, and memory. In addition, the diabetics had significantly more deep white matter lesions, cortical and subcortical atrophy, and small infarcts. Manschot et al. concluded that the cognitive deficits experienced by the diabetics could be attributed to the structural changes in the brain (white matter lesion and infarcts) but did not rule out that the cognitive deficits could be the result of changes at the nonvascular, cellular level as evidenced by the global increases in atrophy for the diabetics. Similar findings have been documented by Brands et al. (2007).

Diabetes has been demonstrated to be a factor increasing post-stroke mortality and adversely affecting post-stroke outcomes as compared with stroke patients without diabetes (Kissela & Air, 2006). The damaging effects of diabetes are evident in individuals recovering from their first stroke. Individuals with diabetes have demonstrated a significantly reduced improvement compared with stroke survivors without diabetes (Nys et al., 2005). Moreover, stroke patients with diabetes mellitus are significantly more likely to have additional strokes and a poorer functional recovery compared to patients without diabetes (Bokura et al. 2005).

Diabetes: Evidence for Lateralization

In addition to evidence supporting the notion that diabetes disrupts cognitive performance, particularly during hyperglycemia, there is some evidence to suggest that diabetes may lateralize to either the left or the right hemisphere. For example, in a comparison between diabetics with retinopathy and diabetics without retinopathy (retinopathy was used as a marker for microvascular disease brought on by long term episodes of hyperglcyemia), Wessels et al. (2006) compared grey matter density using voxel morphometry with MRI slides. Relative to healthy controls and diabetics without retinopathy, the diabetics with retinopathy had

significantly reduced grey matter density in the right inferior frontal gyrus and right occipital lobe. No explanation was provided to elucidate why the right frontal lobe and right occipital lobe were preferentially affected.

Using baseline EEG magnitudes, Hyllienmark et al. (2005) reported that global increases in delta and theta magnitudes were evident in the frontal regions for diabetics relative to non-diabetics. In addition, alpha peak frequency was negatively correlated with the number of severe hypoglycemic events across electrode positions. This effect was most pronounced over the right fronto-polar region ($p<0.01$). Taken together, these results reflect a slowing of brain activation, especially in the frontal lobes of diabetics, with some indication of a specific reduction of activation over the right frontal pole.

Hostility and Diabetes

In addition to the cognitive consequences of diabetes, there is also evidence that this disease process affects emotional functioning. In a sample of 116 diabetic patients, anger was reported in 34% (n=38) and hostility was reported in 17% (n = 17) (Chyun et al., 2006). As part of the Atherosclerosis Risk in Communities Study (ARIC), Golden et al., (2006) examined the influence of anger, and its associated constructs, on the development of diabetes. These researchers demonstrated that angry temperament, as measured by the Speilberger Trait Anger Scale, was predictive of diabetes during follow-up. Here, participants scoring high on angry temperament had a 34% increase in developing diabetes during the 6 year follow-up. This relationship remained even when controlling for unhealthy behaviors (smoking, alcohol intake, caloric intake, and physical activity).

Although not labeled directly as hostility, Sommerfield et al. (2004) compared emotional functioning in Type II diabetics during euglycemic and hyperglycemic states. As depicted by the

University of Wales Institute of Science and Technology checklist, during hyperglycemia, the diabetics reported significantly more “tense arousal” which includes components of feeling anxious and nervous.

Examining the influence of psychosocial variables on the Insulin Resistance Syndrome (IRS), Raiikkonen et al. (1996) demonstrated that hostility, among other constructs, was associated with the variables of hyperinsulinemia, hyperglycemia, dyslipidemia, hypertension, and increased abdominal adipose tissue among others. These associations were found in healthy, middle-aged men employed as managers after a 12 hour fast and were argued to confirm the effects of personality, behavioral patterns, and a stress- inducing lifestyle on insulin resistance.

As part of the Normative Aging Study, Niaura et al. (2000) reported that hostility was positively associated with fasting insulin level and a number of other metabolic factors. Here, subjects were initially enrolled in 1986 and followed thereafter. High scores on the Cook Medley Hostility Scale (CMHO II) were positively associated with insulin levels and also with waist/hip ratio, body mass index, total caloric intake, and serum triglycerides. Although, path analyses revealed that the effects of hostility on insulin, triglycerides, and high-density lipoprotein cholesterol were mediated by body mass index.

The relationship between hostility and heightened levels of glucose may be evident even in childhood and adolescence. In a sample of 134 African American and European American children, Raikkonen et al. (2003) found that baseline hostility scores on the CMHO II predicted future metabolic syndrome diagnoses for children and adolescents free from the metabolic syndrome at baseline at the time of a 3 year follow up. The authors suggested that insulin resistance and obesity were primarily responsible for this relationship.

Rationale

Research has demonstrated an exaggerated and prolonged stress response in hostile men. In the present study, the *Limited Capacity Model* was utilized as a guide to understand the hostility construct. Frontal lobe function and the associated capacity to regulate the stress response was examined in an "at risk" population of hostile-diabetics. As previously stated, the rational behind testing this population is that individuals with dysregulated fuel supply to their brain (diabetics) with an increased and exaggerated response to stress (hostility) should demonstrate robust responses to stress as a function of the combination of these two characteristics.

The *Limited Capacity Model* implicates a dysfunctional right hemisphere in hostile men. Specifically, there is a limited capacity for the right frontal lobe to regulate negative emotion (hostility and anger) concurrent with regulation of sympathetic arousal under stress. Paralleling this research, there is moderate evidence to suggest that diabetics are more likely to experience hostility and anger (Chyun et al., 2006; Golden et al.,2006; Niaura et al., 2000; Raikkonen, et al. 2003). Moreover, there is research evidence implicating dysfunction within the right frontal lobe in this population (Hyllienmark et al., 2005; Wessels et al., 2006).

Unlike previous experiments that examine either hostility or diabetes, this experiment tested the frontal lobe function of hostile-diabetics. It is argued that this study is unique in that there is no known research on this population. In addition, there is a heightened level of specificity in the present study as previous research has examined cognitive dysfunction with diabetics as a global phenomena (Arvanitakis et al, 2006; Brands et al. 2007; Debling et al. 2006). The present research progressed to a specific, and lateralized, examination of the frontal lobes.

Moreover, traditional research on diabetes examines differences between groups at baseline or within group during altered glucose states. This experiment provided for the assessment of physiological responses to lateralized frontal lobe stress. Specifically, this experiment examined frontal lobe function with lateralized verbal and non-verbal fluency tasks. Reactance to these stressors was assessed using QEEG (alpha, beta, theta, delta magnitude). As asserted by the *Limited Capacity Model*, it was predicted that the hostile-diabetics would be unable to regulate their arousal levels subsequent to the right frontal lobe (nonverbal) stressor due to a limited capacity of the right frontal lobe.

Hypotheses: Reactance

1. Using the left (verbal) and right (nonverbal) frontal lobe fluency-stressors, it was predicted that the high hostile-diabetic group would demonstrate heightened reactance to the right frontal lobe fluency-stressor relative to the low hostile-diabetic group as indicated by increases in glucose.
2. Subsequent to the right frontal lobe fluency-stressor, the high hostile-diabetic group was expected to evidence increased QEEG magnitudes of delta and theta, relative to baseline levels experienced before the fluency-stressor.

Hypotheses: Behavioral Performance

1. The high hostile-diabetic groups would have poorer performance on the design fluency task (RFFT).
2. High hostile-diabetic group would have an increased performance on the negatively valanced portions of the affective verbal learning test (AAVLT) in comparison with the neutral and the positively valanced learning trials.

3. The high hostile-diabetic group would demonstrate increased grip strength at the left hand relative to the low hostile-diabetic group.
4. The high hostile-diabetic group would demonstrate decreased finger tapping rate at the left hand relative to the low hostile-diabetic groups.

Method

Participants

The participants were recruited from advertisements placed in local newspapers, fliers placed in local businesses and in physician's offices. Presentations and information was also given to diabetic education groups in the local area.

All of the participants included in the study were adult men volunteering from the local community. Each participant was required to be between the ages of 20 and 70 with diagnosis of type II diabetes given by a physician. The ADA (2005) prefers the diagnosis of diabetes to be made with the fasting glucose test. As indicated by the ADA, a fasting blood glucose level of 126 mg/dl or higher, results in a diagnosis of diabetes. Additional methods of detecting diabetes are available, such as the Oral Glucose Tolerance Test, or the random plasma glucose test. Only men volunteering to participate and reporting to have previously met the diabetic diagnostic criteria were included in the study.

Initially, it was proposed that all of the participants would begin the study by completing an online screening that included the CMHO, medical history questionnaire, and laterality questionnaire. Only those participants scoring in the bottom 1/3 of the CHMO (low hostile) or in the upper 1/3 (high hostile) without significant medical histories (other than diabetes), and who reported a right-sided hemibody preference were going to be to be invited to the experimental portion of the study. In accord with previous research, both the low and high hostile group was

proposed to contain 15 participants in each group (Demaree & Harrison, 1997; Demaree, et al., 2002; Harrison & Gorelczenko, 1990). However, due to modest interest in the community and the participant's inability to access the online screening due computer illiteracy, this proposed screening method was modified. Specifically, the online screening was removed and the participants completed the entirety of the study in the laboratory, which included the personality measures, medical history and handedness questionnaires, as well as all of the testing measures. Additional modifications included increasing the financial compensation from $20 to $50 and providing the participants with feedback on their performance on the AAVLT.

Given these changes, the only measure used to assess appropriateness for the study was the medical history questionnaire in addition to the type II diabetes diagnosis. The CMHO was used as a grouping measure (high or low hostile) and while the participants completed other personality and handedness questionnaires, these measures were not used to prevent participation in the study.

A total of 38 participants completed the experimental portion of the study. This sample consisted of 36 Caucasian men, 2 African-American men, and 1 Middle Eastern man. From this sample, one participant was removed after he reported a number of head traumas as well as multiple electric shocks. Another participant was removed after informing the experimenters that he was receiving insulin via an inserted insulin pump. Ultimately, 36 participants were included in the study. The participants were aged 34-70 (M = 55, SD = 10.13) with an average education level of 16.30 years (SD = 2.98). It should be noted that 15 participants completed 18 or more years of education. As a sample, the participants weighed between 154 and 370 (M = 222.16 lbs, SD = 43.25) with a waist-to-hip ratio of 1.02 (SD =.065).

The scores on the CMHO ranged from 3 to 35 with a mean score of 18.11 (*SD* = 7.19). The total number of participants that were included in the analyses was 36. The distribution of the hostility scores was bimodal. Specifically, there were two clearly identifiable clusters of scores from which a low hostile-diabetic group and a high hostile-diabetic group were delineated, providing for 21 low hostile-diabetic and 15 high hostile-diabetic men. This selection process of high and low hostile groups is in contrast to the traditional selection of participants to these groups for the college-aged population. Specifically, high hostile participants have traditionally been defined as those scoring 28 or above on the CHMO (maximum score = 50). Low hostile participants have been defined as those scoring 19 or below on the CHMO. These cut-off scores have represented the upper and lower thirds of the CHMO distribution (Demaree & Harrison, 1997; Demaree, et al., 2002; Harrison & Gorelczenko, 1990).

Group membership was not significantly correlated with weight, hypertension diagnosis, hip size, waist size, or waist-to-hip ratio. Although not significant, there was a trend for group membership and education level [$r(36)=-.255$, $p=.069$)]. The mean education for the high hostile-diabetic group was 15.43 (SD=3.14) and for the low hostile-diabetic group it was 16.95 (*SD* = 2.5). However, the high hostile-diabetic group had a greater range in education level (14 years) relative to the low hostile-diabetic group (8 years). Moreover, both the highest (24 years) and lowest (10 years) level of completed education was in the high hostile-diabetic group. For the variable of age, there was significant correlation with age and group membership [$r(32) =-.455$, $p=.009$]. Further review revealed that the low hostile group was significantly older ($M = 59.11$, $SD = 8.2$) than the high hostile group ($M = 49.64$, $SD = 10.11$).

The participants' medical history was free of head injury, stroke, or neoplasm, or other significant medical diagnoses. Hypertensive individuals were included in the experiment as it

believed that a significant number of individuals, almost half of all participants with diabetes, will also be hypertensive (Maahs et al., 2005). Of the 36 participants, previous hypertension diagnoses were was recorded in 28 participants (data not recorded in all participants due to a data recording error). Of the 28 recorded responses, 18 participants reported either previous or current hypertensive diagnosis.

Women participants were not included due to sex differences in cerebral laterality (Harrison, Gorelczenko, & Cook, 1990; Higgins & Harrison, 1999; Synder, Harrison, and Gorman, 1996).

