THE INFLUENCE OF PERCEIVED STRESS ON INSULIN RESISTANCE
IN ADULTS WITH TYPE 2 DIABETES

Amanda S. Phillips

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APPROVED:

Charles A. Guarnaccia, Major Professor
Kimberly S. Kelly, Committee Member
John M. Ruiz, Committee Member
Vicki Campbell, Chair of the Department of Psychology
Mark Wardell, Dean of the Toulouse Graduate School
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Objective: To identify whether perceived stress is a risk-factor for higher cortisol levels and greater insulin resistance in Type 2 diabetic patients, using data from participants with and without diabetes in the National Survey of Midlife Development in the United States (MIDUS), specifically MIDUS II, Project 4. The following hypotheses were tested: (H1a) greater perceived stress would be associated with higher cortisol for Type 2 diabetic participants, (H1b) the perceived stress/cortisol relationship would be stronger for people with Type 2 diabetes than for those without it, (H2) greater perceived stress would be associated with higher Homeostatic Model Assessment-Insulin Resistance (HOMA-IR, insulin-resistance) for Type 2 diabetic participants, (H3a) subjective well-being would moderate the perceived stress/insulin resistance relationship for Type 2 diabetic participants, and (H3b) depression would moderate the perceived stress/insulin resistance relationship for Type 2 diabetic participants. Method: MIDUS, a longitudinal study of over 7,000 American adults, explores biopsychosocial factors that could contribute to variance in mental/physical health. Only complete data were utilized. Type 2 participants (n=115) consisted of 54 males and 62 females ranging in age from 36 to 81 years. Non-diabetic participants (n=1097) consisted of 470 males and 627 females ranging in age from 34 to 84 years. Results: None of the predicted relationships were statistically significant. Waist to hip ratio was significantly related to insulin resistance ($r = .31, p = .001$). Conclusions: Future studies should collect information about the type and duration of stressors in addition to perceptions about stress for those with Type 2 diabetes.
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# TABLE OF CONTENTS

**LIST OF TABLES** ........................................................................................................................................ v

**CHAPTER I  INTRODUCTION** ........................................................................................................ 1  
  Psychological Stress ........................................................................................................ 1  
  Perceived Stress ........................................................................................................ 1  
  Perceived Stress and Cortisol ................................................................................ 2  
  Subjective Well-being ............................................................................................................ 5  
  Diabetes Overview .......................................................................................................... 6  
  Type 1 Diabetes ........................................................................................................ 7  
  Type 2 Diabetes ........................................................................................................ 8  
  Diabetes and Psychological Stress ........................................................................ 12  
  Diabetes and Depression ............................................................................................... 12  
  Hypotheses ........................................................................................................................ 13

**CHAPTER II  METHOD** ................................................................................................................. 15  
  Participants ....................................................................................................................... 15  
  Procedures and Materials ................................................................................................... 16  
    Diabetes Diagnosis ........................................................................................................ 16  
    Medication Data ........................................................................................................... 16  
    Biomarker Assessments .................................................................................................. 17  
    Self-Administered Questionnaire Data ............................................................................. 18  
    Perceived Stress Scale ................................................................................................... 18  
    Subjective Well-Being Scale .......................................................................................... 18  
    Center for Epidemiologic Studies Depression Scale ....................................................... 19  
  Data Analysis ................................................................................................................... 19  
    Descriptive Statistics ..................................................................................................... 20  
    Inferential Statistics ....................................................................................................... 20  
    Testing of Hypotheses .................................................................................................... 22

**CHAPTER III  RESULTS** ............................................................................................................... 26  
  Hypothesis 1a .................................................................................................................... 26  
  Hypothesis 1b .................................................................................................................... 26
LIST OF TABLES

Table 1 Descriptive Statistics for Continuous Variables .............................................................. 34
Table 2 Correlations of Scale Variables ....................................................................................... 34
Table 3 Independent Samples $t$-tests comparing Type 2 Diabetic and Non-diabetic Participants 35
Table 4 Participant Counts and Chi-square Test Comparing Type 2 Diabetic and Non-diabetic Participants on Gender................................................................. 35
Table 5 Predictors of Insulin Resistance Testing the Effects of Perceived Stress with Subjective Well-being as a Moderator ................................................................. 36
Table 6 Predictors of Insulin Resistance Testing the Effects of Composite Perceived Stress and Subjective Well-being Variable ................................................................. 37
Table 7 Predictors of Insulin Resistance Testing the Effects of Perceived Stress with Depression as a Moderator ......................................................................................... 38
Table 8 Predictors of Insulin Resistance Testing the Effects of Composite Perceived Stress and Depression Variable ................................................................. 39
CHAPTER I
INTRODUCTION

Approximately 347 million people across the globe have diabetes and the incidence of Type 2 diabetes is expected to increase, becoming the seventh leading cause of premature death by the year 2030 (World Health Organization, 2013). Diabetes is a chronic, metabolic condition that can lead to life-threatening complications such as heart disease and kidney failure. It is possible that perceived stress and its associated increased cortisol levels can increase insulin resistance and eventually lead to increased diabetic complications in people who have Type 2 diabetes. In order to reduce the risk of these outcomes, it is important that we understand how perceived stress impacts cortisol levels and insulin resistance.

Psychological Stress

Studies of psychological stress have primarily focused on objective events believed to be stressful to most people or on the reactions individuals have to these stressors events. According to the latter approach, psychological stress is a subjective experience that results from stressor events for which there are perceived insufficient coping resources. This means an appraisal of a stressor can induce psychological stress in one person and not another. This stress reaction may be acute or chronic, depending on the individual (Cohen, Janicki-Deverts, & Miller, 2007). The effect of this individual difference in the experience of psychological stress can be demonstrated using the construct developed by Cohen, Kamarck, and Mermelstein (1983) called perceived stress.

Perceived Stress

Perceived stress takes place when a person appraises a potentially stress inducing situation and determines they do not have the resources necessary to cope with the stressor.
When perceived stress occurs, the potential for a physiological stress response leading to disease is created (Cohen & Williamson, 1988). Cohen, Tyrell, and Smith (1993) conducted an experimental study which illustrated the effect of perceived stress on disease progression. They recruited 420 healthy participants and exposed them to a cold virus. Higher ratings on scales measuring perceived stress, negative life events, and negative affect were associated with increases in illness. Negative life events were associated with rates of illness, mediated by number of symptoms, and perceived stress was associated with increased infection. The authors concluded that these two experiences, negative life events versus perceived stress, have different effects of the progression of disease.

_Peceived Stress and Cortisol_

When a person experiences perceived stress, an acute physiological reaction occurs in which the hypothalamic-pituitary-adrenal axis (HPA) releases hormones such as cortisol, the primary endocrine indicator of the stress response. Cortisol can be measured using saliva, urine, hair, blood serum and cerebrospinal fluid. Saliva and urine collection are preferred due to their non-invasive collection procedures and because participants can self-collect specimens, which reduces anticipatory stress (Hellhammer, Wüst, & Kudielka, 2009).

Salivary cortisol is used in experimental studies with a pre-post challenge design and also to monitor cortisol awakening response, which is the diurnal increase in cortisol levels in the first hour after a person awakes from sleep (Sarkar, Zeng, Chen, Salvante, & Nepomnaschy, 2013). Salivary cortisol is typically measured as free cortisol, meaning it is not bound to protein. Studies have shown cortisol awakening response has high intraindividual reliability, is independent of the effects of time of waking, sleep duration and quality, physical activity, and alcohol consumption, but is affected by chronic stress and burnout (Hibel, Mercado, & Trumbell, 2019).
2012; Pruessner et al., 1997; Pruessner, Hellhammer, & Kirschbaum, 1999; Schmidt-Reinwald et al., 1999; Wüst, Federenko, Hellhammer, & Kirschbaum, 2000). However, Federenko et al. (2004) found the time of awakening had a significant effect on cortisol levels in adult nurses working various shifts, with those who woke early in the morning showing the most pronounced rise in cortisol levels. They also found students’ cortisol levels decreased after waking from a nap in the evening.

