Association of sleep and inflammation in law enforcement

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ABSTRACT

The law enforcement profession has been associated with an increased risk for cardiovascular diseases (CVD), but the mechanisms are unclear. Previous research suggests a mechanism other than traditional CVD risk factors may be an underlying cause. Sleep health has been reported as an issue among LEO. Poor sleep health has been associated with increased CVD risk. Sleep disorders have been shown to increase biomarkers of inflammation. CVD is increasingly being recognized as an inflammatory disease. We sought to further investigate this issue by evaluating the sleep health, CVD risk, mental health, and inflammatory biomarkers of 133 LEO in the Iowa Department of Public Safety to determine if inflammation and sleep play a role in the occupational CVD risk in LEO.

Officers were divided into three groups based on their sleep health (GOOD, BRDL, POOR). POOR reported significantly higher shiftwork disorder ($P < 0.05$) than GOOD or BRDL. POOR also had significantly higher depression (Center for Epidemiology Studies Depression Scale), life stress (Perceived Stress Scale), and occupational stress scores (Operational and Organizational Police Stress Questionnaires) ($P < 0.05$). No significant differences were found in inflammatory biomarkers or traditional CVD risk factors between GOOD, BRDL, or POOR. In conclusion, sleep disorders may contribute to unfavorable mental health disorders and predispose LEO to negative long-term health consequences including depression and neurodegenerative diseases.

CHAPTER ONE: INTRODUCTION

Law enforcement officers (LEO) present a unique challenge for cardiovascular researchers. Several studies have found the law enforcement profession to be associated with higher rates of cardiovascular disease (CVD) morbidity and mortality (Calvert et al, 1999, Dubrow et al, 1988; Sardinas et al, 1986; Franke et al, 1998). Researchers have attempted to explain the high risk of CVD morbidity and mortality in LEO by attributing a high prevalence of conventional CVD risk factors such as tobacco use, physical inactivity, hypertension, hypercholesterolemia, hyperglycemia, and obesity (Williams et al, 1987; Franke et al, 1997; Richmond et al, 1998). The high incidence of CVD risk in LEO could be a reflection of the general U.S. population (Go et al, 2013). In a cross-sectional study, Franke and colleagues (1998) examined CVD morbidity and mortality and traditional CVD risk factors among a cohort of retired police officers compared to the general U.S. population. LEO were found to have a high incidence of traditional CVD risk factors. However, when controlling for these traditional risk factors, Franke and coworkers found the law enforcement profession itself to have an odds ratio of 2.34 (95% CI = 1.5-3.6).

With a large body of evidence suggesting high CVD morbidity and mortality among LEO, identifying the underlying mechanism becomes the issue. As mentioned previously, a number of studies have found LEO to have elevations of traditional CVD risk factors (Williams et al, 1987; Franke et al, 1997; Richmond et al, 1998). However, according to the Heart Disease and Stroke statistics from the American Heart Association (2013), a large number of the general population has these common CVD risk factors also. Thus, the increased CVD morbidity and mortality in LEO cannot be fully explained by traditional CVD risk factors. Furthermore,

traditional risk factors also do not explain the association between CVD risk and duration of law-enforcement employment (Ramey et al, 2011).

Recent studies have recognized CVD as an inflammatory disease, as several inflammatory biomarkers play a role in atherogenesis (Ridker, 2004; Koenig, 1999; Pai et al, 2004). Studies have linked several inflammatory biomarkers with CVD. C-reactive protein (CRP), a marker of inflammation, has been linked with CVD in several studies (Pai et al, 2004; Ridker et al 2000; Koenig et al 1999; Wang et al, 2006). Interleukins such as TNF-α, IL-β, IL-6 have also been associated with CVD (Pai et al 2004, Ridker et al, 2000). Obesity, smoking, and physical activity have been linked to higher levels of inflammatory mediators (Ridker, 2004).