Self Report Measures

CMHO II

The 50-item CMHO II (Appendix A) has been frequently used as a valid predictor of hostility (Helmer, Ragland, & Syme, 1991.; Larkin, Martin, & McClain, 2002; Scherwitz et al., 1992). Originally based on portions of the Minnesota Multiphasic Personality Inventory (Surwit et al., 2002), the CMHO II is the most commonly used hostility measure and is a valid predictor of medical, psychological, and interpersonal outcomes of trait based hostility (Contrada, 1992). According to Christensen et al. (1997) the CMHO II has proven to have reliable internal consistency (coefficient alpha r = .86). Test-retest consistency confirmation is also reliable (r=.84). Further supporting the reliability of this measure, research within our lab has resulted in a test-retest reliability factor of r=.95 (Walters & Harrison, 2006).

Laterality

The Coren, Porac, and Duncan Laterality Questionnaire (1979) (Appendix B) was used to assess hemibody preference. The questionnaire consisted of 13 items assessing preference for left or right hand, foot, eye, and ear. The items were scored +1 for right, −1 for left, and 0 for

both. The scores range from +13 to −13. Laterality scores of +7 were considered to have a right hemibody preference.

Behavioral Measures

Verbal Stressor (Verbal Fluency)

The Controlled Oral Word Association Test (COWAT) (Appendix C) is a measure of verbal fluency (Benton & de Hamsher, 1976). The COWAT often consists of three one-minute trials in which participants are instructed to say as many words that begin with a specific letter as possible. Proper names, numbers, and the same word with a different suffix did not qualify and were not scored. This experiment employed five trials of verbal fluency. As reported by Lezak (1995), participants completing verbal fluency tasks with the letters F, A, S, T, and R average 11-12 words per letter.

Individuals with left frontal lobe deficits often have lower scores on this verbal fluency test when compared to a normal population (Johnstone, Holland, & Larimone, 2000; Ruff, Light, Parker, & Levin, 1997). In addition, individuals with lesions in the left frontal lobe have decreased performance when compared to individuals with right frontal lobe lesions (Baldo, Shimamura, Delis, Kramer, & Kaplan, 2001; Tucha, Smely, & Lange, 1999.)

Nonverbal Stressor (Nonverbal Fluency)

The Ruff Figural Fluency Test (RFFT) is a paper and pencil test consisting of five sections and is used as a measure of nonverbal fluency. Within each section there are 35 dot matrices arranged in a 5” x 7” pattern. The participants were given one minute to connect three or more dots, making as many unique patterns as possible in the time allotted. The total score was considered to be the total number of patterns minus the number of perseverative errors. A

perseverative error was defined as any repetition in design by the participant. To maintain uniformity with the verbal fluency procedure, 5 trials of the RFFT were completed.

The RFFT was thought to be a measure of right frontal lobe functioning. Previous research has demonstrated that individuals with right frontal lobe strokes or brain injuries have significantly lower scores, or increased error ratios on nonverbal fluency tasks, compared to those without right frontal lobe deficits (Ruff, Allen, Farrow, Niemann, & Wylie, 1994). More recently, Foster et al. (2005) demonstrated the significant relationship between performance on the RFFT and right frontal capacity in healthy young adults. More specifically, the low design fluency group evidenced increased delta magnitude over the right frontal lobe relative to the high fluency group using quantitative electroencephalography (QEEG).

Auditory Affective Verbal Learning Test

The AAVLT (Appendix D) (Snyder & Harrison, 1997) is composed of three word lists differing in either a positive, negative, or neutral valence. The words comprising each of the affectively laden word lists were chosen from word norms established by Toglia and Battig (1978). Each list is comprised of 15 words. The negative list includes words, such as "morgue," "murder," and "kill," while the positive list includes words, such as "sunset," "garden," and "beach." The neutral list consists of words, such as "drum," "curtain," and "bell." The word lists were read so that participants hear approximately 1 word per second.

Hand Grip, Perseveration, and Fatigue Test

In accordance with Harrison and Pauly (1990), Demaree et al. (2002), and Everhart et al. (2002), the Hand Grip, Perseveration and Fatigue Test (Appendix E) was used to assess maximal grip strength, perserevative errors grip strength (or overshoot in estimating one half full grip strength), and fatigue. This test requires a hand dynamometer that is either analog (Demaree et al., 2002; Everhart et al. 2002) or digital (Walters & Harrison, 2007) and measures grip strength

in kilograms. The first trial of this test required the participant to squeeze the hand dynamometer at full strength at the left hand. This was then repeated for the right hand. The participant was then instructed to place the hand dynamometer in his left hand and to squeeze ½ full grip strength. This was then repeated at the right hand. The participant was then instructed to place the hand dynamometer in the left hand and squeeze at full strength for five consecutive trials. This procedure was then repeated at the right hand. At no time was the participant informed of his grip strength score.

Finger Tapping Test

As reviewed by Lezak (1995), the Finger Tapping Test (FTP) (Appendix F) was traditionally used as part of the Halstead Reitan Neuropsychological Assessment Battery to assess for manual dexterity and strength by simply employing a tapping device that records the number of finger taps per unit of time. The participant used each hand to complete five, 10-second trials with very brief rest periods between trials. In addition to the each trial, the score for each hand was the average of the 5 trials.

The FFT has long been used to assess for differences in laterality within the frontal lobes (Kiziltan, Barut, Gelir, 2006). Moreover, the FTT has been used to track patients with head injuries over decades (Prigatano, Johnson, Gale 2004). Groot-Driessen, van de Sande, and van Heugten (2006) demonstrated that initial speed of finger tapping was predictive of recovery and daily living functioning in patients recovering from their first stroke.

Physiological Measures

Blood Glucose Measurement

The current research on glucose measurement indicates marked benefits from obtaining glucose from the forearm (Lee, Weinart, Miller, 2002; Pfutzner et al., 2003; Tieszen & New,

2003). The Therasense Freestyle Glucometer is a leading device for forearm testing (Demers, Kane, Bakst, Busch, & Hamilton, 2003). The Freestyle Glucometer maintains increased accuracy; demonstrates more clinically acceptable readings when compared to intravenous blood samples; and requires fewer sticks (White, Braco, & Malone, 2002).

There is much controversy concerning the at-home, self-test measurement of blood glucose levels and, of all the glucometers assessed to date, all have failed to meet the 95% accuracy rating standard set by the ADA (Brunner et al., 1998; Nichols, et al., 1995; Rheney & Kirk, 2000). Historically, manufacturers of home glucose monitoring devices have recommended obtaining blood samples from the fingertips to assess blood sugar levels. There is some controversy over the accuracy of forearm testing particularly concerning the difference between forearm and finger sites when glucose levels are rapidly ascending or descending. Peled, Wong, & Gwalani (2002) had participants sugar load and found the forearm testing to be less accurate at detecting the swift change in glucose levels when compared to the finger tip sites, yet found the forearm to be reliable, otherwise. Lee et al. (2002) demonstrated a few significant differences in the level of accuracy after employing the two methods for 190 diabetics over the course of the day. Other researchers have found no difference between finger-prick testing and forearm measurements (Pfutzner et al., 2003) even with rapid changes in participants' glucose levels (Jungheim & Koschinsky, 2002). Regardless of the controversies, marked benefits in forearm testing have been the ease of obtaining a blood sample and the noteworthy decrease in pain (Lee et al., 2002; Pfutzner et al., 2003; Tieszen & New, 2003). Forearm testing further increases the readiness for testing, particularly when frequent blood samples are attained (Pfutzner et al., 2003).

Quantitative Electroencephalography (QEEG)

In accordance with Foster et al. (2005), monopolar QEEG recordings were taken from 19 electrode sites, arranged according to the International 10/20 System using with a NeuroSearch-24 (Lexicor Medical Technology, Inc., Boulder, CO). Housed in the lycra electrode cap are 19 silver-silver chloride electrodes. The magnitudes of alpha delta (0-4 Hz), theta (4.1-8.0 Hz), alpha (8.1.-13 Hz), and beta (13.1- 20.0 Hz) were recorded. Each of the 19 electrode sites, along with the associated magnitudes, were included as a dependent variables. A sampling rate of 256 Hz was used without the use of highpass filter. The impedance value for each electrode site was below 5 ohms. QEEG values were formatted with magnitude (uV) using peak values. After each recording, all artifacts were removed.

Procedure

Initially, all potential participants in the experiment completed an online screening. As noted earlier, this online screening was advertised in physicians' offices and in local newspapers. The online screening included questionnaires on medical history, laterality, and hostility. Those participants with reporting a diagnosis of type II diabetes, an unremarkable medical history, with CMHO scores approaching either 0-19 (low hostile) or 27-50 (high hostile) were contacted to participate in the experiment. However, due to poor community participation, the recruitment procedures were streamlined to allow greater ease of access and additional incentives were added to enhance participation, namely increased financial compensation and feedback concerning the participant's memory scores. Due to reported difficulties using the computer and problems accessing the online measures, the online screening portion was removed. This allowed each participant to complete all requirements for the experiment in the laboratory during one session.

These changes increased participant dramatically and also resulted in a more heterogeneous sample. Moreover, as described above, this hostility sample is markedly different and unlike the traditional, college-aged hostile population.

After the incorporation of the updated recruitment procedures, the remainder of the participants called the experimenter directly to schedule a time to enter the laboratory. Participants were screened briefly over the phone to assess for diabetic diagnosis, age, handedness, and medical history. Participants were then scheduled an appointment time for completion of the self-report measures and experimental portion of the study. Prior to the start of the experiment, the participants were asked to make no changes in their eating patterns or medication regimens.

Upon entering the laboratory, the participants read and signed the Informed Consent form. Next, the participants were administered the hostility questionnaire (CMHO) and completed medical history and laterality questionnaires. The participants' weight and waist-to-hip ratio (WHR) were also measured.

The participants were then fitted with the QEEG cap. Once fitted, the researcher left the room and repeated the following instructions: "Please take about one minute to become accustomed to your surroundings. Please sit still in the chair and face forward." After a 90-second adaptation period, the experimenter reentered the room and recorded baseline measures of glucose. After completion of these baseline measures, a two-minute baseline of QEEG magnitudes was taken.

Participants then completed either the verbal or nonverbal fluency measures in a counterbalanced fashion. Instructions for the fluency measure were read to the participants and the task was then completed. After completion of the task, glucose levels were again assessed.

Immediately after these measures were completed, the QEEG magnitudes of delta (0-4 Hz) and theta (4.1-8 Hz), and a reduction in alpha (8.1-13) and beta (13.1-20 Hz) were recorded for 45 seconds. This time length was in accord with Foster & Harrison (2004) and was thought to provide the most robust changes in electrical activity after a stressor. After a 90 second adaptation period, this process was repeated for the remaining fluency measure. Once the COWAT and the RFFT were completed, the FTT, the Hand Grip, Preseveration, and Fatigue Test, and AAVLT were completed. Any questions the participants had, including questions pertaining to their memory, were answered. The participants were then debriefed, paid, and excused.

Results

Physiological Measures: Glucose

To assess between group differences occurring before and after each fluency-stressor for the dependent variable of glucose (mg/dl), a 3-factor mixed design ANOVA was conducted with a fixed factor of Group (high hostile-diabetic, low hostile-diabetic) and repeated measures of Condition (verbal fluency-stressor and nonverbal-fluency stressor) and Trial (pre and post stress). As stated above, the COWAT was employed as the verbal fluency-stressor, whereas the RFFT was employed as the nonverbal fluency-stressor. For each ANOVA, post hoc comparisons were made using Tukey's LSD (Winer, 1971). An a priori level of significance was set at $p \leq .05$.

It was predicted (H_1) that the high hostile-diabetic men would demonstrate heightened reactance to the nonverbal fluency-stressor (right frontal lobe stressor) relative to the low hostile-diabetic men as indicated by increases in glucose after the fluency-stressor. Support for this interaction was not found for Group x Condition x Trial, $F(1,33) = 1.76$, $p=.19$. Contrarily, glucose values demonstrated a trend in reduction in value rather than in increase in value after

both the right and left frontal lobe stressor for both groups. Post hoc analyses revealed that in the high hostile-diabetic group, glucose levels dropped from a mean score of 185.71 (*SD* = 95.04) to 181.71 (*SD* = 101.29) after the nonverbal stressor and from 189.29 (*SD* = 118.51) to 176.36 (*SD* = 100.04) after the verbal stressor. A similar trend was seen in the low hostile-diabetic group. Here, mean glucose scores dropped from 146.48 (*SD* = 69.5) to 133.62 (*SD* = 49.58) after the nonverbal fluency-stressor. For the verbal fluency-stressor, post hoc analysis revealed that the low hostile-diabetic group's mean glucose level dropped from 139.90(*SD* = 51.29) to 137.19 (*SD* = 54.17) after the fluency-stressor (see Table 1). When the factors of Group (low hostile-diabetic and high hostile-diabetic) and Condition (nonverbal fluency-stressor and verbal fluency-stressor) were removed there was a main effect for the variable of Trial, $F(1)=12.5$, $p<.001$. For the entire sample, post hoc analyses revealed a reduction in mean glucose before the fluency-stressor (*M* =165.35, *SE* = 13.92) to after the fluency-stressor (*M*=157.22, *SE* = 12.89).