Urinary cortisol is typically used in longitudinal studies to examine intrapersonal or interpersonal differences. It can be free, or non-conjugated, meaning it is not bound to a protein. Urinary cortisol may also be conjugated, meaning that it is bound to sulfonide (antibiotic) or glucuronide (used in excretion) groups. The advantage to using an overnight urine sample in measuring cortisol is that the subject is asleep, and is not being exposed to additional stressors or activities that may affect cortisol levels. Additionally, the importance of specific timing in collecting the specimen is less critical, though one would need to control for overnight voids (Shakar et al., 2013)

In a longitudinal study comparing salivary free cortisol to first morning urinary cortisol, researchers found these two measures were weakly, but significantly, related and first morning urinary cortisol levels were much higher in free cortisol than salivary samples. The authors attributed this difference in part to circadian rhythm, which causes cortisol levels to rise dramatically in the first hour after waking and decline throughout the day. They also cited that salivary cortisol represents cortisol production over the previous 10-20 minutes, while first morning urinary cortisol is the collection of cortisol from the time of the last urinary void, often before the participant went to bed the night prior, and the morning urinary void. Due to the larger quantity of free cortisol in urine samples, the authors concluded changes in HPA activity
could be more easily detected in first morning urinary cortisol samples (Shakar et al., 2013). However, only about 1% of free blood cortisol is excreted through urine, along with cortisol metabolites. In order to get a more accurate measure of free cortisol levels, these metabolites, which represents approximately 80% of secreted cortisol, can be also be assessed, in addition to free cortisol. This requires using a gas chromatography/mass spectrometry method (Hellhammer et al., 2009). Furthermore, because diuresis and urine concentration can affect urinary cortisol levels, creatinine, which excreted into urine at a steady rate, is used to standardize cortisol levels (Glei et al., 2013).

Psychological and endocrine stress responses are considered to both be indicators of the same stress construct. The assumption that psychological and endocrine stress responses are indicators of an overall stress construct indicates there should be a high degree of association between perceived stress and cortisol levels. Neuroanatomical connections between the HPA and the limbic and cortical structures associated with perceived stress responses lend support to this association (Hellhammer et al., 2009). However, when self-report measures are used to assess perceived stress, the results are mixed in demonstrating this relationship. Pruessner, Hellhammer, and Kirschbaum (1999) found perceived stress correlated significantly with cortisol awakening response in teachers. Although additional studies have found positive associations between perceived stress and cortisol (Edwards, Hucklebridge, Clow, & Evans, 2003; Gersten, 2008), others have found negative associations (O’Connor et al., 2009; Yang et al., 2001) or no associations (Fischer, Calame, Dettling, Zeier, & Fanconi, 2000; Kurina, Schneider, & Waite, 2004).

Several sources of variability in measuring the relationship between psychological stress and cortisol have been identified in the literature. Neuroendocrine factors such as the lag time
between psychological and endocrine responses to stress can affect covariance (Campbell & Ehlert, 2012; Schlotz et al., 2008) and chronic secretion of cortisol could lead to down regulation of cortisol receptors and production (Miller, Chen, & Zhou, 2007). From a psychological perspective, stress self-report measures used in various studies are based upon different underlying constructs. In addition, self-reports of stress are affected by both gender, with females reporting greater stress, and personality traits, such as greater neuroticism related to greater stress (Hellhammer, Wüst, & Kudielka, 2009).

Subjective Well-being

Subjective well-being (SWB) describes the emotions and judgments individuals incorporate into evaluations of quality of life. Researchers have examined a number of factors included in assessment of SWB, such as positive affect, life satisfaction, and satisfaction with particular life domains, such as work or family (Diener, Suh, Lucas, & Smith, 1999). Previous research has shown adaptation to life conditions, both favorable and unfavorable, varies at the individual level in terms of SWB. Some individuals may experience a stressor, such as unemployment, which only temporarily reduces their level of SWB. Other individuals who experience this stressor may take many years to adapt and return to their previous level of SWB (Diener, 2012).

Higher SWB has been shown to have protective health effects. A meta-analysis of 35 studies conducted by Chida and Steptoe (2008) showed that higher SWB was associated with reduced mortality due to cardiovascular events, renal failure, and HIV infections. The potential link between SWB and insulin resistance has not been examined in previous research. However, since SWB is associated with a protective effect for physical health, it is possible that people
who are higher in SWB may not incur the same degree of insulin resistance (a factor in the development of diabetes discussed immediately below) due to perceived stress.

Diabetes Overview

Diabetes mellitus is a group of chronic metabolic diseases in which a person becomes hyperglycemic due to the inability of the pancreas to produce insulin or enough insulin, a failure of muscle or adipose cells to respond to insulin (insulin resistance), or both issues occurring simultaneously. This group consists of Type 1 diabetes, where there is a complete inability to produce insulin but typically no difficulty related to insulin resistance, and Type 2 diabetes, where there is an inability to produce enough insulin and/or insulin resistance. There is also gestational diabetes, which is similar to, potentially temporary, Type 2 diabetes that occurs during pregnancy, and diabetes which is secondary to an illness or an injury, which can be similar to either Type 1 or Type 2 diabetes depending upon the nature of the causal illness or injury. This least common form of diabetes, secondary to an illness or an injury, will not be discussed further, but is listed for sake of comprehensiveness.

Individuals are tested for diabetes using a glycated hemoglobin (A1c) test, a fasting or incidental blood glucose test, and/or a glucose tolerance test after reporting clinical symptoms such as excessive thirst, hunger and urination (Van Belle, Coppieters, & Von Herrath, 2011). Symptoms are typically more severe for Type 1 diabetes and there is also some differentiation of symptom clusters between Type 1 and Type 2 diabetes.

The A1c test is a measure that correlates with average blood glucose levels over the previous two or three months by assessing the amount of blood glucose attached to hemoglobin proteins found in red blood cells. However, the A1c test has a telescoping effect, meaning that more recent blood glucose levels will have a greater effect on the results of the test. An A1c
level above 6.5% on two consecutive tests, two or three months apart, is generally considered to be indicative of diabetes.

The fasting blood glucose test and glucose tolerance test are also taken on two separate occasions. After an overnight fast, blood glucose levels greater than 126 mg/dL on two fasting blood glucose tests is indicative of diabetes. For both these tests, a very high initial level typically will be enough to make a diagnosis of diabetes. The glucose tolerance test, used to diagnose gestational diabetes, involves an initial glucose challenge in which the patient drinks a glucose solution with a known glycemic profile and a blood test is performed one hour later. A blood glucose level greater than 140 mg/dL indicates the patient is at risk for gestational diabetes and must take a follow-up test. Here the patient fasts overnight and then blood glucose is measured. Finally, the patient drinks a more concentrated glucose solution and their blood glucose level is checked once an hour for three hours. If at least two of the three blood tests show a blood glucose level higher than 140 mg/d, the patient will be diagnosed with gestational diabetes (Mayo Clinic, 2013a).

Once a person has been diagnosed with diabetes, they are encouraged to maintain A1c levels around 7% or lower (American Diabetes Association, 2013a), because higher levels can lead to serious complications including coronary heart disease, neuropathy, and kidney disease. Fortunately, the three most common types of diabetes, Type 1, Type 2, and gestational diabetes, can be managed through medical and lifestyle interventions (WHO, 2013).

Type 1 Diabetes

Type 1 diabetes most often begins in childhood, but can develop at any time during the lifespan. It is characterized by the death of insulin producing β-cells in the pancreas, and is believed to be the result of an autoimmune reaction. However, the exact mechanism of this
autoimmunity is unknown and there are several theories concerning its etiology. Korsgren et al. (2012) conducted a study with animal models, which suggests that intestinal bacteria entering the pancreas may prompt an immunity response leading to the destruction of β-cells. Other researchers believe there is a lifetime genetic vulnerability in which environmental triggers, such as viruses, can facilitate this autoimmune response (Van Belle, Coppieters, & Von Herrath, 2011).

Although there is no cure or preventative measure for Type 1 diabetes, the disease can be managed through a regimen designed to maintain safe blood glucose levels. This is accomplished through insulin replacement via insulin injections or an insulin pump and carbohydrate counting. People who have this disease must also check their blood sugar levels frequently throughout the day and participate in regular A1c testing (Mayo Clinic, 2013). In addition, life-style, weight, and dietary management are beneficial to the management of all types of diabetes, including Type 1.

*Type 2 Diabetes*

Type 2 diabetes was once considered to be primarily adult onset, but is increasingly being diagnosed in adolescents and children and accounts for 95%, or more, of diabetes cases overall. The common factor among Type 2 cases is obesity and metabolic deregulation. Approximately 80% of people who have Type 2 diabetes are overweight or obese (U. S. Department of Health and Human Services, 2012). The obesity that characterizes Type 2 diabetes is one factor that can contribute to insulin resistance, a metabolic condition in which the body produces insulin, but does not use it effectively to facilitate the absorption of glucose into cells (NDIC, 2013). Along with insulin resistance, reduction in production of insulin due to β-cell death contributes to the development of Type 2 diabetes.
Type 2 diabetes is managed through monitoring blood sugar and lifestyle changes. A healthy diet, weight maintenance and regular exercise are often sufficient to keep blood glucose levels in a safe range. However, it may become necessary for a person with Type 2 diabetes to take oral medications, which either stimulate insulin production or reduce insulin resistance if the disease progresses. If β-cells are destroyed, exogenous insulin, administered through injection, as with Type 1 diabetes, will be needed to maintain diabetic control for such individuals with advanced Type 2 diabetes (Mayo Clinic, 2012).