Shiftwork refers to rotating, varied s work hours, or working at constant, unusual hours such as afternoon or night shifts. Varied scheduling can cause disruptions in circadian rhythm, fatigue, and sleep disturbances (Aschoff et al, 1975; Knutsson, 2003). In addition, Blom's lab (2011) found short sleep duration (< 6 hours) and poor sleep quality to be associated with higher incidence of CVD and coronary heart disease (CHD). Studies suggest sleep deprivation causes increased stimulation of the autonomic nervous system and increased catecholamine levels which can lead to the production of inflammatory mediators (Mullington, 2009). Sleep deprivation has also been associated with elevated blood pressure, increasing the stress on the endothelial layer of blood vessels. The increased sheer stress on the endothelial layer of blood vessels can lead to the production of inflammatory mediators such as IL-6 and adhesion molecules (Mullington, 2009). Hoevenaar-Blom and colleauges (2011) found short sleep duration (< 6 hrs) and poor sleep quality to be associated with higher incidence of CVD and coronary heart disease (CHD). Clinical studies have shown sleep restriction to stimulate the

gene expression and molecular signaling of the inflammatory pathway and increase systemic circulation of inflammatory biomarkers (Irwin et al, 2006; Irwin et al, 2008; van Leeuwen et al, 2009).

The total number of studies examining the relationship between shiftwork, sleep quality or duration, and inflammatory mediators are relatively sparse. The results of the literature are inconclusive as some studies suggest a relationship between shiftwork and elevated inflammatory mediators (Sookoian et al, 2007; Okun et al, 2009; Nishitani et al 2007), while other studies found no association between shiftwork and elevated inflammatory mediators (Taheri et al, 2007; Dowd et al, 2011). Further research is needed to better understand the association between shiftwork and inflammatory mediators.

Shiftwork schedules are common among LEO, leaving officers susceptible to sleep disorders. Other studies have found associations between short sleep duration and poor sleep quality to be associated with health issues among LEO, but levels of inflammatory biomarkers were not measured in these studies (Yoo et al, 2013; Violanti et al, 2009). Franke's study (2010) attempted to link elevated inflammatory mediators and stress in a cohort of LEO. They found inflammatory mediators to be elevated in LEO compared to the general population. However, work-related stress was not strongly associated with elevated levels of inflammatory mediators. Interestingly, 77% of LEO reported working shiftwork or irregular work hours compared to 27% in the general population, but sleep health was not assessed in this study (Franke et al, 2010). The findings from Franke and coworkers (2010) suggest a need for a study examining the relationship between shiftwork, inflammatory mediators, and LEO. The purpose of the current study is to compare levels of inflammation between LEO with good, borderline, and poor sleep

hygiene. It is also of interest if poor sleep hygiene is associated with shiftwork disorder. It is hypothesized that after controlling for all confounding variables, LEO with poor sleep hygiene will have elevated systemic inflammation when compared with LEO with good sleep hygiene will exist . Furthermore, we want to see if there is a significant difference in traditional CVD risk factors in officers with good and bad sleep hygiene.

CHAPTER TWO: REVIEW OF LITERATURE

Prevalence of CVD in Law Enforcement Officers

Law enforcement officers (LEO) are a unique population at risk for CVD. Calvert and colleagues (1999) examined the relationship between occupation and mortality from ischemic heart disease in 16 to 60 year old males. Calvert and colleagues (1999) used the National Occupational Mortality Surveillance system to conduct proportional mortality ratios as a means to examine the relationship between occupation and ischemic heart disease mortality. LEO were among the highest proportional mortality ratios with sheriffs at 1.26 (95% CI = 1.11-1.43), correctional officers at 1.21 (95% CI = 1.07-1.36), and 1.14 (95% CI = 1.06-1.21) for police and detectives. A study conducted by Dubrow and colleagues (1988) also supports the notion that police officers are more at risk for mortality from CVD. In this study, Dubrow's lab examined death certificates from 1968 to 1978 in Rhode Island and Utah. Mortality of ischemic heart disease was divided into two sub-categories: acute myocardial infarction and other ischemic heart disease. LEO risk for mortality from an acute myocardial infarction was significantly elevated in both Rhode Island and Utah ($P<0.05$). Risk of other ischemic heart disease in both Rhode Island and Utah was also significantly elevated for LEO ($P< 0.05$). Sardinas and coworkers (1986) conducted another study which supports the higher relationship of CVD and LEO. In this study, Sardinas and colleagues used death certificate data from 1960-1978 to calculate mortality odds ratios in firemen and police officers from ischemic heart disease. Police officers were found to have ischemic heart disease prevalance higher than their firefighting counterparts.

Other studies suggest LEO have a similar mortality rate as the general U.S. public. In one study, Feuer and colleagues (1986) constructed proportionate mortality ratios for LEO and firefighters in New Jersey. Neither LEO nor firefighters differed significantly from the New Jersey population. However, working police were found to have a significantly higher proportional mortality rate from heart disease, whereas retired police were not. The findings by Feuer's lab were supported by Demers and colleagues (1992) in a study comparing the mortality ratios in firefighters and police officers. LEO were found to have a standardized mortality ratio of 0.87 (95% CI = 0.81-0.93) when compared to the U.S. white male population from all-causes and a standardized mortality ratio of 0.85 (95% CI = 0.75-0.96) from heart disease (Feuer et al, 1992). Vena et al (1986) also found LEO to have a similar CVD mortality risk compared to the general U.S. population. However, risk of mortality from CVD tended to increase with increased number of years employed.