It should be noted that the variability within the high hostile-diabetic scores was nearly double that of the low hostile-diabetic group's. Several transformations of the high hostile-diabetic group's glucose values were employed to reduce the variability of these scores. However, these transformation scores did had no discernable effects on the analyses.

Although not originally proposed as an analysis, the factor of Time was reviewed. Despite the order of Condition being counterbalance (verbal fluency-stressor and nonverbal fluency-stressor), this factor was examined to assess for ordering effects as well as to assess glucose responsivity over the course of time. As stated earlier, glucose levels were measured at four different times, specifically before and after both the verbal and nonverbal fluency-stressors. This analysis examined the glucose levels fluctuations over time while disregarding the variables of Condition and Trial. Here, a one-factor mixed ANOVA was conducted with the fixed effect of

group (high hostile-diabetic and low hostile-diabetic) with the repeated measure of Time (glucose time 1-4). There was a non-significant trend for the interaction of Group x Time, $F(1,33)=2.761$, $p<.11$, thereby further supporting the general pattern of a reduction in glucose levels after each stressor. It should be noted that glucose values increased in value during the 90-second adjustment period regardless of the prior condition, followed by a second drop after the stressor (see Table 2). To explore the cumulative differences of glucose values between groups over time, the variable of Time (1-4) was averaged. A one-way ANOVA was conducted and revealed no significant differences between groups for glucose levels. However, a non-significant trend [$F(1,33)=3.03$, $p=.09$] was evident between the two groups for the average glucose level. Post hoc analysis revealed that the average glucose level for the low hostile-diabetic group was 139.30 (SD = 54.94) and the average glucose level for the high hostile-diabetic group was 184.23 (SD = 99.25). Further analysis revealed a substantial variation in the high hostile-diabetic glucose levels relative to the low hostile-diabetic glucose levels (see Table 4).

Physiological Measures: QEEG

To assess between group differences occurring before and after each fluency-stressor for the dependent variables of QEEG magnitude, separate 3-factor mixed design ANOVA were conducted with a fixed factor of Group (high hostile-diabetic, low hostile-diabetic) and repeated measures of Condition (verbal fluency-stressor and nonverbal-fluency stressor) and Trial (pre and post stress) for the QEEG the magnitudes of delta (0-4 Hz), theta (4.1-8.0 Hz), alpha (8.1.-13 Hz), and beta (13.1- 20.0 Hz). Given the *Limited Capacity Model's* focus on the right frontal lobe as well as a concern for increasing the probability of a Type I error, only frontal lobe magnitudes were examined to compare changes in a pre-post stress paradigm. Specifically, the

right frontal lobe sites included FP2, F4, and F8 and the left frontal lobe sites included FP1, F3, and F7.

It was predicted (H_2) that subsequent to the right frontal lobe stressor, the high hostile-diabetics would evidence increased delta (0-4 Hz) and theta (4.1-8 Hz), and a reduction in alpha (8.1-13), relative to baseline levels experienced before the stressor. Analyses were conducted for the right frontal lobe sites of FP2, F4, and F8 and for the left frontal lobe sites of FP1, F3, and F7. For the delta magnitude (0-4 Hz) at FP1a significant interaction was found for Group x Trial $F(1,22)=3.99$, $p\leq.05$. Here, post hoc analysis revealed that the low hostile-diabetic mean delta magnitude was 8.41 (*SD* = .91) before the stressor and dropped to 8.25 (*SE* = 1) after the stressor, whereas the high hostile-diabetic mean delta magnitude was 9.58 (*SE* = 1.16) before the stressor to 11.68 (*SE* = 1.28) after the stressor.

For the magnitude of delta (0-4 Hz), an interaction effect was found for Group x Trial, $F(1,22) = 7.36$, $p\leq.01$ at the location of F3. Post hoc analysis revealed that the low hostile-diabetic mean delta magnitudes were 7.54 (*SE* = .70) before the stressor and 6.85(*SE* = .692) after the stressor, whereas the high hostile-diabetic mean pre-stress value was 7.46 (*SE* = .83) that increased to 8.8 (*SE* = .824) after the stressor (see Table 5).

Further comparisons examined relative left and right frontal lobe activation/deactivation in relation to both the type of fluency-stressor as well examining changes in a pre-post stress paradigm between the low hostile-diabetic and high hostile-diabetic group. Here a 4-factor ANOVA was employed with the fixed factor of Group (high hostile-diabetic, low hostile-diabetic) and repeated measures of Location [left frontal (FP1) and right frontal (FP2)], Condition (verbal fluency-stressor and nonverbal-fluency stressor), and Trial (pre and post stress). For the magnitude of delta (0-4 Hz), there were no main effects or interaction effects with

the variable of Location. This analysis was repeated for Location of F3 and F4 and then again for F7 and F8 and no between group differences were found.

For the magnitude of theta (4.1-8 Hz) at FP1 there was a main effect for the variable of Trial $F(1)=4.66$, $p<.05$. This finding indicated that theta increased after the completion of each stressor for the entire sample. For this magnitude, the sample began with a mean magnitude of 3.87 (SE = .218) and ended with a mean magnitude of 4.19 (SE = .223). There was interaction effect for Group x Trial, $F(1,27)=4.61$, $p<.05$ at the site of F3 for magnitude of theta (4.1-8 Hz). Here, post hoc analysis revealed that the low hostile-diabetic men demonstrated a reduction in theta from pre-stress (M = 4.12, SE = .27) to post-stress (M = 4.10, SE = .23) whereas the high hostile men demonstrated an increase in theta from pre-stress (M=4.10, SE= .33) to post-stress (M = 4.42, SE = .35) (see Table 6).

Further comparisons examined relative left and right frontal lobe activation/deactivation in relation to both the type of fluency-stressor as well examining changes in a pre-post stress paradigm between the low hostile-diabetic and high hostile-diabetic group. Here a 4-factor ANOVA was employed with the fixed factor of Group (high hostile-diabetic, low hostile-diabetic) and repeated measures of Location [left frontal (FP1) and right frontal (FP2)], Condition (verbal fluency-stressor and nonverbal-fluency stressor), and Trial (pre and post stress). This analysis was repeated for the locations of F3 and F4 as well as for F7 and F8. No between group differences were found for the magnitude of theta (4.1-8.0 Hz).

There were no significant findings for the magnitude of alpha (8.1-13 Hz) for any of the frontal lobe sites.

For the magnitude of beta (13.1-20) there was a main effect for the variable of Trial at F8 $F(1)=4.362$, $p<.05$. Post hoc analysis revealed an increase in magnitude from the pre-stress

(*M*=3.58, *SE*=.206) to the post-stress (*M* = 3.942, *SE* = .255) regardless of Condition or Group. There were no other main effects or interaction effects for the remaining electrode sites.

Behavioral Measures

To assess for differences among the behavioral measures, 2-factor mixed design ANOVAs were conducted with the fixed factor of Group (diabetic-hostile and diabetic low-hostile) and repeated measures of Condition (verbal and nonverbal fluency-stressors) to assess for differences in the dependent variables of Total Score and Total Error.

There was no support for the behavioral prediction (H_1) that the high hostile group would have poorer performance on the nonverbal fluency-stressor task (RFFT). In direct contrast to this prediction, 2-factor mixed ANOVA revealed that while there was a significant interaction for Group x Total Error, $F(1,34)=3.893$, $p \leq .05$. Post hoc analysis revealed that the Total Error was significantly more elevated for low hostile-diabetic group (*M* = 42.29, *SD* = 39.13) rather than for the high hostile-diabetic group (*M*=20.47, *SD* = 20.3) (see Table 7). It should be noted that the while the high hostile-diabetic Total Error score for the RFFT is equivalent to previous high hostile Total Error rates (Walters & Harrison, 2006), the Total Error for the low hostile-diabetic group is markedly elevated. For the dependent variable of Total Score on the nonverbal fluency task, there were there were no significant differences between the low hostile-diabetic group (*M* = 75.10, *SD* = 22.42) and the high hostile-diabetic group (*M* = 69.73, *SD* = 16.36).

For the verbal fluency task (COWAT), both groups averaged around 12 words per trial while making 2-4 errors for the entire task. No significant differences between groups were found for the verbal Total Score or Total Error.

No support was found for the behavioral prediction (H_2) that the high hostile-diabetic men would have an increased performance on the negatively valanced portions of the affective

verbal learning test (AAVLT) in comparison with the neutral and the positively valanced learning trials (see Table 8).

No support was found for the behavioral prediction (H_3) the high hostile-diabetics would demonstrate increased grip strength at the left hand relative to the low hostile diabetics. Here there were no differences on the Grip Strength, Perseveration, and Fatigue Test (see Table 9).

No support was found for the behavioral prediction (H_4) that the high hostile-diabetics would demonstrate decreased finger tapping rate (FTT) at the left hand relative to the low hostile diabetics. Post hoc analysis revealed that at the right hand, the low hostile-diabetic men were able to tap an average of 46.08 (*SD* = 6.25) per trial and the high hostile-diabetic men were able to tap an average of 45.25 (*SD* = 6.65) per trial. At the left hand, the low hostile-diabetic men were able to tap an average of 50.44 (*SD* = 8.09) per trial and the high hostile-diabetics were able to tap an average of 48.89 (*SD* = 6.35) per trial.

Demographic Measures

There were no between group differences for the variables of weight, hip size, waist size, or WHR.

Discussion

As an extension of *The Limited Capacity Model* of hostility (Carmona, Holland, & Harrison, 2009; Walters & Harrison, 2006; Williamson & Harrison, 2005; Williamson, Harrison, & Walters, 2007), it was predicted that high hostile-diabetic men would demonstrate prolonged and exaggerated responses to stress as a result of a limited stress management capacity attributable to a diminished capacity within the right frontal lobe. In a pre-post stress paradigm, both peripheral glucose levels and the QEEG magnitudes of delta, theta, alpha, and beta at the left and right frontal lobes were examined to measure the proposed hyperreactivity to stress. It

was also expected that the high hostile-diabetic men would show a diminished performance on neuropsychological indicants (behavioral measures) of the right frontal functions as another reflection of a limited capacity within this region.

Concerning the variable of peripheral glucose, increases were not demonstrated in the high hostile-diabetic as a result of nonverbal fluency-stressor as predicted. Moreover, glucose levels significantly reduced in value rather than increased in value after both fluency-stress conditions for the entire sample. While this pattern of glucose responsivity did not support the initial prediction, the findings are consistent with newly published research on glucose changes after cognitive tasks in diabetic men. Perlmuter et al. (2009) administered the neuropsychological measures of Digit Symbol Substitution, Trial Making Test A and B, and the COWAT to both diabetic men. Glucose levels were measured before and after each stressor. To examine the changes in glucose levels, the researchers created a rate variable by dividing the change in glucose level by the time required to complete each timed test. In the diabetic population, peripheral glucose levels dropped after the completion of all the tests except for the COWAT. This decrease was found regardless of the type or amount of diabetes medication at the time of the experiment. Perlmuter et al. argued that peripheral glucose levels reduced in value after the cognitive testing because individual neurons required more resources to complete the mental demands. These authors suggested that this theory may explain why the glucose reductions were seen in tests that required psychomotor skills, attention, visuoperceptual ability, sequencing skills, mental flexibility, and planning; and why glucose levels did not change as a function completing the COWAT which is a test that is based upon an internal language system with no motor component. There was detailed theoretical explanation in these findings other than at the level of the neuron substrate.

In relation to the *Limited Capacity Model*, the glucose findings from the current experiment require further exploration. Here, future research will be needed to assess if the drop in glucose levels in the high hostile-diabetics is larger relative to the drop in glucose levels in the low hostile-diabetics due to diminished capacity. Additionally, there was a relatively high level of variability for the high-hostile diabetic glucose levels, a finding that requires further exploration. The high hostile-diabetic group mean glucose level was 184.23 (SD=99.25) with a range of glucose levels from 76 mg/dl to 383 mg/dl (see Table 4). The low hostile-diabetic group's glucose levels tended to cluster closer to the mean (M = 139.30, SD = 54.94) (see Figure 1). More research is required to determine if this variability is a descriptor of the high hostile-diabetic group or if it is an atypical finding.