Type 2 Diabetes and Insulin Resistance

Insulin resistance is the leading risk factor for the onset of Type 2 diabetes and persists throughout the course of the disease, thus it is important to understand how insulin resistance develops (Saltiel & Kahn, 2001). Several theories exist concerning its etiology. The adipose tissue expandability hypothesis states each individual has a limited number of adipocytes, the cells in which fat, or lipid, is stored. These adipocytes store a limited amount of lipid and once that limit is reached, lipid begins to accumulate in the cells of non-adipose organs. If this accumulation occurs in muscle, liver, or β-cells, the result can be insulin resistance or apoptosis, both of which could lead to Type 2 diabetes. However, there is not a universal adipose mass at which this insulin resistance occurs in all people, which means this is not a universal explanation for the development of insulin resistance (Van Belle et al., 2011).

In addition to the adipose expandability hypothesis, adipose cells may be involved in insulin resistance by ceasing to respond to insulin when they are filled to capacity and releasing hormones that signal other adipocytes and muscle cells to stop responding to insulin. This leads to a build-up of glucose in the blood stream, which signals the β-cells in the pancreas to produce more insulin. This cycle of unresponsive cells and insulin production continues until the body
becomes insulin-resistant. This process overworks the β-cells and can eventually lead to their destruction, and thus a reduction in insulin production ability (Hirosumi et al., 2002).

Psychological stress may also contribute to the development of insulin resistance and Type 2 diabetes. Li, Li, Zhou, and Messina (2013) conducted a study using a mouse model in which they administered 180 episodes of inescapable foot shock. When compared with mice that did not receive the shocks, the mice that received the shocks and failed to escape shocks during behavioral escape tests experienced impaired glucose metabolism and impaired insulin signaling in the liver, meaning that the liver was not absorbing excess glucose. The results of this study suggest acute psychological stress can affect glucose metabolism and insulin function. Cortisol, the primary endocrine indicator of stress, has also been shown to contribute to insulin resistance, Type 2 diabetes, and diabetic complications (Chiodini et al., 2005; Lehrke et al., 2008; Prunell et al., 2008; Roy, Roy & Brown, 1998). Cortisol signals adipose and muscle tissue to become less responsive to insulin, and thus stop taking in glucose. Over time, these signals from excess cortisol can lead to insulin resistance (Björntorp, 1999).

The degree of insulin resistance a person has can be measured using a mathematical model called homeostatic model assessment-insulin resistance (HOMA-IR). This norm based structural model quantifies insulin resistance by dividing the product of fasting plasma glucose (FPG) and fasting plasma insulin (FPI) by a constant (FPG × FPI/405). FPG is a measure of basal blood glucose levels after an overnight fast and FPI is a measure of basal blood insulin levels after an overnight fast (National Diabetes Information Clearinghouse, 2014). This relationship between FPG and FPI is demonstrative of the secretion of insulin from β-cells in response to basal glucose levels, with 1 as a normal HOMA-IR value (Wallace, Levy, & Matthews, 2004). The HOMA-IR model is highly correlated with other reliable measures of
insulin resistance (Bonora et al., 2000; Garcia-Estevez et al., 2003; Matthews et al., 1985). It is preferable to take a mean of three samples in order to determine HOMA-IR. However, the common practice is to take a single sample, which is considered acceptable for large datasets. The HOMA-IR equation yields estimates of insulin resistance that can be used to compare populations using similar assays and observes relative change over time (Wallace et al., 2004). However, HOMA-IR is based on a model derived in 1985 (Matthews et al., 1985), and has not been calibrated to current assay methods. This means HOMA-IR should not be used to assess absolute insulin resistance (Wallace et al., 2004).

Type 2 Diabetes and Cortisol

There is a debate concerning whether higher cortisol levels can be attributed to differential HPA functioning in those with Type 2 diabetes compared with non-diabetics. Several studies have provided data that support a difference in HPA activation in those who have Type 2 diabetes compared with non-diabetics (Bruehl, Wolf, & Convit, 2009; Champaneri et al., 2012; Reynolds et al., 2010). In addition, a study by Chiodini et al. (2007) found 170 people with Type 2 diabetes had higher cortisol levels than 71 non-diabetic age-matched controls, and Type 2 diabetics experiencing complications had still higher cortisol levels than Type 2 diabetics not experiencing complications. Chiodini et al, and other similar studies did not evaluate other potential causes of these differences in HPA activity. Diabetes can be comorbid with Alzheimer’s disease, depression, and mild cognitive impairment, which are all associated with elevated cortisol levels (Castillo-Quan & Pérez-Osorio, 2007). However, the data presented by the above studies is compelling and merits further study.
Diabetes and Psychological Stress

Psychological stress has been shown to increase blood glucose levels people who have Type 1 and Type 2 diabetes (Chida & Hammer, 2008). It is possible psychological stress can affect blood glucose levels through direct and indirect routes. The release of stress hormones, such as cortisol, intended to mobilize glucose during the stress response can be problematic for a person who has diabetes. Once these stress hormones began breaking down tissue into glucose, the lack of insulin or insulin resistance causes a build-up of glucose in the blood stream, which can lead to complications over a prolonged time, especially when the stress is chronic. There may also be an indirect effect, in which people who have diabetes and are experiencing psychological stress may neglect health behaviors important to maintaining diabetic control, such as healthy eating and exercise. They may also engage in harmful behavior, such as increasing alcohol consumption, eat less healthful food, and decreasing physical activity. If psychological stress becomes chronic, tissue damage due to increased blood glucose levels may occur more quickly than it would in similar non-diabetic individuals (ADA, 2013c).

Diabetes and Depression

Previous research has demonstrated a link between diabetes and depression. In some cases, depression develops first and may be a risk factor for the onset of Type 2 diabetes (Brown, Varghese, & McEwen, 2004). However, depression may also be a consequence of having been diagnosed with diabetes. Mezuk et al. (2013) performed a study in which they demonstrated a 4.3 fold increase in the development of depression after having been being diagnosed with diabetes, while un-diagnosed diabetes was not significantly associated with depression. Additionally, people who have diabetes, on average, have twice the base-rate of depression than does the general population (Sacco et al., 2007).
In those who have diabetes, depression is often associated with poorer glycemic control (Rush, Whitebird, Rush, Solberg, & O'Connor, 2008), an increased risk of complications (de Groot, Anderson, Freedland, Clouse, & Lustman, 2001), and an increased risk of mortality (Katon et al., 2005). This increased risk may be related to a decrease in important health behaviors as a consequence of depression (Rush et al.), and may also be related to physiological changes associated with depression, such as increased cortisol levels (Brown et al., 2004). The direction of the relationship between depression and diabetic complications is unknown, and could potentially be a non-recursive model (i.e., reciprocal causation over time) and/or the result of an unmeasured third-variable. Additionally, it is possible that chronically high cortisol levels due to depression could lead to insulin resistance (Björntorp, 2001).

**Hypotheses**

The aim of the present study was to determine whether perceived stress significantly co-varied with cortisol and insulin resistance in Type 2 diabetic individuals, and to compare the nature of this relationship to non-diabetic individuals. Understanding such a relationship for Type 2 diabetic patients may allow health care providers to quickly assess, possibly with a few questions related to perceived stress, whether their diabetic patients are at a higher risk of becoming insulin resistant or more insulin resistant.

Hypothesis 1a: It was predicted that participants who have Type 2 diabetes and report greater perceived stress would have higher cortisol levels.

Hypothesis 1b: It was predicted that the relationship between perceived stress and cortisol would be stronger for people with Type 2 diabetes than for individuals without diabetes.

Hypothesis 2: It was predicted that for participants who have Type 2 diabetes, those who report greater perceived stress would have higher insulin resistance.

In addition, it has been observed that individuals who experience stress may or may not become insulin resistant. Understanding ways the relationship between perceived stress and
insulin resistance may be moderated for people who have diabetes would be clinically useful for physicians who identify patients for whom perceived stress is a greater risk-factor for increased insulin resistance. Hypotheses 3a and 3b investigates two potential mechanisms of this possible moderation effect.

Hypothesis 3a: The present study aimed to test whether subjective well-being moderated the perceived stress/insulin resistance relationship with the expectation that greater subjective well-being would be related to a decrease the strength of the relationship between perceived stress and insulin resistance.