Mortality may not tell the whole story when it comes to CVD prevalence in LEO. Mortality from CVD is decreasing in the United States, and assessing CVD prevalence by using a mortality ratio method may underestimate the relationship of CVD prevalence in LEO. CVD morbidity has been used as a method of examining CVD incidence in LEO. In the Normative Aging Study, a longitudinal study starting in 1963, Sparrow et al (1983) followed both LEO and non-LEO for a period of 10 years. Both groups were CVD free at the beginning of the study. Sparrow and colleagues found police to have a coronary heart disease risk ratio of 1.40 (95% CI = 0.7-2.4), but this number was not statistically significant from the non-LEO group – even after being adjusted for additional factors such as age, cholesterol, smoking, and blood pressure still no significant differences were found. On the contrary, Franke and colleagues (1998) reported

higher CVD morbidity in LEO than in the general population. In this study, Franke's used self-report methods with a cohort of 232 retired LEO (age ≥ 55) and a sample of the general population of Iowa (n = 817) to compare incidence of CVD and traditional risk factors of CVD. LEO were found to have a higher CVD morbidity compared to the general population ($P < 0.001$). Ramey and colleagues (2009) provided further evidence for high CVD morbidity in LEO. In this study, Ramey and colleagues assessed CVD risk in a sample of retired officers from the Milwaukee police department compared to a sample from the general population. The Milwaukee LEO had an increased prevalence of several CVD risk factors compared to the control group (CVD 15.2% vs. 9.5%, $p = .036$; hypertension 51.5% vs. 36.2%, $p = .001$; hypercholesterolemia 62.4% vs. 44.4%, $p = .001$; overweight and obesity 85.1% vs. 74.7%, $p = .005$). Working in the law enforcement profession was found to have a CVD prevalence odds ratio of 1.70 (95% CI = 1.03-2.79). These results suggest a strong association between the law enforcement profession and CVD morbidity (Ramey et al, 2009).

A primary issue in studying CVD morbidity and mortality in LEO is a phenomenon known as the "Healthy Worker Effect." The "Healthy Worker Effect" is a concept in which employees who are too unhealthy to work would not contribute to the data. This would allow only healthier employees to be studied. For example, if a large number of LEO are forced to change profession or retire at an early age due to increased CVD risk, those employees would not be included in studies examining the health of LEO. Healthy, often younger employees who have not developed any serious health complications are more likely to be surveyed. Surveying a large cohort of healthier employees could skew the results of these studies, diminishing the true morbidity and mortality ratio of CVD in LEO (Franke et al, 2002).

As can be seen, CVD prevalence has been examined in several studies. There are several studies suggesting increased CVD morbidity and mortality in LEO (1962; Calvert et al, 1999, Dubrow et al, 1988; Sardinas et al, 1986; Franke et al, 1998, Ramey et al, 2009)) and studies which suggest CVD morbidity and mortality to be similar in LEO compared to the general population (Feuer et al, 1986; Demers et al, 1992; Vena et al, 1986; Sparrow, 1963). Despite some conflicting literature, it is generally accepted that there is a relationship of increased CVD prevalence among LEO.

Conventional CVD Risk Factors and LEO

As mentioned previously, several studies have established a correlation between CVD and LEO. Studies have found LEO to have increased CVD risk factors such as physical inactivity, hypertension, hypercholesterolemia, smoking, hyperinsulinemia and obesity (Williams et al, 1987; Franke et al, 1997; Richmond et al, 1998). Pollack et al (1978) found middle-aged police officers to be of lower physical fitness levels than age-based norms. The American Heart Association (2013) has shown that a large percentage of the U.S. population has these risk factors; in which case the prevalence of CVD in LEO may just be a reflection of the general population.