In addition to illuminating the directional change in glucose values after a fluency-stressor, the glucose results reveal two key qualitative findings. The first is that cognitive stress, here a fluency-stressor, resulted in peripheral glucose changes. This finding provides further evidence that cognitive functioning can result in arousal system changes seen peripherally. Secondly, the glucose values changed rapidly as a function of the fluency-stressor in a repeated fashion. This finding may be beneficial to the diabetes literature as it provides another avenue of analysis. Diabetes research on cognitive functioning typically compares diabetic performance to non-diabetic performance (Debling et al. 2006; Kanaya et al., 2004; Reaven et al., 1990) or provides within subject comparisons between euglyemic episodes and hyperglycemic episodes (Cox et al., 2005; Sommerfield et al., 2004). The current experimental design allowed for glucose levels to be measured before and after both fluency-stressors. Moreover, it demonstrated that a 90-second recovery period between stressors was a sufficient recovery time for glucose levels to return to near their initial values. As noted in the literature (Arvanitakis et al., 2006;

Van den Berg et al., 2007; Biessels et al, 2004) the exact regulator mechanisms behind the fluctuations in glucose levels is not well understood and additional research is required, although it is clear that the brain does indeed play a role in these changes.

Concerning the QEEG findings, there was no support for the initial prediction that there would be increases in slow wave magnitudes at the right frontal lobe for the high hostile-diabetics after the nonverbal fluency-stressor task. In contrast to this prediction, the high hostile-diabetics demonstrated increases in delta and theta at the left frontal lobe, rather than the right frontal lobe after a fluency-stress condition, whereas the low hostile-diabetics demonstrated decreases in delta and theta at the left frontal lobe after a fluency-stress condition. This effect was seen regardless of the type of fluency-stressor.

This finding of deactivation in the left frontal lobe after stress rather than at the right frontal lobe in the high hostile-diabetic men is unusual in that it stands in direct opposition to the hostility research from our lab that has repeatedly demonstrated diminished right frontal lobe functioning in high hostile men for motor (Demaree et al. (2002) and premotor systems (Walters & Harrison, 2006; Williamson & Harrison, 2005; Williamson et al., 2007). The findings from the current research also contrast with previous research on both the structural and functional changes that support the lateralized effects of diabetes on the frontal lobes. Using MRI, Wessels et al. (2006) found that diabetics, relative to non-diabetics, had significantly reduced grey matter density in the right inferior frontal gyrus and right occipital lobe. In addition to these structural changes within the right frontal lobe, Hyllienmark et al. (2005) demonstrated that, relative to non-diabetics, diabetics demonstrated a specific reduction of activation over the right frontal pole. It should be noted that both the research by Wessels et al. (2006) and Hyllienmark et al.

(2005) used non-diabetics as a control group and did not examine emotional contributors, such as hostility.

For the current experiment, the differential response of delta and theta magnitudes at the left frontal lobe as a function of hostility group provide evidence that the low hostile-diabetics and the high hostile-diabetics are two distinct groups with differing electrophysiological responses to stress. Given the left frontal deactivation, perhaps additional resources are being allocated to the right frontal regions via inter-hemispheric connections, namely the corpus callosum. Originally proposed by Tucker (1981) with regard to emotion in a theoretical sense, this theory postulates that interhemispheric mechanisms involving contralateral inhibition across interhemispheric commissures are responsible for emotion. Relative activation of the right hemisphere was predicated with negative emotion and relative activation of the left hemisphere with positive emotion (Tucker & Williamson, 1984). More recently, Stephan et al. (2005) conducted a literature review on fMRI research that examined the inter-hemispheric inhibition and activation via the corpus callosum for task demands (rather than Tucker's original focus on emotion.) Stephan et al. reported that the interhemispheric interactions are a function of task demands, resulting in an asymmetry of activation that exits when the new task demands are placed on an individual. Here, the relative activation and deactivation is a function of the type of task demand. Given the historical nature of the research supporting a diminished capacity within the right frontal lobe of the high hostile men, perhaps the left frontal deactivation seen in the high hostile-diabetic men is due to rechanneling of resources from the left frontal lobe to the right frontal lobe via the corpus callosum. Further analysis of the potential activation seen in this dense white matter structure is not possible at this time due the limitations of the QEEG only being able to record electrical activation changes on the surface of the brain.

The rechanneling of resources between the frontal lobe is also supported by the *Balance Model of Emotion* (Carmona, Holland, and Harrison, 2009; Carmona, Holland, Stratton, and Harrison, 2008; Foster, Drago, Ferguson, and Harrison, 2008). Here, a functional cerebral systems approach has been employed to explain frontal regulatory capacity over posterior regions. Essentially, this model posits that the brain can be divided into four functional quadrants: left and right hemispheric functioning as well as anterior and posterior. Support has been found for the regulatory control over both vestibular and cardiovascular functioning in populations with an increased negative emotional bias. An essential feature of the *Balance Model of Emotion* is it's increased scope and incorporation of multiple brain regions that are working together in concerted fashion. As it applies to the current experiment, future research will be required to assess the influence of these regions on peripheral glucose levels as well as slow wave QEEG magnitudes.

Curiously, the increase in slow-wave magnitude over the left frontal lobe for the high hostile-diabetic group had no bearing on the verbal and nonverbal fluency-stressor variables of Total Score or Total Error. For example, while the high hostile-diabetic group did evidence some errors on the nonverbal fluency-stressor (RFFT), it was the low hostile-diabetic group that evidenced marked impairment for this task. The low hostile-diabetic Total Error for the nonverbal fluency-stressor was double the rate of the high hostile-diabetics.' This behavioral measure was not associated with changes in QEEG magnitude. These findings are unlike previous research on fluency in which poor performance on the RFFT was shown to be predictive of increased delta wave magnitudes over the right frontal regions (Foster et al. 2004). Given the significant impairment of the low hostile-diabetic population, future research is warranted to further elucidate these findings, particularly since the error scores were so robust

and widespread within this group.

Unlike the initial prediction, there were no group differences in scores for affective memory as measured by the AAVLT. Mollet and Harrison (2007) and Snyder et al. (1996) demonstrated significant impairments for the high hostile performance relative to the low hostile performance on this affective memory measure. The current experiment also did not demonstrate between group differences on any measure of motor performance for finger tapping speed (FFT) or on the Hand Grip, Perserveration, and Fatigue Test, as has been repeatedly documented by Demaree & Harrison (1997) and Demaree et al. (2002).

Both the absence of findings on the behavioral measures, as well as the unexpected glucose and QEEG findings may be attributed to differences in the sample used for the current experiment relative to the samples used for development of research in our lab to date. In addition to carrying a diagnosis of type II diabetes, the sample used for the current research consisted of adult men, aged 34-70, volunteering from the local community, that were predominately hypertensive. Unlike the college-aged samples, the participants in this experiment were highly educated with an average education level equivalent to a master's degree. Moreover, 15 participant's had earned a doctorate of philosophy, theology, or education. The increased education level is somewhat curious given the robust Total Error rates on the fluency-stressors.

Of additional significance, the traditional recruitment methods and compensation varied from the college-aged samples. Historically, over 100 undergraduate students were required to complete the CMHO before an appropriate number of low and high hostile participants, endorsing a right hemibody preference, agreed to participate in research conducted in the laboratory (Demeree et al., 1997; Walters & Harrison, 2006; Mollet & Harrison, 2007). The

current experiment discontinued the online pre-screening due to computer illiteracy and removed the right hemibody preference to increase subject participation.

The hostile-diabetic men were compensated both with financial gains ($50) as well as feedback on the memory performance instead of being rewarded with extra credit as is typically done with the undergraduate population. It is arguable that the compensation employed biased the participants in some fashion. A subset of the participants reported interest in the financial compensation and five participants stated that they were not employed at the time of the study. Aside from the monetary compensation, a significant number of participants were highly interested in their memory scores, and nearly half of the participants noted that they felt their memory has been worsening over time, a pattern attributed to normal aging. Three participants also stated that they had recently lost weight. They reported being eager to participate in diabetes research to determine the effects of their weight loss on their diabetes and mental ability. Finally, the variable of age was a possible confounding variable. Here, the low hostile-diabetic group was, on average, 10 years older than the high hostile-group.

In addition to problems related to the sample, the current experiment contains some methodological flaws. The primary methodological issue pertains to this issue of not using a "non-diabetic" control group, which has been the standard comparison group for diabetes research (Debling et al. 2006; Hyllienmark et al., 2005; Perlmuter et al., 2009; Reaven et al. 1990; Wessels et al., 2006). Future research warrants further assessment of between group differences among low and high hostile-diabetics and low and high hostile-nondiabetics.

The second methodological issue has to with the differing group sizes. While the low hostile-diabetic group included 21 participants, the high hostile-diabetic group included 15 participants. This smaller group size of the high hostiles is unexpected given the literature

documenting the relationship between diabetes and both hostility and anger (Chyun et al., 2006; Golden et al., 2006; Niaura et al., 2000; Raiikkonen et al. 1996; Sommerfield et al. 2004). The implication of the seeming lack of interest in the community, specifically on the part of the high hostile-diabetics, is that some unknown occurrence is preventing participation. This unknown factor may be related to medical noncompliance as has been documented within the diabetic community (Hauber, Mohamed, Johnson, and Falvey, 2009; Schmittdiel et al. 2007). It is arguable that engaging in unhealthy behaviors that include cigarette smoking, high alcohol intake, and caloric intake (Kawachi, Sparrow, Spiro, Vokonas, & Weiss,1996; Knox, Weidner, Adelman, Stoney, and Ellison, 2004; Scherwitz et al. 1992; Siegler, Peterson, Barefoot, and Williams, 1992; Yan et al. 2003; Zhang et al. 2005) as well as being statistically more likely to suffer from cardiovascular disease (Boyle et al. 2004; Brydon, Magid, & Steptoe, 2005; Miller, Smith, Turner, Guijarro, & Hallet, 1996), hypertension (Yan et al. 2003; Zhu et al. 2005), and atherosclerosis (Iribarren et al. 2000) reduce the interest of participating in research. Any combination of these factors could potentially inhibit participation in the study. Future research will be forced to address this dilemma to increase community member involvement.

The current experiment applied a theoretical model of hostility to a population with a potentially progressive and dysregulated fuel supply, specifically type II diabetes. Several existing bodies of literature were integrated, allowing for the examination of the emotional, behavioral, and physiological aspects of this newly defined, hostile-diabetic population. As guided by the *Limited Capacity Model,* the frontal lobe functioning as well as peripheral glucose responses of the hostile-diabetic population was examined before and after lateralized stressors. The findings revealed that peripheral glucose levels reduce in value after the completion of frontal lobe stressors, while the left frontal lobe of the high hostile-diabetic group evidenced

increased slow wave activity, potentially to compensate for other regions with diminished capacity. Given the relatively uncharted aspects of the hostile-diabetic population, as well as the issues related to the sample, future exploration of the stress response and frontal lobe functioning is warranted.

References

American Diabetes Association (2005). *American Diabetes Association Complete Guide to Diabetes (4th Edition)*. United States of America: Author.

Anand, S.G., Mehta, S.D., Adams, W.G. (2006). Diabetes mellitus screening in pediatric primary care. *Pediatrics, 118*(5), 1888-95

Ali, S., Stone, M.A., Peters, J.L., Davies, M.J., Khunti, K. (2006). The prevalence of co-morbid depression in adults with Type 2 diabetes: A systematic review and meta-analysis. *Diabetic Medicine, 23*(11), p. 1165-73.

Arvanitakis, Z., Wilson, R.S., Bennett, D.A. (2006). Diabetes mellitus, dementia, and cognitive function in older persons. *Journal of Nutrition, Health & Aging, 10*(4), 287-91.

Arvanitakis, Z., Wilson, R.S., Li, Y., Aggarwal, N.T., Bennett, D.A. (2006). Diabetes and function in different cognitive systems in older individuals without dementia. *Diabetes Care, 29*(3), 560-5.

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, 26*(8), 1044-80.

Baldo, J.V., Shimamura, A.P., Delis, D.C., Kramer, J., & Kaplan, E. (2001). Verbal and design fluency in patients with frontal lobe lesions. *Journal of the International Neuropsychological Society, 7*(5), 586-96.

Barefoot, J.C., Williams, R.B. (1992). Hostility during late adolescence predicts coronary risk factors at mid-life. *American Journal of Epidemiology, 136*(2), p. 146-154.

Benton, A., de Hamsher, K.S., (1976). *Multilingual aphasia examination.* Iowa City: University of Iowa.