Hypothesis 3b: Similar to 3a, the present study aimed to test whether depression moderated the perceived stress/insulin resistance relationship with the expectation that greater depression would be related to an increase in the strength of the relationship between perceived stress and insulin resistance.
CHAPTER II

METHOD

Participants

Project 4 from the MIDUS II longitudinal study is a biomarker supplement, which contains data from a subsample of 1,255 participants ranging in age from 35 to 86. These data were collected during a 24-hour stay at one of three General Clinical Research Centers (GCRCs) located at UCLA, University of Wisconsin, and Georgetown University (Ryff et al., 2013). To recruit participants for Project 4, staff at the three primary data collection sites located at UCLA, University of Wisconsin, and Georgetown University sent a recruitment packet to those who had been involved in Project 1. A few weeks later they followed up by phone to answer questions, schedule a visit to the data collection site and facilitate travel arrangements. Verbal informed consent was obtained at the time respondents scheduled a visit and written consent was given at the facility before data collection. (Ryff et al., 2013).

Type 2 diabetic participants for the present work (n = 115) were included in the analyses along with a comparison sample of non-diabetics (n = 1097). The Type 2 diabetic sample was selected by including participants who self-reported they had received a diagnosis of diabetes from a physician, then using an SPSS filter to screen out self-reported diabetic participants who also reported a subcutaneous route of medication (the required method for taking insulin in Type 1 diabetics), thus limiting the sample to only Type 2 diabetics. It is possible this method may have removed Type 2 diabetics who are at a very advanced stage of the disease. However, this was the only way to ensure no Type 1 diabetics were included in the sample. This Type 2 diabetic sample consisted of 54 males (46.6%) and 62 females (53.4%) ranging in age from 36 years to 81 years. These participants selected Caucasian (62.9%), Black (3.4%), Native
American/Alaskan Native (1.7%), Asian (0.9%), and Don’t Know (0.9%) to describe their race/ethnicity (30.2% were system missing). For the non-diabetic sample, participants who indicated they had received a diagnosis of diabetes from a physician were excluded. This sample consisted of 470 males (42.8%) and 627 females (57.2%) who ranged in age from 34 years to 84 years. Participants selected Caucasian (79.8%), Black (2.1%), Native American/Alaskan Native (1.0%), Asian (0.2%), Other (2.6%), Don’t know (0.1%), and Refused (0.1%) to describe their race/ethnicity (14.1% were system missing).

Procedures and Materials

The National Survey of Midlife Development in the United States (MIDUS) (Ryff, Seeman, & Weinstein, 2013) is a longitudinal study of over 7,000 Americans between the ages of 25 and 74, which began collecting data in 1994. The multidisciplinary team who developed the study sought to explore biopsychosocial factors, which could contribute to age-related variance in mental and physical health.

The present study used data from MIDUS II, Project 4, which was conducted from 2004 to 2006. The objective of MIDUS II was to follow up with MIDUS I respondents using the same previously administered phone interview questionnaire and SAQ, and with the addition of neurological and biological data collection. Project 4 was the component of MIDUS II to include a physical exam and collect biomarker data.

Diabetes Diagnosis

A medical history was obtained via interview, in which participants were asked if a physician had diagnosed them as having diabetes. Participants answered 1 (Yes) or 2 (No).
Medication Data

Participants were instructed to bring all their medications in the original packaging to the interview site. This procedure was implemented so the researchers could ensure accuracy in recording the medication names and dosages. Upon arrival at the GCRC, medication data, including route and frequency of administration, and how long the participant had been taking the medication, were recorded on the Medication Chart (UW-Madison Institute on Aging, 2010). For the purposes of the current study, data from participants who brought insulin to the testing site and reported that they had been taking this medication subcutaneously were excluded. Since the MIDUS study did not directly ask whether participants had been diagnosed with Type 1 versus Type 2 diabetes, this is the best method of limiting the analysis to only participants with Type 2 diabetes. Additionally, certain medications which could affect cortisol levels or HOMA-IR results were controlled for in the statistical analysis. These medications included estrogens, androgens, contraceptives, corticosteroids, and common diabetic medications (Meglitinides, Sulfonylureas, Biguanides, Thiazolidinediones, and other miscellaneous Anti-diabetic Agents).

Biomarker Assessments

Physical Exam

The physical exam was performed at all three GCRCs. During the physical exam, measurements such as waist and hip circumference were measured in order to calculate waist-to-hip ratio, which was controlled for in the statistical analysis.

Tissue Sample Assays

Tissue samples were gathered and processed at each GCRC, then shipped to the MIDUS Biocore Lab for assay. These samples included a 12-hour (overnight) urine sample. Frozen urine was shipped once per month to assay for cortisol. Stored serum samples were analyzed
during the summer of 2010 to determine insulin and glucose levels, which were used to calculate HOMA-IR and cortisol levels (Ryff et al., 2013). Cortisol levels were standardized for diuresis by dividing cortisol values by urinary creatinine values (Glei et al., 2013).

**Self-Administered Questionnaire Data**

The Self-Administered Questionnaire (SAQ) is a 25-page booklet, which includes the following three psychosocial scales. It was self-administered after the medical history and took participants approximately 30 minutes to complete.

**Perceived Stress Scale**

The Perceived Stress Scale (PSS) consists of 10 items which ask participants to rate stress related thoughts and feelings as occurring 1 (*never*), 2 (*almost never*), 3 (*sometimes*), 4 (*fairly often*), or 5 (*very often*) over the past month. They were asked not to count the number of times a particular thought or feeling occurred, but to circle an answer that seems like a reasonable estimate. This 10-item Perceived Stress Scale was developed and tested for validity and reliability by Cohen, Kamarck, and Mermelstien (1983). After reverse coding items such that a higher score indicated greater perceived stress, a mean of these 10 items was taken.

**Subjective Well-Being Scale**

The Subjective Well-being Scale (SWS) is an 8 item overall measure of subjective well-being. It contains 3 subscales with items taken from multiple sources (Lyubomirsky & Ross, 1997; McCullough, Emmons & Tsang, 2002; Pavot & Diener, 1993). All of these items are rated on a 7-point Likert-type scale, with the following responses: 1 (*strongly disagree*), 2 (*disagree*), 3 (*slightly disagree*), 4 (*neutral*), 5 (*slightly agree*), 6 (*agree*), or 7 (*strongly agree*). This scale was scored by taking and a mean of the 8 item scores. Participants were asked to rate their agreement with the following statements:
• Compared to most of my peers, I consider myself to be more happy.
• In most ways my life is close to my ideal.
• The conditions of my life are excellent.
• I am satisfied with my life.
• So far I have gotten the important things I want in life.
• If I could live my life over, I would change almost nothing.
• I have so much in life to be thankful for.
• I am grateful to a wide variety of people.

*Center for Epidemiologic Studies Depression Scale.*

The Center for Epidemiologic Studies Depression Scale (CES-D) is a 20-item self-report questionnaire designed for use with the general population (Radloff, 1977). Participants rated the occurrence of these 20 items over the past week using a 4-point Likert-type scale with the following response options: 1 (*rarely or none of the time [less than one day]*), 2 (*some or a little of the time [1-2 days]*), 3 (*occasionally or a moderate amount of the time [3-4 days]*), 4 (*Most or all of the time [5-7 days]*) After reverse coding items as necessary, such that a higher number indicates more depressive symptoms, this scale was scored by taking a mean of the 20 items.

**Data Analysis**

MIDUS data for this project was retrieved from the Inter-university Consortium for Political and Social Research (ICPSR) website. The ICPSR is a division of the Institute for Social Research at the University of Michigan. The significance level for all analyses was $p < .05$.  

19
Descriptive Statistics

Descriptive statistics were conducted to determine the characteristics of the sample. Means, standard deviations, minimums, maximums, skew and kurtosis were calculated for continuous variables and can be found in Table 1. In addition to the above statistical analyses, Cronbach’s alpha internal consistency reliability was calculated for the PSS (.81), CES-D (.90) and SWS (.84), as well as a combined PSS/SWS scale (.86) and a combined PSS/CES-D scale (.92), which are described below.

The data were examined to determine if any outliers were present. An outlier value of 212 μg/dL was found for cortisol (a value of 92 μg/dL is sufficient to diagnose Cushing’s disease) and this case (16421) was removed. An outlier value of 26.48 was found for HOMA-IR, which was approximately 10 points higher than the next highest value (16.44), so this case (18869) was also removed. An outlier was found for regression predicted values (14475, Zpred = 7.88). This case was removed as well. In addition, the data were examined to ensure that assumptions of normality and linearity were adequately met. Tests to check these assumptions included skew, kurtosis, and bivariate scatterplots. The data were found to adequately meet these assumptions.

Inferential Statistics

One possible interpretation of potential results from testing hypotheses 3a and 3b is perceived stress, subjective well-being, and depression are related, meaning they are measuring the same construct. Therefore, collinearity diagnostics were conducted and a lower triangular correlation matrix of all scale variables was used to examine the relationship among these constructs (Table 2). Correlations with correction for attenuation due to unreliability of measurement, a statistical method to examine the correlation of the latent constructs if the
measurement of these constructs could be made perfectly reliable (Carmines & Zeller, 1991), were further conducted to more fully determine whether any collinearity was present.

The collinearity diagnostics, including tolerance and VIF, showed there were not any violations of regression assumptions for scale variables. In order to fully explore the data for possible collinearity, correlations of scale variables were analyzed with correction for attenuation. Both before, and more strongly, after this correction for attenuation, perceived stress was negatively correlated with subjective well-being (zero order correlation: $r = -.52$) (correction for attenuation: $r_{PSS*SWS} = -.63$). These correlations indicate a possible collinearity problem, therefore a composite variable was created in addition to the individual scale variables in order to explore whether the possibility that this degree of relatedness would affect the outcome of the analyses. Items from both scales were incorporated into a single variable by reverse coding and then multiplying the 8 SWS items by 5/7 and then averaging these items with the 10 PSS items. Multiplying the SWS items by 5/7 converted this 7-point scale to a 5-point scale, making it more comparable the 5-point PSS. Using this single variable, an additional test of hypothesis 3a was conducted using a simple linear regression. Cronbach’s alpha internal consistency reliability for this composite PSS and SWS variable was $\alpha = .86$.

In addition, perceived stress and depression were highly positively correlated (zero order correlation: $r = .73$) (correction for attenuation: $r_{PSS*CESD} = .85$). Because these correlations indicate a possible collinearity problem, a similar procedure to that above was conducted. The 20 CES-D items (4-point) were multiplied by 5/4 and averaged with the 10 PSS items (5-point). Using this composite variable, an additional test of Hypothesis 3b was conducted using a simple linear regression. Cronbach’s alpha internal consistency reliability for this composite PSS and CES-D was $\alpha = .92$. 
To further explore any group differences between Type 2 diabetic participants and non-diabetic participants, \( t \)-tests were conducted for key variables. The results of these \( t \)-tests can be found in Table 3. In addition, a chi-square test was conducted to examine group differences in gender. The results of this chi-square test can be found in Table 4.

**Testing of Hypotheses**

**Hypothesis 1a**

It was predicted that participants who have Type 2 diabetes and report greater perceived stress would have higher cortisol levels. A one-tailed correlation was conducted to test this relationship. A one-tailed partial correlation was next conducted to test this relationship, controlling for estrogens, androgens, contraceptives, and corticosteroids, which could influence cortisol levels. Next, a one-tailed partial correlation was conducted to test this relationship with age as a control variable in addition to the above medications. Finally, a one-tailed partial correlation was conducted to test this relationship with gender as a control variable in addition to the above medications.

**Hypothesis 1b**

It was predicted that the relationship between perceived stress and cortisol would be stronger for people with Type 2 diabetes than for individuals without diabetes. A one-tailed correlation was conducted to test this relationship for the non-diabetic sample. A one-tailed partial correlation was next conducted examining the relationship between perceived stress and cortisol for this non-diabetic sample, controlling for the above medications that could affect cortisol. Next, a one-tailed partial correlation was conducted to test this relationship for non-diabetics with age as a control variable in addition to the above medications. Finally, a one-tailed partial correlation was conducted to test this relationship for non-diabetics with gender as a
control variable in addition to the above medications. These correlations would have been compared using Hotelling’s $t$-test if they were significantly different from zero. In this case no comparison was necessary. In addition, independent samples $t$-tests were conducted to compare the means of the two groups on perceived stress and cortisol.

Hypothesis 2

It was predicted that participants who have Type 2 diabetes and report greater perceived stress would have higher insulin resistance. A one-tailed correlation was conducted to test this relationship. A one-tailed partial correlation was next conducted to test this relationship, controlling for waist-to-hip ratio and use of diabetes medications (meglitinides, sulfonylureas, biguanides, thiazolidinediones, and other miscellaneous anti-diabetic agents). Next, a one-tailed partial correlation was conducted to test this relationship with age as a control variable in addition to the above medications and waist to hip ratio. Finally, a one-tailed partial correlation was conducted to test this relationship with gender as a control variable in addition to the above medications and waist to hip ratio.

Hypothesis 3a

The present study aimed to test whether subjective well-being moderated the perceived stress/insulin resistance relationship in people with Type 2 diabetes, with the expectation that greater subjective well-being would be related to a decrease the strength of the relationship between perceived stress and insulin resistance. A hierarchical regression analysis, using subjective well-being (SWS) as a moderator of the perceived stress (PSS) and insulin resistance (HOMA-IR) relationship. (i.e., a PSS × SWS cross-product was created with centered variables, [Cohen et al., 2003]), and controlling for waist-to-hip ratio, the above diabetic medications, age, and gender was used to predict insulin resistance. Waist to hip ratio was entered in the first step
followed by diabetic medications, which were entered in the second step. Age and gender were entered in the third step. The centered SWS variable was entered in the fourth step followed by the centered PSS variable, which was entered in the fifth step. The PSS×SWS cross-product was entered in the final step.

Because the perceived stress and subjective well-being correlation was large, these two scales were combined into a composite variable for a modified repetition of the above analysis. A hierarchical regression analysis was conducted, using the combined perceived stress/subjective well-being variable, controlling for waist-to-hip ratio, the above diabetic medications, age, and gender with insulin resistance as the outcome variable. Waist to hip ratio was entered in the first step followed by diabetic medications, which were entered in the second step. Age and gender were entered in the third step. The composite PSS and SWS variable was entered in the final step.

Hypothesis 3b

Similar to 3a, the present study aimed to test whether depression moderated the perceived stress/insulin resistance relationship, with the expectation that greater depression would be related to an increase in the strength of the relationship between perceived stress and insulin resistance. A hierarchical regression analysis similar to the analysis for 3a was conducted to test this relationship. Waist to hip ratio was entered in the first step followed by diabetic medications, which were entered in the second step. Age and gender were entered in the third step. The centered CES-D variable was entered in the fourth step followed by the centered PSS variable, which was entered in the fifth step. The PSS×CES-D cross-product was entered in the final step.

Because the perceived stress and depression correlation was large, these two scales were combined into a single variable for a modified repetition of the above analysis. A hierarchical regression analysis was conducted, using the combined perceived stress/depression variable,
controlling for waist-to-hip ratio, the above diabetic medications, age, and gender with insulin resistance as the outcome variable. Waist to hip ratio was entered in the first step followed by diabetic medications, which were entered in the second step. Age and gender were entered in the third step. The composite PSS and CES-D variable was entered in the final step.
CHAPTER III

RESULTS

Hypothesis 1a

It was predicted that participants who have Type 2 diabetes and report greater perceived stress would have higher cortisol levels, but this was not supported \( r = -.04, p = .69 \), two-tailed). A one-tailed partial correlation was next conducted to test this relationship, controlling for estrogens, androgens, contraceptives, and corticosteroids, which could influence cortisol levels. This relationship was also not significant \( r = -.04, p = .34 \). Next, a one-tailed partial correlation was conducted to test this relationship with age as a control variable in addition to the above medications. This relationship was also not significant \( r = -.02, p = .42 \). Finally, a one-tailed partial correlation was conducted to test this relationship with gender as a control variable in addition to the above medications. This relationship was also not significant \( r = -.04, p = .34 \).

Hypothesis 1b

It was predicted that the relationship between perceived stress and cortisol would be stronger for people with Type 2 diabetes \( r = -.04, p = .69 \) than for individuals without diabetes \( r = -.02, p = .43 \), but this was not supported. A one-tailed partial correlation was next conducted examining the relationship between perceived stress and cortisol for this non-diabetic sample, controlling for the above medications that could affect cortisol. The relationship between perceived stress and cortisol for Type 2 diabetic participants \( r = -.04, p = .34 \) was again essentially the same as non-diabetic participants \( r = -.02, p = .23 \). Next, a one-tailed partial correlation was conducted to test this relationship for non-diabetics with age as a control variable in addition to the above medications. The relationship between for Type 2 diabetic participants \( r = -.02, p = .42 \) was again essentially the same as non-diabetic participants \( r = -
Finally, a one-tailed partial correlation was conducted to test this relationship for non-diabetics with gender as a control variable in addition to the above medications. Again, the relationship between for Type 2 diabetic participants ($r = -.04, p = .34$) was essentially the same as non-diabetic participants ($r = -.03, p = .16$). Independent samples $t$-tests were conducted, which show the means between these two groups are not significantly different with regard to perceived stress and the means of these two samples are not significantly different with regard to cortisol. The results of these $t$-tests can be found in Table 3.