Benton, D., Kumari K., Brain, P.F. (1982). Mild hypoglycemia and questionnaire measures of aggression. *Biological Psychology, 14*, 129-135.

Biessels, G.J., Bravenboer, B., Gispen, W.H. (2004). Glucose, insulin and the brain: modulation of cognition and synaptic plasticity in health and disease: a preface. *European Journal Pharmacology, 19*, 490(1-3), 1-4.

Biessels, G.J., Staekenborg, S., Brunner, E., Brayne, C., Scheltens, P. (2006). Risk of dementia in diabetes mellitus: a systematic review. *Lancet Neurology, 5*(1), 64-74.

Boyle, S.H., Williams, R.B., Mark, D.B., Brummett, B.H., Siegler, I.C., Helms, M.J., Barefoot, J.C. (2004). Hostility as a predictor of survival in patients with coronary artery disease. *Psychosomatic Medicine, 66*(5), p. 629-32.

Bokura, H., Kobayashi, S., Yamaguchi, S., Takahashi, K., Iijima, K., Nagai, A., Oguro, H. (2006). Clinical characteristics and prognosis in stroke patients with diabetes mellitus: retrospective evaluation using the Japanese Standard Stroke Registry database (JSSRS). No To Shinkei, 58(2), 135-9.

Brands, A.M., Biessels, G.J., Kappelle, L.J., de Haan, E.H., de Valk, H.W., Algra, A., Kessels, R.P. (2007). Cognitive Functioning and Brain MRI in Patients with Type 1 and Type 2 Diabetes Mellitus: *A Comparative Study. Dementia and Geriatric Cognitive Disorders, 23*(5), 343-350

Brands, A.M., van den Berg, E., Manschot, S.M., Biessels, G. J., Kappelle, L.J., de Haan, E.H.F. & Kessels, R.P.C. (2007). A detailed profile of cognitive dysfunction and its relation to psychological distress in patients with type 2 diabetes mellitus. *Journal of the International Neuropsychological Society, 13,* p. 228- 297.

Brands, A.M., Biessels, G.J., de Haan, E.H., Kappelle, L.J., Kessels, R.P. (2005). The effects of type 1 diabetes on cognitive performance: a meta-analysis. *Diabetes Care, 28*(3), 726-35.

Brower, M.C. & Price, B.H. (2000). Neuropsychiatry of frontal lobe dysfunction in violent and criminal behavior: a critical review. *Journal of Neurology, Neurosurgery, and Psychiatry, 71,* p. 720-726.

Brunner, G.A., Ellmerer, M., Sendlhofer, G., Wutte, A., Trajanoski, Z., Schaupp, L., Quehenberger, F., Wach, P., Krejs, G.J., Pieber, T.R. (1998). Validation of home blood glucose meters with respect to clinical and analytical approaches. *Diabetes Care, 21,* (4), 585- 590.

Brydon, L., Magid, K., Steptoe, A. (2005). Platelets, coronary heart disease, and stress. *Brain and Behavioral Immunology, Sept 22*.

Carmona, J.C., Holland, A.K., Harrison, D.W. (2009). Extending the functional cerebral systems theory of emotion to the vestibular modality: A systematic and integrative approach. *Psychological Bulletin, 135* (2), 286-302.

Carmon, J.C., Holland, A.K., Stratton, H.J., and Harrison, D.W. (2008). Sympathetic arousal to a vestibular stressor in high and low hostile men. *Brain and Cognition, 66*, 150-155.

Christensen, A.J., Wiebe, J.S., Lawton, W.J. (1997). Cynical hostility, powerful others control expectancies, and patient adherence in hemodialysis. *Psychosomatic Medicine, 59*, 307 312.

Chyun, D.A., Melkus, G.D., Katten, D.M., Price, W.J., Davey, J.A., Grey, N., Heller, G., Wackers, F.J. (2006). The association of psychological factors, physical activity, neuropathy, and quality of life in type 2 diabetes. *Biological Research for Nursing, 7*(4), 279-88.

Coren, S. P., Porac, C., & Duncan, P. (1979). A behaviorally validated self-report inventory to assess 4 types of lateral preferences. *Journal of Clinical Neuropsychology, 1*, 55–64.

Cox, D.J., Kovatchev, B.P., Gonder-Frederick, L.A., Summers, K.H., McCall, A., Grimm, K.J., Clarke, W.L. (2005). Relationships between hyperglycemia and cognitive performance among adults with type 1 and type 2 diabetes. *Diabetes Care, 28*(1), 71-7.

Debling D., Amelang, M., Hasselbach, P., Sturmer, T. (2006). Diabetes and cognitive function in a population-based study of elderly women and men. *Journal of Diabetes Complications, 20*(4), 238-45.

Demakis, G.J. & Harrison, D.W. (1997). Relationships between verbal and nonverbal fluency measures: implications for assessment of executive functioning. *Psychological Reports, 81*(2), 443-448.

Demaree, H.A., & Harrison, D.W. (1996). Case study: topographical brain mapping in hostility following mild closed head injury. *International Journal of Neuroscience, 87*(1-2), 97 101.

Demaree, H.A., & Harrison, D.W. (1997). Physiological and neuropsychological correlates of hostility. *Neuropsychologia 35,* 10, 1405-1411.

Demaree H.A., Harrison, D.W. (1997). A neuropsychological model relating self-awareness to hostility. *Neuropsychology Review, 7*(4):171-85.

Demaree, H.A., Higgins, D.A., Williamson, J., Harrison, D.W. (2002). Asymmetry in hand grip strength and fatigue in low- and high-hostile men. *International Journal of Neuroscience, 112*(4), p. 415-28.

Demers, J., Kane, M.P., Bakst, G., Busch, R.S., Hamilton, R.A. (2003). Accuracy of home blood glucose monitors using forearm blood samples: Freestyle versus One Touch Ultra. *American Journal of Health-System Pharmacy,60*(11), 1130-1135.

Domasio, A.R. & Anderson, S.W. (2003). The frontal lobes. In *Clinical Neuropsychology, 4th Edition* by K.M. Heilman & E. Valenstein (eds.). Oxford University Press: New York.

Dwyer, D.S. (2002). *Glucose Metabolism in the Brain*. Academic Press: Amsterdam

Eren, I., Erdi, O., Sahin, M. (2007). The effect of depression on quality of life of patients with type II diabetes mellitus. *Depression and Anxiety, 0*, 1-9

Everhart, D.E. & Harrison, D.W. (2002).Heart rate and fluency performance among high- and low-anxious men following autonomic stress. *International Journal of Neuroscience, 112*(10), p.1149-71.

Everhart, D.E., Harrison, D.W., Shenal, B.V., Williamson, J., and Wuensch, K.L.(2002). Grip strength, fatigue, and motor perseveration in anxious men without depression. *Neuropsychiatry Neuropsychology and Behavioral Neurology, 15*(2), p. 133-42.

Fehm, H.L., Kern, W., Peters, A. (2006). Chapter 7: The selfish brain: competition for energy resources. *Progress in Brain Research, 153*, 129-40.

Foster, P.S. & Harrison, D.W. (2004). The covariation of cortical electrical activity and cardiovascular responding. *International Journal of Psychophysiology, 52*(3), 239-55

Foster, P.S., Williamson, J.B. & Harrison, D.W. (2005). The Ruff Figural Fluency Test: heightened right frontal lobe delta activity as a function of performance. *Archives of Clinical Neuropsychology.*

Foster, P.S., Drago, V., Ferguson, B.J., Harrison, D.W. (2008). Cerebral moderation of cardiovascular functioning: A functional cerebral systems perspective. *Clinical Neurophysiology, 1999*, 2846-2854.

Fontbonne, A., Berr, C., Ducimetiere, P., Alperovitch, A. (2001). Changes in cognitive abilities over a 4-year period are unfavorably affected in elderly diabetic subjects: results of the Epidemiology of Vascular Aging Study. *Diabetes Care, 24*(2), 366-70.

Golden, S.H., Williams, J.E., Ford, D.E., Yeh, H.C., Sanford, C.P., Nieto, F.J., Brancati, F.L. (2006). Anger temperament is modestly associated with the risk of type 2 diabetes mellitus: the Atheroslcerosis Risk in Communities Study. *Psychoneuroendocrinology, 31*(3):325-32.

Gothelf, D., Apter, A, van Praag, H.M. (1997). Measurement of aggression in psychiatric patients. *Psychiatry Research, 4*, 71(2), 83-95.

Groot-Driessen, D, van de Sande, P., van Heugten, C. (2006). Speed of finger tapping as a predictor of functional outcome after unilateral stroke. *Archives of Physical Medicine and Rehabilitation, 87*(1), 40-4.

Hauber, A.B., Mohamed, A.F., Johnson, F.R., Falvey, H. (2009). Treatment preferences and medication adherence of people with Type 2 diabetes using oral glucose-lowering agents. *Diabetes Medicine, 26*(4), p. 416-24.

Harrison, D.W., Gorelczenko, P.M., & Cook J. (1990). Sex differences in the functional asymmetry for facial affect perception. *International Journal of Neuroscience, 52,* p.11 16.

Harrison, D.W., Pauly, R.S. (1990). Manual dexterity, strength, fatigue, and perseveration: an initial test of asymmetry in cerebral activation. *Perceptual Motor Skills, 70*(3 Pt 1), p. 739-44.

Helmer, D.C., Ragland, D.R., Syme, S.L. (1991). Hostility and coronary artery disease. *American Journal of Epidemiology, 133,* (2), 112-122.

Herridge, M.L., Harrison, D.W., & Demaree, H.A. (1997). Hostility, facial configuration, and bilateral asymmetry on Galvanic skin response. *Psychobiology, 25,* 71-76.

Herridge, M.L., Harrison, D.W., Mollet, G.A., Shenal, B.V. (2004). Hostility and facial affect recognition: effects of a cold pressor stressor on accuracy and cardiovascular reactivity. *Brain and Cognition, 55*(3), 564-71.

Hewing, J., Hagemann, D., Seifert, J., Naumann, E., and Bartussek, D. (2004). On the selective relation of frontal cortical asymmetry and anger-out versus anger-control. *Journal of Personality and Social Psychology, 87*(6), 926-939.

Higgins, D.A., & Harrison, D.W. (1999). Sex differences in the functional cerebral laterality of cardiovascular reactivity to speech and a cold pressor. *Archives of Clinical Neuropsychology, 14* (8), 771.

Hillbrand, M., Waite, B.M., Rosenstein, M., Harackiewicz, D., Lingswiler, V.M., Stehney, M. (2005). Serum cholesterol concentrations and non-physical aggression in healthy adults. *Journal of Behavioral Medicine, 28*(3), 295-299.

Hu, G., Rico-Sanz, J., Lakka, T.A., Tuomilehto, J. (2006). Exercise, genetics and prevention of type 2 diabetes. *Essays Biochemistry, 42*, 177-92

Hu, G., Lindstrom, J., Valle, T.T., Eriksson, J.G., Jousilahti, P., Silventoinen, K., Qiao, Q., Tuomilehto, J. (2004). Physical activity, body mass index, and risk of type 2 diabetes in

patients with normal or impaired glucose regulation. *Archives of Internal Medicine, 26*,164(8), 892-6.

Hyllienmark, L., Maltez, J., Dandenell, A., Ludvigsson, J., Brismar, T. (2005). EEabnormalities with and without relation to severe hypoglycaemia in adolescents with type 1 diabetes. *Diabetologia, 48*(3), 412-9.

Iribarren, C., Sidney, S., Bild, D.E., Liu, K., Markovitz, J.H., Roseman, J.M., Mathews, K. (2000). Association of hostility with coronary artery calcification in young adults: The CARDIA study. *Journal of the American Medical Association, 17*(19), 2546-2551.

Johnstone, B., Holland, D., Larimone, C. (2000). Language and Academic Abilities. In *Neuropsychological Assessment in Clinical Practice,* Groth-Marnat (editor), New York: John Wiley and Sons, Inc

Jungheim, K., Koschinksy, T. (2002). Glucose monitoring at the thenar: evaluation of upper dermal blood glucose kinetics during rapid systemic blood glucose changes. *Hormonal Metabolic Research, 34*(6), 325-329.

Kanaya, A.M., Barrett-Connor, E., Gildengorin, G., Yaffe, K. (2004). Change in cognitive function by glucose tolerance status in older adults: a 4-year prospective study of the Rancho Bernardo study cohort. *Archives of Internal Medicine, 28*, 164(12):1327-33.