Hypothesis 2

It was predicted that participants who have Type 2 diabetes and report greater perceived stress would have higher insulin resistance, but this was not supported ($r = -.06, p = .52$, two-tailed). A one-tailed partial correlation was next conducted to test this relationship, controlling for waist-to-hip ratio and use of diabetes medications (Meglitinides, Sulfonylureas, Biguanides, Thiazolidinediones, and other miscellaneous Anti-diabetic Agents). This relationship was also not significant ($r = -.12, p = .11$). Next, a one-tailed partial correlation was conducted to test this relationship with age as a control variable in addition to the above medications and waist to hip ratio. This relationship was also not significant ($r = -.11, p = .14$). Finally, a one-tailed partial correlation was conducted to test this relationship with gender as a control variable in addition to the above medications and waist to hip ratio. This relationship was also not significant ($r = -.09, p = .17$).

Hypothesis 3a

The present study aimed to test whether subjective well-being moderated the perceived stress/insulin resistance relationship in people with Type 2 diabetes, with the expectation that greater subjective well-being would be related to a decrease the strength of the relationship
between perceived stress and insulin resistance, but this was not supported. A hierarchical regression analysis was conducted to test this relationship and is shown in Table 5. The overall model was significant \(F(7,107) = 2.20, p = .04\), with perceived stress, subjective well-being, and the control variables accounting for 12.6% for the variance in insulin resistance (Adjusted \(R^2 = .07\)). However, perceived stress did not significantly predict insulin resistance (\(\beta = -.13, p = .26\)). There was not a significant interaction (\(\beta = -.07, p = .49\)) and waist to hip ratio, a control variable, was the only predictor with a statistically significant beta.

Because the perceived stress and subjective well-being correlation was large, these two scales were combined into a single variable for a modified repetition of the above analysis. A hierarchical regression analysis was conducted, using the above covariates and the composite perceived stress and subjective well-being variable, and is shown in table 6. The results were similar to the above analysis. Although the overall model was significant \(F(5, 109) = 2.97, p = .02\), with the composite perceived stress and subjective well-being variable and control variables accounting for 12% of the variance in insulin resistance (Adjusted \(R^2 = .08\)). The composite perceived stress and subjective well-being variable did not significantly predict insulin resistance (\(\beta = -.12, p = .20\)) and waist to hip ratio, a control variable, was the only predictor with a statistically significant beta.

**Hypothesis 3b**

Similar to hypothesis 3a, the present study aimed to test whether depression moderated the perceived stress/insulin resistance relationship, with the expectation that greater depression would be related to an increase in the strength of the relationship between perceived stress and insulin resistance, but this was not supported. A hierarchical regression analysis similar to the analysis for 3a was conducted to test this relationship and is shown in table 7. The overall model
was significant $F(7,107) = 2.39, p = .03$), with perceived stress, depression, and the control variables accounting for 13.5% of the variance in insulin resistance (Adjusted $R^2 = .08$). However, perceived stress was not significant in predicting insulin resistance ($\beta = -.24, p = .09$). There was not a significant interaction ($\beta = .008, p = .94$).

Because the perceived stress and depression correlation was large, these two scales were combined into a single variable for a modified repetition of the above analysis. A hierarchical regression analysis was conducted, using the combined perceived stress/depression variable, and is shown in table 8. The results were similar to the above analysis. The overall model was significant $F(5,109) = 2.67, p = .03$) with the composite perceived stress and depression variable and control variables accounting for 10.9% of the variance in insulin resistance (Adjusted $R^2 = .068$). However, the composite perceived stress and depression variable did not significantly predict insulin resistance ($\beta = -.05, p = .53$).
CHAPTER IV
DISCUSSION

The purpose of this study was to test whether perceived stress would influence cortisol levels and insulin resistance in people who have been diagnosed with Type 2 diabetes. These hypotheses make intuitive sense, because cortisol is considered the primary biomarker for stress (Hellhammer et al., 2009) and is known to influence insulin resistance (Lehrke et al., 2008). Contrary to expectations, the relationship between perceived stress and cortisol level was not significant. The relationship between perceived stress and insulin resistance also was not significant. This remained true when using subjective well-being and depression as moderators.

The data from the present study indicate there is not a relationship between cortisol and perceived stress. The above-cited study by Chiodini et al. (2005) found Type 2 diabetics experiencing complications had still higher cortisol levels than Type 2 diabetics not experiencing complications. Although not part of the proposed analyses, subsequent examination of complications found in the current, Type 2 diabetic sample showed 20 participants (16.9%) had been previously diagnosed with heart disease and 76 (64.4%) had been diagnosed with high blood pressure. Contrary to the Chiodini et al. findings, having heart disease ($r = .11, p = .24$) and high blood pressure ($r = .01, p = .96$) were not significantly related to cortisol levels. Data concerning other diabetic complications, such as neuropathy, retinopathy, and kidney disease were not collected in the MIDUS study. Perhaps further analyses of how diabetic complications may affect cortisol levels should be pursued in futures studies. It should also be noted that the Chiodini et al. study involved hospitalized diabetic patients and the current study used diabetics who were not selected because of any patient status, but simply because there were present in a
randomly selected sample. The effect of studies that examine patient versus community
dwelling individuals with a similar disease process is not well understood.

It is also possible these results may be due to cortisol levels varying based on the duration
and type of stressor involved (Miller et al., 2007). Previous studies have shown an acute rise in
cortisol levels soon after experiencing a stressor (Schlotz et al., 2008; Wirtz, Ehlert, Kottwitz, La
Marca, & Semmer, 2013), while studies involving chronic stress have demonstrated a decline in
cortisol levels (Miller, Chen, & Ritchey, 2002; Seedat, Stein, Kennedy, & Hauger, 2003), though
not all studies show these patterns (Simpson et al., 2008). Because the perceived stress scale
asks about stress related thoughts and feelings that occurred over the last month, but not about
the duration of the stressor, it is possible that some participants may have been reporting about
chronic stressors while others were reporting about more recent stressors, which may have
affected cortisol levels differently and lead to the above results. In addition, different types of
stressors, such as those involving social threat (Dickerson & Kemeny, 2004), and traumatic
versus non-traumatic threats can affect HPA activity differently (Miller et al., 2007). The type of
stressor is not documented using the perceived stress scale data used in this study, and could not
be taken into account in the analyses.

Other studies attempting to find a relationship between perceived stress and cortisol have
produced non-significant results. Fischer et al. (2000) found nurses and physicians produced
spikes in cortisol that were related to stressful events, but 71.3% of these spikes occurred without
the participant consciously perceiving an increase in psychological stress. If these medical
professionals are not able to consciously perceive they are having a stress response or are not
able to remember having a stress response, it is possible participants in other scenarios, such as
the MIDUS study, may have the same difficulty. Kurina, Schneider, and Waite (2004) found
average cortisol slopes (representing the pattern of cortisol levels throughout the day) and average cortisol levels among their 91 participants were approximately normally distributed. This observation was unexpected, because prior research suggests cortisol levels follow either a normal diurnal pattern, which is characterized by a peak in cortisol levels in the morning followed by a decline throughout the day, or an abnormal pattern in which there is a morning peak and very little decline throughout the day. Cortisol levels examined in this study did not follow a normal distribution, so this could not have affected the results.

The reasons for the lack of an observed relationship between perceived stress and insulin resistance are unknown. It is possible the lack of association is due to the measurement of perceived stress rather than acute stress. Acute stress produces reliable responses, while perceived stress has no known reliable biological indicators (Goldman, Glei, Seplaki, Liu, & Weinstein, 2005). Additionally, the expectation was that perceived stress would result in higher cortisol levels, which would subsequently affect insulin resistance. Previous research shows insulin resistance begins to occur almost immediately after an acute stressor (Kruyt, van Westerloo, & DeVries, 2012; Li et al, 2013). However, the amount of time a person must be exposed to a chronic stressor before insulin resistance becomes more consistently elevated has not been established. Although experiencing stress for a month (as participants reported in the perceived stress scale) is enough time to establish chronic stress is taking place, it may not have been a long enough period of time for insulin resistance to become consistently elevated.

Waist to hip ratio was significantly related to insulin resistance for Type 2 diabetic participants in this study \( (r = .31, p = .001) \), which is not surprising because waist-to-hip ratio is considered a risk factor for insulin resistance (Shakeri-Manesch et al., 2009). Greater insulin resistance increases the risk of developing Type 2 diabetes and diabetic complications, and
increasing insulin resistance can make Type 2 diabetes progressively more difficult to manage (Masuo, Rakugi, Ogiehara, Esler, & Lambert, 2010). This finding illustrates the importance of central adiposity in the development of insulin resistance in those who have Type 2 diabetes.

The strength of this study was that data was collected from community-dwelling participants were collected and analyzed in a controlled environment during an over-night lab stay. Furthermore, this study tested the use of subjective well-being as a moderator for the perceived stress and insulin resistance relationship, which had not been previously examined. Future studies seeking to understand the relationship between perceived stress and cortisol or insulin resistance should collect information about the type and duration of stressors in addition to perceptions about stress.
Table 1

Descriptive Statistics for Continuous Variables

<table>
<thead>
<tr>
<th></th>
<th>Observed Minimum</th>
<th>Observed Maximum</th>
<th>Mean</th>
<th>SD</th>
<th>Skew(SE)</th>
<th>Kurtosis(SE)</th>
<th>Cronbach’s Alpha</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS</td>
<td>1.1</td>
<td>4.4</td>
<td>2.30</td>
<td>0.59</td>
<td>0.44(.23)</td>
<td>.99(.45)</td>
<td>.81</td>
</tr>
<tr>
<td>CES-D</td>
<td>1.3</td>
<td>3.4</td>
<td>1.70</td>
<td>0.36</td>
<td>1.76(.23)</td>
<td>4.36(.45)</td>
<td>.90</td>
</tr>
<tr>
<td>SWS</td>
<td>2.0</td>
<td>6.8</td>
<td>4.99</td>
<td>1.00</td>
<td>-0.93(.23)</td>
<td>0.71(.45)</td>
<td>.84</td>
</tr>
<tr>
<td>PSS and SWS*</td>
<td>1.1</td>
<td>4.2</td>
<td>2.23</td>
<td>0.56</td>
<td>.75(.23)</td>
<td>.83(.45)</td>
<td>.86</td>
</tr>
<tr>
<td>PSS and CES-D*</td>
<td>1.48</td>
<td>4.3</td>
<td>2.18</td>
<td>.46</td>
<td>1.38(.23)</td>
<td>3.79(.45)</td>
<td>.92</td>
</tr>
<tr>
<td>Cortisol</td>
<td>1.6</td>
<td>61.0</td>
<td>13.50</td>
<td>11.82</td>
<td>1.89(.23)</td>
<td>4.08(.45)</td>
<td></td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0.9</td>
<td>16.44</td>
<td>4.93</td>
<td>3.41</td>
<td>1.36 (.23)</td>
<td>1.91 (.45)</td>
<td></td>
</tr>
</tbody>
</table>

Note. PSS = Perceived Stress Scale, SWS = Subjective Well-being Scale, CES-D = Center for Epidemiologic Studies Depression Scale, HOMA-IR = Homeostatic Model Assessment – Insulin Resistance.

* As described in text PSS and SWS combined into a single 5-point scale and PSS and CES-D combined into a single 5-point scale.

Table 2

Correlations of Scale Variables

<table>
<thead>
<tr>
<th></th>
<th>PSS</th>
<th>CES-D</th>
<th>SWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS</td>
<td>(.81)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CES-D Correction for Attenuation</td>
<td>.73**</td>
<td>(.90)</td>
<td></td>
</tr>
<tr>
<td>SWS Correction for Attenuation</td>
<td>-.52**</td>
<td>-.56**</td>
<td>(.84)</td>
</tr>
</tbody>
</table>

**Significant at the 0.01 level (two-tailed)

Note. Items in parentheses are scale reliabilities before correction for attenuation. PSS = Perceived Stress Scale, SWS = Subjective Well-being Scale, CES-D = Center for Epidemiologic Studies Depression Scale
### Table 3

**Independent Samples t-tests comparing Type 2 Diabetic and Non-diabetic Participants**

<table>
<thead>
<tr>
<th></th>
<th>Type 2</th>
<th>Non-diabetic</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td></td>
<td>n</td>
<td>M</td>
<td>SD</td>
<td>n</td>
<td>t</td>
<td>df</td>
<td>Sig</td>
</tr>
<tr>
<td>PSS</td>
<td>2.27</td>
<td>.57</td>
<td>116</td>
<td>2.21</td>
<td>.63</td>
<td>1,096</td>
<td>1.01</td>
<td>1,210</td>
<td>.31</td>
<td>[-.06, .18]</td>
</tr>
<tr>
<td>SWS</td>
<td>5.00</td>
<td>.99</td>
<td>116</td>
<td>5.17</td>
<td>1.06</td>
<td>1,095</td>
<td>-1.74</td>
<td>1,209</td>
<td>.08</td>
<td>[-.38, .02]</td>
</tr>
<tr>
<td>CES-D</td>
<td>1.48</td>
<td>.04</td>
<td>116</td>
<td>1.43</td>
<td>.01</td>
<td>1,097</td>
<td>1.33</td>
<td>1,211</td>
<td>.18</td>
<td>[-.03, .13]</td>
</tr>
<tr>
<td>Cortisol</td>
<td>49.65</td>
<td>2.77</td>
<td>117</td>
<td>49.84</td>
<td>1.05</td>
<td>1,096</td>
<td>-.06</td>
<td>1,211</td>
<td>.95</td>
<td>[-6.75, 6.36]</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>4.89</td>
<td>3.30</td>
<td>114</td>
<td>3.18</td>
<td>3.29</td>
<td>1,084</td>
<td>5.27</td>
<td>1,196</td>
<td>&lt;.001</td>
<td>[1.07, 2.34]</td>
</tr>
<tr>
<td>Waist to hip</td>
<td>.94</td>
<td>.10</td>
<td>117</td>
<td>.89</td>
<td>.10</td>
<td>1,097</td>
<td>5.80</td>
<td>1,212</td>
<td>&lt;.001</td>
<td>[.04, .07]</td>
</tr>
<tr>
<td>Age</td>
<td>57.94</td>
<td>11.75</td>
<td>117</td>
<td>54.11</td>
<td>11.67</td>
<td>1,099</td>
<td>3.37</td>
<td>1,214</td>
<td>.001</td>
<td>[1.60, 6.06]</td>
</tr>
</tbody>
</table>

### Table 4

**Participant Counts and Chi-square Test Comparing Type 2 Diabetic and Non-diabetic Participants on Gender**

<table>
<thead>
<tr>
<th></th>
<th>Type 2 (n = 117)</th>
<th>Non-diabetic (n = 1,099)</th>
<th>Group Difference</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>$\chi^2$(df)</td>
</tr>
<tr>
<td>Male</td>
<td>54</td>
<td>46.2%</td>
<td>471</td>
<td>42.9%</td>
<td>.47(1)</td>
</tr>
<tr>
<td>Female</td>
<td>63</td>
<td>53.8%</td>
<td>628</td>
<td>57.1%</td>
<td></td>
</tr>
</tbody>
</table>
### Table 5

**Predictors of Insulin Resistance Testing the Effects of Perceived Stress with Subjective Well-being as a Moderator**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Model 2&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Model 3&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Model 4&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Model 5&lt;sup&gt;e&lt;/sup&gt;</th>
<th>Model 6&lt;sup&gt;f&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>-1.33 .19</td>
<td>-1.29 .20</td>
<td>-.64 .52</td>
<td>-.70 .49</td>
<td>-.57 .57</td>
<td>-.56 .58</td>
</tr>
<tr>
<td>Waist to Hip</td>
<td>.28 3.05 .003</td>
<td>.27 2.86 .01</td>
<td>.32 2.55 .01</td>
<td>.33 2.64 .01</td>
<td>.31 2.46 .02</td>
<td>.31 2.44 .02</td>
</tr>
<tr>
<td>Medications</td>
<td>.05 .54 .59</td>
<td>.04 .41 .68</td>
<td>.04 .45 .66</td>
<td>.02 .25 .80</td>
<td>.02 .22 .83</td>
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</tr>
<tr>
<td>Gender</td>
<td>.06 .50 .62</td>
<td>.08 .64 .53</td>
<td>.07 .57 .57</td>
<td>.07 .56 .58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-.16 -1.68 .10</td>
<td>-.18 -1.85 .07</td>
<td>-.17 -1.78 .08</td>
<td>-.17 -1.81 .07</td>
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<td></td>
</tr>
<tr>
<td>SWS</td>
<td>.08 .87 .39</td>
<td></td>
<td>.02 .17 .87</td>
<td>.04 .32 .74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSS</td>
<td></td>
<td>-.11 -1.04 .30</td>
<td>-.13 -1.14 .26</td>
<td>-.07 -.69 .49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSS×SWS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R&lt;sup&gt;2&lt;/sup&gt;</td>
<td>.076</td>
<td>.078</td>
<td>.11</td>
<td>.11</td>
<td>.12</td>
<td>.13</td>
</tr>
<tr>
<td>F</td>
<td>9.29</td>
<td>4.76</td>
<td>3.29</td>
<td>2.77</td>
<td>2.50</td>
<td>2.20</td>
</tr>
<tr>
<td>ΔR&lt;sup&gt;2&lt;/sup&gt;</td>
<td>.076</td>
<td>.002</td>
<td>.028</td>
<td>.006</td>
<td>.009</td>
<td>.004</td>
</tr>
<tr>
<td>ΔF</td>
<td>9.29</td>
<td>.289</td>
<td>1.75</td>
<td>.756</td>
<td>1.09</td>
<td>.480</td>
</tr>
</tbody>
</table>