Kawachi, I., Sparrow, D., Spiro, A., Vokonas, P., Weiss, S.T. (1996). Myocardial Ischemia/Coronary Artery Vasoconstriction/Thrombosis/Myocardial Infarction: A prospective study of anger and coronary artery disease: the normative aging study. *Circulation 94,* (9), 2090-2095

Keltikangas-Jarvinen, L. & Heinonen, K. (2003). Childhood roots of adulthood hostility: Family factors as predictors of cognitive and affective hostility. *Childhood Development, 74*(6), 1751-1768.

Kimbrell, T.A., George, M.S., Parekh, P.I., Ketter, T.A., Podell, D.M., Danielson, A.L., Repella, J.D., Benson, B.E., Willis, M.W., Herscovitch, P., Post, R.M. (1999). Regional brain activity during transient self-induced anxiety and anger in healthy adults. *Biological Psychiatry, 46*(4), p. 454-65.

Kinsbourne, M. (1980). Mapping a behavioral cerebral space. *International Journal of Neuroscience, 11*, p. 45-51.

Kinsbourne, M. & Hicks, R.E. (1978). Functional Cerebral Space: a model for overflow, transfer, and interference effects in human performance: a tutorial review. In *Attention and Performance, VII* by Jean Requin (ed). Lawrence Erlbaum Associates: Hissdale, New Jersey.

Kissela, B., Air E. (2006). Diabetes: impact on stroke risk and poststroke recovery. *Seminars in Neurology, 26*(1), 100-7.

Kiziltan, E., Barut, C., Gelir, E. (2006). A high-precision, low cost system for evaluating finger tapping tasks. *International Journal of Neuroscience, 116*(12), p. 1471-80.

Knox, S.S., Weidner, G., Adelman, A., Stoney, C.M., Ellison, R.C. (2004). Hostility and Physiological Risk in the National Heart, Lung, and Blood Institute Family Heart Study. *Archives of Internal Medicine*, *164*, p. 2442-2448.

Larkin, K.T., Martin, R.R., McClain, S.E. (2002). Cynical hostility and the accuracy of decoding facial expressions of emotions. *Journal of Behavioral Medicine, 25,* (3), 285 292.

Lee, D.M., Weinert, S.E., Miller, E.E. (2002). A study of forearm versus finger stick glucose monitoring. *Diabetes Technology Therapy,4*(1), 13-23.

Lezak, M.D. (1995). *Neuropscyhological Assessment, 3rd Edition*. Oxford University Press: New York.

Lovallo, W. (2005). *Stress and Health: Biological and Physical Interactions.* Sage Publications: Thousand Oaks, California.

Luria, A. (1973). *The Working Brain; An Introduction to Neuropsychology.* Basic Books: Penguin Press.

Lustman, P.J. & Clouse, R. E. (2005). Depression in diabetic patients; The relationship between mood and glycemic control. *Journal of Diabetes and Its Complicaitons,19,* p. 113-122.

Lustman, P.J., Clouse, R. E., Griffith, L. S., Carney, R. M., Freedland, K. E. (1997). Screening for depression in diabetes using the beck depression inventory. *Psychosomatic Medicine, 59*(1), p. 24-31.

Maahs, M.D., Kinney, G.L., Wadwa, P., Snell-Bergeon, J.K., Dabelea, D., Hokanson, J., Ehrlich, J., Garg, S., Eckel, R.H., Rewers, M.J. (2005). Hypertension Prevalence, Awareness, Treatment, and Control in an Adult Type 1 Diabetes Population and a Comparable General Population. *Diabetes Care, 28*, 301-306.

Manschot, S.M., Brands, A.M., van der Grond, J., Kessels, R.P., Algra, A., Kappelle, L.J., Biessels, G.J. (2006). Brain magnetic resonance imaging correlates of impaired cognition in patients with type 2 diabetes. *Diabetes, 55*(4), 1106-13.

Martin, R., Watson, D., & Wan, C.K. (2000). A three-factor model of trait anger: Dimensions, of affect, behavior, and cognition. *Journal of Personality, 68*(5), p.869-897.

McCrimmon, R.J., Ewing, F.M.E., Frier, B.M., Deary, I.J. (1999). Anger state during acute insulin-induced hypoglycemia. *Physiology and Behavior, 67*, (1), 35-39.

Messier C. (2005). Impact of impaired glucose tolerance and type 2 diabetes on cognitive aging. *Neurobiology of Aging, 26*(1), 26-30.

Miller. T.Q., Smith, T.W., Turner, C.W., Guijarro, M.L., and Hallet, A.J. (1996). A meta analytic review of research on hostility and physical health. *Psychological Bulletin, 119*(2), p.322-348.

Mollet, G.A. & Harrison, D.W. (2007). Affective verbal learning in hostility: An increased primacy effect for negative emotional material. Archives of Clinical Neuropsychology, 22(1), p. 53-62.

Moore, D.S. (2002). *The Dependent Gene: The Fallacy of "Nature vs Nurture."* Times Books: New York.

Niaura, R., Banks, S.M., Ward, K.D., Stoney, C.M., Spiro, A. 3rd, Aldwin, C.M., Landsberg, L., Weiss, S.T. (2000). Hostility and the metabolic syndrome in older males: the normative aging study. *Psychosomatic Medicine*, 62(1), p.7-16.

Nichols, J.H., Howard, C., Loman, K., Miller, C., Nyberg, D., Chan, D.W., (1995). Laboratory and bedside evaluation of portable glucose meters. *American Journal of Clinical Pathology, 103* (2), 244-251.

Nys, G.M., Van Zandvoort, M.J., De Kort, P.L., Jansen, B.P., Van der Worp, H.B., Kappelle, L.J., De Haan, E.H. (2005). Domain-specific cognitive recovery after first-ever stroke: a follow-up study of 111 cases. Journal of the International Neuropsychological Society, 11(7), 795-806.

Peled, N., Wong, D., Gwalani, S.L. (2002). Comparison of glucose levels in capillary blood sample. *Diabetes Technology Therapy,4* (1), 35-44.

Perlmuter, L.C., Shah, P.H., Flanagan, B.P., Surampudi, V., Kosman, Y., Singh, S.P., Al Jaghbeer, E. (2009). Rate of peripheral glucose change during cognitive testing predicts performance in diabetes mellitus. *Journal of Diabetes, 1*, p. 43-49.

Pfutzner, A., Hermanns, N., Schroder, S., Wegenstien, M., Larbig, M., Mondok, A. Frost,T., Haak, T. (2002). Cross-sectional investigation on the accuracy of alternate site glucose testing using the Soft-Sense glucose monitor. *Swiss Medical Weekly, 132*(25-26), 351-357.

Prigatano, G.P., Johnson, S.C., Gale, S.D. (2004). Neuroimaging correlates of the Halstead Finger Tapping Test several years post-traumatic brain injury. *Brain Injury, 18*(7), p. 661-9.

Qiu, W.Q., Price, L.L., Hibberd, P., Buell, J., Collins, L., Leins, D. et al. (2006). Executive dysfunction in homebound older people with diabetes mellitus. *Journal of the American Geriatric Society, 54*(3), 496-501.

Raiikkonen, K., Keltikangas-Jarvinen, L., Adlercreutz, H., & Hautanen, H. (1996). Psychosocial stress and the insulin resistance syndrome. *Metabolism, 45,* 1533-1538.

Raikkonen, K., Matthews, K.A., Salomon, K. (2003). Hostility predicts metabolic syndrome risk factors in children and adolescents. *Health Psychology, 22*(3), 279-86.

Ramchandani, N. (2004). Type 2 diabetes in children. A burgeoning health problem among overweight young Americans. *American Journal of Nursing, 104*(3), 65-8.

Ramirez, J.M. & Andreu, J.M.(2006) Aggression, and some related psychological constructs (anger, hostility, and impulsivity); some comments from a research project. *Neuroscience and Biobehavioal Reviews, 30*(3), 276-291

Reaven, G.M., Thompson, L.W., Nahum, D., & Haskins, E. (1990). Relationship between hyperglycemia and cognitive function in older NIDDM patients. *Diabetes Care, 13*(1), 16-21.

Reuter-Lorenz, P.A., Kinsbourne, M. & Moscovitch, M. (1990). Hemispheric control of spatial attention. *Brain and Cognition, 12*, 240-266.

Rheney, C.C., & Kirk, J.K., (2000). Performance of three blood glucose meters. *Annals of Pharmacotherapy, 34*(3), 317-321.

Rhodes & Harrison (2007). Hostility and Electromyography. Manuscript in preparation.

Richards, J.C., Hof, A., Alvarenga, M., (2000). Serum lipids and their relationships with hostility and angry affect and behaviors in men. *Health Psychology, 19*(4), 393-398

Rubia, K., Lee, F., Cleare, A.J., Tunstall, N., Fu., C.H.Y., Brammer, M., McGuire, P. (2005). Tryptophan depletion reduces right inferior prefrontal activation during response inhibition in fast, event-related fMRI. *Psychopharmacology, 179*, 791-803.

Rubin, R.R., Ciechanowski, P., Edede, L.E., Lin, E.H., and Lustman, P.J. (2004). Recognizing and treating depression in patients with diabetes. *Current Diabetes Reports, 4*(2), p.119 125.

Ruff, R.M., Allen, C.C., Farrow, C.E., Niemann, H., Wylie, T. (1994). Figural fluency: differential impairment in patients with left versus right frontal lobe lesions. *Archives of Clinincal Neuropsychology*, *9*(1), p. 41-55.

Ruff, R.M., Light, R.H., Parker, S.B., Levin, H.S., (1997). The psychological construct ofword fluency. *Brain Language, 57* (3), 394-405.

Rujescu, D., Giegling, I., Bondy, B., Gietl, A., Zill, P., Moller, H.J (2002). Association of anger related traits with SNPs in the TPH gene. *Molecular Psychiatry, 7*(9), 1023-1029.

Sato, T., Morimoto, N, Tsutsub, N., Nakakadob, F., Kinugawac, N., and Nakamurab, Y. (2002). Background factors correlated with the psychological features of 254 outpatients with Type 2 diabetes mellitus in Japan. *Diabetes Research and Clinical Practice, 56*(2), p. 133-140.

Scherwitz, L.W., Perkins, L.L., Chesney, M.A., Hughes, G.H., Sidney, S., Manolio T.A. (1992). Hostility and health behaviors in young adults: the CARDIA Study. Coronary Artery Risk Development in Young Adults Study. *American Journal of Epidemiology, 36*, (2), 136-145.

Schmittdiel, J.A., Uratsu, C.S., Karter, A.J., Heisler, M., Subramanian, U., Mangione, C.M., Selby, J.V., Siegler, I.C., Peterson, B.L. (2007). Why don't diabetes patients achieve recommended risk factor targets? Poor adherence versus lack of treatment medication. *General Internal Medicine, 23*(5), p. 588-94.

Shuldham, C.M., Cunningham, G., Hiscock, M., Luscombe, P. (1995). Assessment of anxiety in hospital patients. *Journal of Advanced Nursing, 22*(1), p. 87-93.

Sinclair, A.J., Girling, A.J., Bayer, A.J. (2000). Cognitive dysfunction in older subjects with diabetes mellitus: impact on diabetes self-management and use of care services. All Wales Research into Elderly (AWARE) Study. *Diabetes Research and Clinical Practice, 50*(3), 203-12

Sluyter, F., Keijser, J.N., Boomsma, D.I., van Doornen, L.J., van den Oord, E.J., Snieder, H. (2000). Genetics of testosterone and the aggression-hostility-anger (AHA) syndrome: A study of middle-aged male twins. *Twin Research, 3*(4), 266-76.

Smith, T.W., Glazer, K., Ruiz, J.M., Gallo, L.C. (2004). Hostility, anger, aggressiveness, and coronary heart disease: An interpersonal perspective on personality, emotion, and health. *Journal of Personality 72*(6)

Smith, T.W., McGonigle, M.A., Benjamin, L.S. (1998). Sibling interactions, self-regulation, and cynical hostility in adult male twins. *Journal of Behavioral Medicine, 21*(4).

Smith, T.W. & Seigman, A.W. (1994). *Anger, Hostility, and the Heart.* Lawrence Erlbaum: Hillsdale, New Jersey.

Snyder, K. A., & Harrison, D. W. (1997). The Affective Verbal Learning Test. Archives of *Clinical Neuropsychology, 12*(5), 477–482.

Snyder K.A., Harrison, D.W., Gorman, W.J. (1996). Auditory affect perception in a dichotic listening paradigm as a function of verbal fluency classification. *International Journal of Neuroscience, 84*(1-4), 65-74.

Sommerfield, A.J., Deary, I.J., Frier, B.M. (2004). Acute hyperglycemia alters mood state and impairs cognitive performance in people with Type II diabetes. *Diabetes Care, 27*(10), 2335-2340.

Spielberger, C. D., Johnson, E. H., Russell, S. F., Crane, R. S., Jacobs, G., & Worden, T. J. (1983). Assessment of anger: The state-trait scale. In J. N. Butcher, & C. D. Spielberger (Eds.), *Advances in Personality Assessment, 2.* Hillside, NJ: Earlbaum.

Stephan, K.E., Penny, W.D., Marshall, J.C., Fink, G.R., Friston, K.J. (2005). Investigating the functional role of colossal connections with dynamic causal models. *Annaul New York Academy of Science, 1064,* p. 16-36.

Suarez, E.C., Kuhn, C.M., Schanberg, S.M., Williams, R.B. Jr, and Zimmermann, E.A. (1998). Neuroendocrine, cardiovascular, and emotional responses of hostile men: the role of interpersonal challenge. *Psychosomatic Medicine, 60*(1), p.78-88.

Surwit, R.S., Williams, R.B., Siegler I.C., Lane J.D., Helms, M., Applegate K.L., Zucker, N., Feinglos, M.N., McCaskill C.M., & Barefoot, J.C. (2002). Hostility, race, and glucose metabolism in nondiabetic individuals. *Diabetes Care, 25,* 835-839.

Tieszen, K.L., New, J.P. (2003). Alternative site for blood glucose testing: do patients prefer it? *Diabetes Medicine,20* (4), 325-328.

Thomas, J., Jones, G., Scarinci, I., Brantley, P. (2003). A descriptive and comparative study of the prevalence of depressive and anxiety disorders in low-income adults with type 2 diabetes and other chronic illnesses. *Diabetes Care, 26*(8), 2311-7.

Toglia, M. P., & Battig, W. F. (1978). *Handbook of word norms*. Hillsdale, NJ: Lawrence Erlbaum.

Tucha, O.W., Smely, C.W., & Lange, K.W. (1999). Verbal and figural fluency in patients with mass lesions of the left or right frontal lobes. *Journal of Clinical and Experimental Neuropsychology, 21*(2), 229-236.

Tucker, D.M., (1981). Lateral brain function, emotion, and conceptualization. *Psychological Bulletin, 89,* 19-46.

Tucker. D.M., & Williamson, P.A. (1984). Asymmetric neural control systems in human self regulation. *Psychological Review, 91*, 185-215.

Urrutia-Rojas, X., Menchaca, J. (2006). Prevalence of risk for type 2 diabetes in school children. *Journal of School Health, 76*(5):189-94.

van den Berg, E., Kessels, R.P., Kappelle, L.J., de Hann, E.H., Biessels, G.J. (2007). Type 2 diabetes, cognitive function and dementia: vascular and metabolic determinants. *Timely Topics in Medicine: Cardiovascular Diseases, 11*(E7).

Vernon, P.A., McCarthy, J.M., Johnson, A.M., Jang, K.L., and Harris, J.A. (1999). Individual differences in multiple dimensions of aggression: A univariate and multivariate genetic analysis. *Twin Research, 2*(1), 16-21.

Virkkunen, R. (1982). Reactive hypoglycemic tendency among habitually violent offenders. A further study by means of the glucose tolerance test. *Neuropsychobiology, 8*(1), 35 40.

Vogele, C. (1997). Serum lipid concentrations, hostility, and cardiovascular reactions to mental stress. *International Journal of Psychophysiology, 28,* 176-179.

Walters, R.P. & Harrison, D.W. (2006). *Frontal Regulation of Blood Glucose Levels in Hostility: Support for the Limited Capacity Model.* Article accepted for publication.

Walters, R.P. & Harrison, D.W. (2007). *Does performance on frontal lobe fluency tasks predict grip strength?* Manuscript in Progress.

Watari., K., Letamendi, A., Elderkin-Thompson, V., Haroon, E., Miller, J., Darwin, C., Kumar, A. (2006). Cognitive function in adults with type 2 diabetes and major depression. *Archives of Clinical Neuropsychology, 21*(8), 787-96.

Weisz, J., Emri, M., Fent, J., Lengyel, Z., Marian, T., Horvath, G., Bogner, P., Tron, L., Adam, G. (2001). Right prefrontal activation produced by arterial baroreceptor stimulation: a PET study. *Neuroreport, 12*(15), p. 3233-8.

Wessels, A.M., Simsek, S., Remijnse, P.L., Veltman, D.J., Biessels, G.J., Barkhof, F., Scheltens, P., Snoek, F.J., Heine, R.J., Rombouts, S.A. (2006). Voxel-based morphometry demonstrates reduced grey matter density on brain MRI in patients with diabetic retinopathy. *Diabetologia, 49*(10), 2474-80.

White, J., Baco, F., Malone, J. (2002). Comparison of the Freestyle and the One Touch Ultra Blood Glucose Monitoring System Using Capillary Blood from the Forearm. Presented at the 62nd Scientific Sessions of the America Diabetes Association. June, 15: San Francisco, CA.

Williamson, J.B. & Harrison, D.W., (2005). Functional cerebral asymmetry in hostility: A dual task approach with fluency and cardiovascular regulation. *Brain and Cognition, 52*, p. 167-174

Williamson, J.B., Harrison, D.W., & Walters (2007). *The influence of lateralized stressors on cardiovascular regulation and dichotic listening in hostile men*. Manuscript in preparation.

Winer, B.J. (1971). *Statistical Principles in Experimental Design (2nd Edition)*. New York: McGraw Hill.

Yan, L.L., Liu, K., Mathews, K.A., Daviglus, M.L., Ferguson, T.F., Kiefe, C.I. (2003). Psychosocial factors and risk of hypertension: The coronary arty risk development in young adults (CARDIA) study. *Journal of the American Medical Association, 290*(16), p.2138-2148

Zhang, J., Niaura, R., Todaro, J.F., McCaffery, J.M., Shen, B.J., Spiro, A. 3rd, Ward, K.D. (2005). Suppressed hostility predicted hypertension incidence among middle-aged men: The normative aging study. *Journal of Behavorial Medicine, 23*, p. 1-12.

Zhu, H., Poole, J., Lu, Y., Harshfield, G.A., Treiber, F.A., Snieder, H., Dong, Y. (2005). Sympathetic nervous system, genes and human essential hypertension. *Current NeurovascularResearch, 2*(4), p.303-17

Table 1

Mean glucose levels as a function of group membership, condition, and trial

Group	Condition	Trial	Glucose Mean	Glucose SD
Low Hostile-Diabetic	Verbal	Pre	139.91	(51.29)
		Post	137.19	(54.17)
	Nonverbal	Pre	146.47	(69.51)
		Post	133.62	(49.58)
High Hostile-Diabetic	Verbal	Pre	189.27	(118.5)
		Post	176.36	(100.04)
	Nonverbal	Pre	185.71	(95.04)
		Post	181.71	(101.29)

Table 2

Mean glucose values as a function of group and time

Group	Time	Glucose Mean	Glucose SD
Low Hostile-Diabetic	1	145.52	(71.18)
	2	135.24	(50.18)
	3	140.86	(49.06)
	4	135.57	(53.68)
High Hostile-Diabetic	1	187.57	(113.10)
	2	177.07	(98.4)
	3	187.43	(101.44)
	4	181.00	(102.92)

Table 3

Mean levels of the QEEG magnitude of delta at the location of FP1 as function group membership and trial.

Group	Trial	Magnitude	SE
Low Hostile-Diabetic	Pre	8.41	(.91)
	Post	8.25	(1)
High Hostile-Diabetic	Pre	9.58	(1.16)
	Post	11.68	(1.28)

Table 4

List of extreme glucose values in both the low and high hostile-diabetic groups.

Extreme Values[a]

	Hostility			Case Number	Value
AveGlucose	LoHostile	Highest	1	26	346.75
			2	19	208.50
			3	24	171.25
			4	29	152.25
			5	13	151.25
		Lowest	1	8	86.75
			2	3	100.00
			3	34	102.50
			4	31	103.50
			5	30	106.25
	HiHostile	Highest	1	25	383.50
			2	4	342.25
			3	22	294.00
			4	21	263.25
			5	2	226.50
		Lowest	1	28	76.00
			2	12	82.50
			3	32	86.25
			4	1	94.25
			5	33	108.25

Table 5

The mean QEEG magnitude of delta at the location of F3 as a function of group membership and trial.

Group	Trial	Magnitude	SE
Low Hostile-Diabetic	Pre	7.54	(.70)
	Post	6.85	(.69)
High Hostile-Diabetic	Pre	7.46	(.83)
	Post	8.84	(.82)

Table 6

The mean QEEG magnitude of theta at F3 as a function of group membership and trial.

Group	Trial	Magnitude	SE
Low Hostile-Diabetic	Pre	4.12	(.27)
	Post	4.10	(.29)
High Hostile-Diabetic	Pre	4.10	(.33)
	Post	4.42	(.35)

Table 7

Total Error on the RFFT as function of group membership.

Group	Total Error	SD
Low Hostile-Diabetic	42.29	(39.13)
High Hostile-Diabetic	20.47	(20.3)

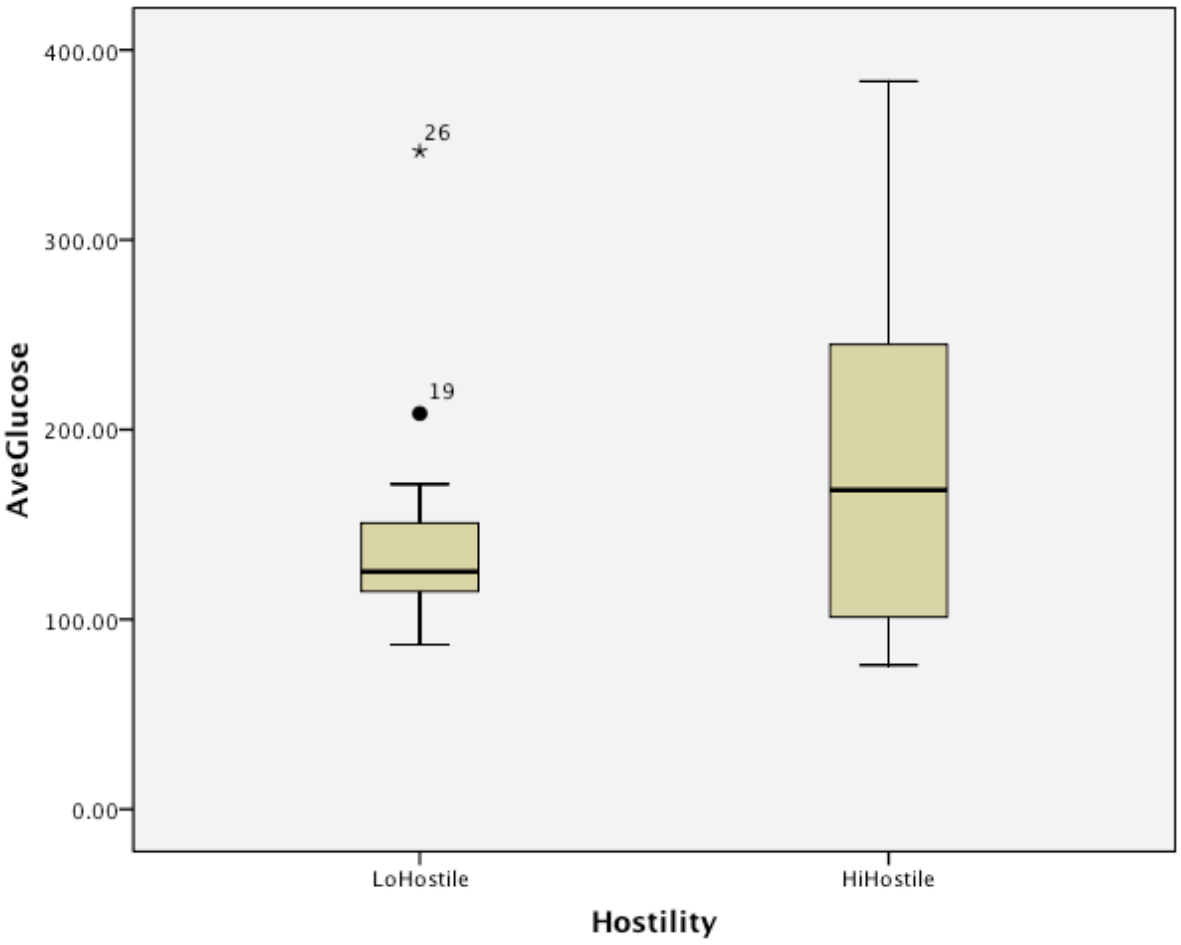
Table 8

Total Score on the AAVLT as a function of group membership.