<sup>a</sup>Predictors: waist to hip ratio.
<sup>b</sup>Predictors: waist to hip ratio, diabetic medications.
<sup>c</sup>Predictors: waist to hip ratio, diabetic medications, age, gender.
<sup>d</sup>Predictors: waist to hip ratio, diabetic medications, age, gender, centered SWS.
<sup>e</sup>Predictors: waist to hip ratio, diabetic medications, age, gender, centered SWS, centered PSS.
<sup>f</sup>Predictors: waist to hip ratio, diabetic medications, age, gender, centered SWS, centered PSS, PSS×SWS cross-product.

Note. PSS = Perceived Stress Scale, SWS = Subjective Well-being Scale.
Table 6

Predictors of Insulin Resistance Testing the Effects of Composite Perceived Stress and Subjective Well-being Variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Model 2&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Model 3&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Model 4&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>-1.33 .19</td>
<td>-1.29 .19</td>
<td>-.64 .52</td>
<td>-.33 .74</td>
</tr>
<tr>
<td>Waist to Hip</td>
<td>.28 3.05 .003</td>
<td>.27 2.86 .01</td>
<td>.32 2.55 .01</td>
<td>.33 2.61 .01</td>
</tr>
<tr>
<td>Medications</td>
<td>.05 .54 .59</td>
<td>.04 .41 .68</td>
<td>.04 .35 .73</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>.06 .50 .62</td>
<td></td>
<td>.08 .65 .52</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-.16 -1.68 .10</td>
<td>-.18 -1.90 .06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSS and SWS</td>
<td></td>
<td>-.12 -1.28 .20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$R^2$</td>
<td>.076</td>
<td>.078</td>
<td>.107</td>
<td>.08</td>
</tr>
<tr>
<td>$F$</td>
<td>9.28</td>
<td>4.76</td>
<td>3.29</td>
<td>2.97</td>
</tr>
<tr>
<td>$\Delta R^2$</td>
<td>.076</td>
<td>.002</td>
<td>.028</td>
<td>.013</td>
</tr>
<tr>
<td>$\Delta F$</td>
<td>9.28</td>
<td>.289</td>
<td>1.73</td>
<td>1.64</td>
</tr>
</tbody>
</table>

<sup>a</sup>Predictors: waist to hip ratio.

<sup>b</sup>Predictors: waist to hip ratio, diabetic medications.

<sup>c</sup>Predictors: waist to hip ratio, diabetic medications, age, gender.

<sup>d</sup>Predictors: waist to hip ratio, diabetic medications, age, gender, PSS/SWS combined variable.

Note. PSS = Perceived Stress Scale, SWS = Subjective Well-being Scale.
Table 7

Predictors of Insulin Resistance Testing the Effects of Perceived Stress with Depression as a Moderator

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Model 2&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Model 3&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Model 4&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Model 5&lt;sup&gt;e&lt;/sup&gt;</th>
<th>Model 6&lt;sup&gt;f&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>t</td>
<td>Sig</td>
<td>B</td>
<td>t</td>
<td>Sig</td>
</tr>
<tr>
<td>(Constant)</td>
<td>-1.33</td>
<td>.19</td>
<td>.19</td>
<td>-1.29</td>
<td>.20</td>
<td>.19</td>
</tr>
<tr>
<td>Waist to Hip</td>
<td>.27</td>
<td>2.86</td>
<td>.01</td>
<td>.27</td>
<td>2.86</td>
<td>.01</td>
</tr>
<tr>
<td>Medications</td>
<td>.04</td>
<td>.41</td>
<td>.68</td>
<td>.04</td>
<td>.41</td>
<td>.68</td>
</tr>
<tr>
<td>Gender</td>
<td>.06</td>
<td>.50</td>
<td>.62</td>
<td>.06</td>
<td>.50</td>
<td>.62</td>
</tr>
<tr>
<td>Age</td>
<td>-.16</td>
<td>-1.68</td>
<td>.10</td>
<td>-.16</td>
<td>-1.67</td>
<td>.10</td>
</tr>
<tr>
<td>CES-D</td>
<td>-.16</td>
<td>-1.68</td>
<td>.10</td>
<td>-.16</td>
<td>-1.67</td>
<td>.10</td>
</tr>
<tr>
<td>PSS</td>
<td>-.25</td>
<td>-1.88</td>
<td>.06</td>
<td>-.25</td>
<td>-1.88</td>
<td>.06</td>
</tr>
<tr>
<td>PSS×CES-D</td>
<td>.01</td>
<td>.07</td>
<td>.94</td>
<td>.01</td>
<td>.07</td>
<td>.94</td>
</tr>
<tr>
<td>$R^2$</td>
<td>.076</td>
<td>.078</td>
<td>.107</td>
<td>.107</td>
<td>.135</td>
<td>.135</td>
</tr>
<tr>
<td>$F$</td>
<td>9.29</td>
<td>4.76</td>
<td>3.29</td>
<td>2.61</td>
<td>2.81</td>
<td>2.39</td>
</tr>
<tr>
<td>$\Delta R^2$</td>
<td>.076</td>
<td>.002</td>
<td>.028</td>
<td>.000</td>
<td>.028</td>
<td>.000</td>
</tr>
<tr>
<td>$\Delta F$</td>
<td>9.29</td>
<td>.289</td>
<td>1.75</td>
<td>.003</td>
<td>3.53</td>
<td>.005</td>
</tr>
</tbody>
</table>

<sup>a</sup>Predictors: waist to hip ratio.
<sup>b</sup>Predictors: waist to hip ratio, diabetic medications.
<sup>c</sup>Predictors: waist to hip ratio, diabetic medications, gender, age.
<sup>d</sup>Predictors: waist to hip ratio, diabetic medications, gender, age, CES-D.
<sup>e</sup>Predictors: waist to hip ratio, diabetic medications, gender, age, CES-D.
<sup>f</sup>Predictors: waist to hip ratio, diabetic medications, gender, age, CES-D, PSS, PSS×CES-D cross-product.

Note. PSS = Perceived Stress Scale, CES-D = Center for Epidemiologic Studies Depression Scale.
Table 8

**Predictors of Insulin Resistance Testing the Effects of Composite Perceived Stress and Depression Variable**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Model 2&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Model 3&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Model 4&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>-1.33 .19</td>
<td>-1.29 .20</td>
<td>-.64 .52</td>
<td>-.51 .62</td>
</tr>
<tr>
<td>Waist to Hip Ratio</td>
<td>.28 3.05 .003</td>
<td>.27 2.86 .01</td>
<td>.32 2.55 .01</td>
<td>.32 2.54 .01</td>
</tr>
<tr>
<td>Diabetic Medications</td>
<td>.05 .54 .59</td>
<td>.04 .41 .68</td>
<td>.04 .39 .70</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>.06 .50 .62</td>
<td>.07 .54 .59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.16 -1.68 .10</td>
<td>.16 -1.72 .09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSS/CES-D Combined</td>
<td></td>
<td></td>
<td>-.05 -.53 .60</td>
<td></td>
</tr>
<tr>
<td>$R^2$</td>
<td>.076 .078</td>
<td>.107 .109</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$F$</td>
<td>9.28 4.76</td>
<td>3.29 2.67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\Delta R^2$</td>
<td>.076 .002</td>
<td>.028 .002</td>
<td></td>
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<tr>
<td>$\Delta F$</td>
<td>9.28 .289</td>
<td>1.74 .279</td>
<td></td>
<td></td>
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</tbody>
</table>

<sup>a</sup>Predictor: waist to hip ratio.
<sup>b</sup>Predictors: waist to hip ratio, diabetic medications.
<sup>c</sup>Predictors: waist to hip ratio, diabetic medications, gender, age.
<sup>d</sup>Predictors: waist to hip ratio, diabetic medications, gender, age, PSS/CES-D combined variable.

Note. PSS = Perceived Stress Scale, CES-D = Center for Epidemiologic Studies Depression Scale.
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