Group	Positive (*M,SD*)	Negative(*M,SD*)	Neutral(*M,SD*)
Low Hostile Diabetic	5.90(1.34)	6.00(1.27)	6.14(1.96)
High Hostile Diabetic	5.93(1.53)	5.27(1.75)	5.73(1.28)

Figure 1

Variability of average glucose levels as a function of group membership.



Appendix A
CMHO II

Direction: If a statement is true or mostly true, as pertaining to you, circle the letter T.
If a statement is false, or usually not true about you, circle the letter F.
Try to give a response to every statement.

1. When I take a new job, I like to find out who it is important to be nice to.	T	F
2. When people do me wrong, I feel I should pay them back if I can, just for the principle of the thing.	T	F
3. I prefer to pass by school friends, or people I know but have not seen for a long time, unless they speak to me first.	T	F
4. I have often had to take orders from someone who did not know as much as I did.	T	F
5. I think a great many people exaggerate their misfortunes in order to gain the sympathy and help of others.	T	F
6. It takes a lot of argument to convince most people of the truth.	T	F
7. I think most people would lie to get ahead.	T	F
8. Someone has it in for me.	T	F
9. Most people are honest chiefly because they are afraid of being caught.	T	F
10. Most people will use somewhat unfair means to gain profit or an advantage rather than lose it.	T	F
11. I often wonder what hidden reason another person may have for doing something nice for me.	T	F
12. It makes me impatient to have people ask my advice or otherwise interrupt me when I am working on something important.	T	F
13. I feel that I have often been punished without cause.	T	F
14. I am against giving money to beggars.	T	F
15. Some of my family have habits that bother and annoy me very much.	T	F
16. My relatives are nearly all in sympathy with me.	T	F
17. My way of doing things is apt to be misunderstood by others.	T	F
18. I don't blame people for trying to grab everything they can get in this world.	T	F
19. No one cares much what happens to you.	T	F
20. I can be friendly with people who do things I consider wrong.	T	F
21. It is safer to trust nobody.	T	F
22. I do not blame a person for taking advantage of people who leave themselves open to it.	T	F
23. I have often felt that strangers were looking at me critically.	T	F
24. Most people make friends because friends are likely to be useful to them.	T	F
25. I am sure that I am being talked about.	T	F
26. I am likely not to speak to people until they speak to me.	T	F
27. My way of doing things is apt to be misunderstood by others.	T	F

28. Most people inwardly dislike putting themselves out to help other people.	T	F
29. I tend to be on my guard with people who are somewhat more friendly than I had expected.	T	F
30. People often disappoint me.	T	F
31. I like to keep people guessing what I'm going to do next.	T	F
32. I frequently ask people for advice.	T	F
33. I am not easily angered.	T	F
34. I have often met people who were supposed to be experts who were no better than I.	T	F
35. It makes me feel like a failure when I hear of the success of someone I know well.	T	F
36. I would certainly enjoy beating criminals at their own game.	T	F
37. I have at times had to be rough with people who were rude or annoying.	T	F
38. People generally demand more respect for their own rights than they are willing to allow for others.	T	F
39. There are certain people whom I dislike so much I am inwardly pleased when they are catching it for something they have done.	T	F
40. I am often inclined to go out of my way to win a point with someone who has opposed me.	T	F
41. I am quite often not in on the gossip and talk of the group I belong to.	T	F
42. The man who had the most to do with me when I was a child (such as my father, step- father, etc.) was very strict with me.	T	F
43. I have often found people jealous of my good ideas, just because they had not thought of them first.	T	F
44.When a man is with a woman he is usually thinking of things related to her sex.	T	F
45. I do not try to cover up my poor opinion or pity of people so that they won't know how I feel.	T	F
46. I have frequently worked under people who seem to have things arranged so that they get credit for good work, but are able to pass off mistakes to those under them.	T	F
47. I strongly defend my own opinions as a rule.	T	F
48. People can pretty easily change my mind even when I have made a decision about something	T	F
49. Sometimes I am sure that other people can tell what I'm thinking.	T	F
50. A large number of people are guilty of bad sexual conduct.	T	F

Appendix B
Laterality Questionnaire

Participant #: _____

Circle the appropriate number after each item.

	Right Hand	Left Hand	Both
With which hand would you throw a ball to hit a target?	1	-1	0
With which hand do you draw?	1	-1	0
With which hand do you use an eraser on paper?	1	-1	0
With which hand do you remove the top card when dealing?	1	-1	0
With which foot do you kick a ball?	1	-1	0
If you had to pick up a pebble with your toes, which foot would you use?	1	-1	0
If you had to step up on a chair, which foot would you place on the chair first?	1	-1	0
Which eye would you use to peep through a keyhole?	1	-1	0
If you had to look into a dark bottle to see how full it was which eye would you use?	1	-1	0
Which eye would you use to sight down a rifle?	1	-1	0
If you wanted to listen to a conversation going on behind a closed door, which ear would you place against the door?	1	-1	0
If you wanted to listen to someone's heartbeat, which ear would you place against his or her chest?	1	-1	0
Into which ear would you place you earphone of a transistor radio?	1	-1	0

# of Right	+	# of Left	=	Total Score
_____	+	_____	=	_____

Is mother right or left hand dominant? _____
Is father right or left hand dominant? _____

Appendix C
COWAT

Subject number: ________
Date:___________

F	A	S	T	R
Errors	Errors	Errors	Errors	Errors
Correct words	Correct words	Correct words	Correct words	Correct words

Appendix D
AAVLT

Neutral List	Recalled	Positive List	Recalled	Negative List	Recalled
Drum		Smile		Morgue	
Curtain		Freedom		Murder	
Bell		Cheerful		Kill	
Coffee		Friend		Pimple	
School		Music		Gun	
Parent		Joy		Greedy	
Moon		Happy		Lice	
Garden		Wisdom		Measles	
Hat		Blossom		Slay	
Farmer		Laugh		Deface	
Nose		Beauty		Cruel	
Turkey		Peace		Failing	
Color		Sunset		Hate	
House		Garden		Acne	
River		Beach		Grave	

Appendix E
Hand Grip Strength, Perseveration, and Fatigue Test

Grip Strength	
LH Full	
RH Full	
LH ½	
RH ½	
LH 1	
LH 2	
LH 3	
LH 4	
LH 5	
RH 1	
RH 2	
RH 3	
RH 4	
RH 5	

Appendix F
Finger Tapping Test

Trial	Left Hand	Right Hand
1		
2		
3		
4		
5		
Average		

Appendix G
General Medical History Questionnaire

1.	Are you a right handed man?	Y	N
2.	Do you have Type II diabetes?	Y	N
3.	Do you have any history of a wrist, forearm, arm injury?	Y	N
4.	Do you have any history of congenital or developmental problems ?	Y	N
5.	Do you have any history of learning disabilities or special education?	Y	N
6.	Do you have any history of hypertension? (high blood pressure)	Y	N
7.	Do you have any history of hypotension? (low blood pressure)	Y	N
8.	Do you have any history of hyperthyroidism?	Y	N
9.	Do you have any history of hypothyroidism?	Y	N
10.	Have you ever suffered a head injury resulting in a hospital stay longer than 24 hours?	Y	N
11.	Have you ever been knocked out or rendered unconscious (more than 5 minutes)?	Y	N
12.	Have you ever suffered "black-out" or fainting spells?	Y	N
13.	Have you ever had a stroke?	Y	N
14.	Have you ever had a brain tumor?	Y	N
15.	Have you ever been diagnosed with a neurological disease, such as epilepsy, Parkinson's Disease, Alzheimer's Disease, or dementia?	Y	N
16.	Do you have any history of heart disease?	Y	N
17.	Do you have any history of pancreatic disease?	Y	N
18.	Are you currently taking any prescription blood-thinning medications?	Y	N
19.	Do you have a history of high blood pressure?	Y	N
20.	Do you have any uncorrected visual or hearing impairments?	Y	N
21.	Have you ever received psychiatric/psychological care or counseling?	Y	N
22.	Have you ever been hospitalized in a psychiatric facility/hospital?	Y	N
23.	Have you ever been diagnosed with a psychiatric/psychological disorder?	Y	N
24.	Have you ever been administered any (neuro)psychological tests or measures?	Y	N
25.	Do you have a history of substance abuse or alcohol abuse?	Y	N
26.	Do you consume three or more alcoholic more than two nights a week?	Y	N
27.	Have you ever used smoked or used tobacco products?	Y	N
28.	Do you use any unprescribed or "illegal/street" drugs?	Y	N
29.	Are you taking any of the following medications: antidepressant, antianxiety, antipsychotic?	Y	N
30.	Are you taking any allergy or cold medication?	Y	N

If you answered "yes" to any of the above please explain fully:

Appendix H
Diabetes Questionnaire

Subject number_____

Date of Birth_____

Education Level _____

Marital Status (circle one)

Married

Single

Divorced

Widowed

Other

Social Situation (circle one)

Living alone

Living with _____

Height _____

Weight _____

Do you have hypertension? If so, please list your last blood pressure reading.

_____

Do you have any difficulties with vision? If so, please list them.

_____

Do you have any kidney related health issues? If so, please list them.

_____

Do you have increased cholesterol levels? If so, please list your last reading?

_____

What is the normal range of your glucose?

_____

What is the highest your glucose has ever been?

_____

What is the lowest your glucose has ever been?

_____

Does diabetes run in your family?

_____

Diabetes

1. When was your diabetes first diagnosed? _____
2. How old were you when you were diagnosed? _____
3. What type of diabetes do you have? _____
4. Is your diabetes controlled with diet alone?_____
5. If you take pills for your diabetes, please list the amount, type, and frequency that you take
   them._____
   _____
   _____
6. Do you use insulin to treat your
   diabetes?_____
   a. If you use insulin, please list the type, amount, and location of
      injections._____

_____

_____

_____

b. If you use insulin, when did you start?

_____

7. How often do you check your blood glucose level?

_____

8. Do you use an insulin pump?

_____

Hypoglycemia

1. Has your blood sugar ever gotten low?

_____

a. If so, how did you know?

_____

b. How low did it get?

_____

2. Does your blood sugar frequently get low?_____

a. If you blood sugar gets low, how many times in the past 12 months has it gotten low? _____

3. Have you ever had a seizure to hypoglycemia?

_____

4. Have you passed out do to hypoglycemia?

_____

Hyperglycemia

1. What are the common symptoms (if applicable) that your blood sugar is elevated?_____

   _____

2. Have you ever been hospitalized due to hyperglycemia?_____
3. Do you often experienced hyperglycemia?_____
    a. If so, do you often experience (circle all that apply)
        i. Thirst
        ii. Hunger
        iii. Fatigue
        iv. Desire to urinate
        v. Blurred vision
        vi. Increased difficulty with infections
        vii. Other:_____

Diabetes and Mood

1. Has diabetes adversely affected your mood? If so, how?

   _____

   _____

2. Would you describe yourself as having increased (circle all that apply):
    1. Anger
    2. Aggression
    3. Hostility
    4. Irritability
    5. Sadness
    6. Depression
    7. Anxiety
    8. Worry
    9. Other:_____
3. Would others describe you has having increased (circle all that apply):

1. Anger
2. Aggression
3. Hostility
4. Irritability
5. Sadness
6. Depression
7. Anxiety
8. Worry
9. Other:_____

4. When your blood sugar is low do you have more problems with (circle all that apply):
    1. Anger
    2. Aggression
    3. Hostility
    4. Irritability
    5. Sadness
    6. Depression
    7. Anxiety
    8. Worry
    9. Other:_____
5. When your blood sugar is high do you have more problems with (circle all that apply):
    1. Anger
    2. Aggression
    3. Hostility
    4. Irritability
    5. Sadness
    6. Depression
    7. Anxiety
    8. Worry
    9. Other:_____

Diet and exercise

1. How many calories do you consume in an average day?

   _____

2. Do you follow a specific type of diet for treatment of your diabetes, such as monitoring the amount and type of calories consumed?

   _____

3. Do you believe your diet to an important factor in your diabetes management?_____
4. Do you have control over what you eat?_____
5. Has diabetes adversely impacted your normal eating habits? If so, how?

   _____

   _____

   _____

6. Do you exercise regularly? If so, please list the type, amount, and frequency of your exercise_____

   _____

   _____

Diabetes and Cognition

1. Does diabetes make it difficult for you to concentration or complete tasks that require a lot thought?

   _____

   _____

   a. If so, are these matter made worse when your sugar levels are:
      i. High (hyperglycemia)

         _____

ii. Low (hypoglycemia)

_____

2. Has diabetes adversely affected your memory? If so how?

_____

_____

_____