Despite the prevalence of traditional CVD risk factors in LEO, these factors may not fully explain the relationship between CVD and LEO. Franke and colleagues (1998) attempted to answer this question in a study examining CVD morbidity and mortality and traditional CVD risk factors in retired LEO compared to the general population in Iowa. As mentioned previously, LEO in this study were found to have a higher CVD morbidity compared to the general

population. Franke's lab found the LEO to have a high incidence of traditional CVD risk factors such as hypercholesterolemia (OR = 2.37; 95% CI = 1.7-3.3); diabetes (OR = 2.22; 95% CI = 1.4-3.6), hypertension (OR = 1.79; 95% CI = 1.3-2.5), tobacco use (OR = 1.67; 95% CI = 1.07-2.6), and age (OR = 1.06; 95% CI = 1.03-1.08). However, when controlling for these traditional risk factors, Franke and colleagues found the law enforcement profession to have an odds ratio of 2.34 (95% CI = 1.5-3.6). This study supports the notion that there is some sort of "unconventional" mechanism contributing to CVD in LEO.

Stress is a non-traditional risk factor which may be a contributor to CVD. The law-enforcement profession has been subjectively viewed as a high-stress occupation. Franke's study (2002) tried to provide insight into the relationship between stress and CVD in the law-enforcement profession. In this study, Franke and coworkers surveyed CVD risk by using the Behavioral Risk Factor Surveillance System (BRFSS) and also perceived job stress using the Perceived Stress Scale (PSS) in a cohort of Iowa police officers compared with the general population. A sample of 2818 LEO responded to the survey along with 1791 subjects in the general population. Interestingly, this study found no significant difference between the general population and LEO in overall CVD prevalence. This lack of a significant difference in CVD was attributed to the previously mentioned "Healthy Worker Effect." However, when evaluating LEO alone, the profession was associated with elevated levels of perceived stress ($P < 0.05$). Perceived stress was affected by duration of time in profession ($P = 0.004$) independent of age. A similar study conducted by Ramey and coworkers (2009) found the law enforcement profession to be an independent CVD risk factor. In this study, Ramey et al surveyed retired LEO and a sample of the general population using the BRFSS. LEO retirees

were found to be 70% more likely to develop CVD than the general population cohort. The LEO in this study had an increased prevalence of conventional risk factors such as hypertension, cholesterol, physical inactivity, diabetes, and hypercholesterolemia. However, when controlling for these risk factors the law enforcement profession itself had an odds ratio of 1.70 (95% CI = 1.03-2.79). Perceived levels of stress were not measured in this study, but based on similar literature Ramey and colleagues believed job-related stress was a likely cause for such a high odds ratio of CVD in the law enforcement profession (Ramey et al, 2009).

The evidence associating stress and CVD in LEO is inconclusive. Franke's lab attempted to answer this question in a study conducted in 2010. Franke and co-workers measured traditional CVD risk factors, inflammatory mediators, and stress measures including perceived stress, job strain, vital exhaustion and effort reward imbalance in a sample of 466 LEO compared with 171 participants from the general population. LEO and the general population did not differ significantly in CVD from traditional risk factors, nor was there a difference in 10-year CVD risk from the Framingham Risk Score. LEO did show significantly increased levels of inflammatory mediators compared to the general population. However, this increase in inflammatory mediators could not be attributed to stress. The control group actually showed significantly higher levels of perceived stress, job strain, and vital exhaustion compared to the LEO in this study ($P < 0.05$). LEO did show increased stress from effort-reward imbalance. Franke and colleagues concluded stress was not the mechanism contributing to CVD in LEO in this study, as many professions other than law enforcement also have stressors.

As mentioned previously, there is much evidence to support a correlation between the law enforcement profession and CVD. Conventional risk factors such as obesity,

hypercholesterolemia, hyperinsulinemia, physical inactivity, and hypertension have been blamed for this (Williams et al, 1987; Franke et al, 1997; Richmond et al, 1998, Pollack, 1978). However, law enforcement as a profession has been associated as a risk factor after controlling for traditional risk factors (Franke et al, 1998). Researchers have attempted to link work-related stress to CVD in LEO, but the results are inconclusive at best (Franke et al, 2002; Ramey et al, 2009, Franke et al, 2010). Franke's lab(2010) found inflammatory mediators to be elevated in LEO compared to the general population, which brings up the next point: is there a relationship between inflammatory mediators and CVD in LEO?

Inflammatory Mediators and CVD

In the aforementioned study by Franke and colleagues (2010), inflammatory mediators were measured in LEO and found to be elevated in this population. These findings are important, as CVD is increasingly being recognized as an inflammatory disease.

Atherosclerosis is a progressive disease occurring from the process of hardening or thickening of artery walls due to accumulation of fatty plaques. Atherosclerosis is a response to chronic injury occurring to the arterial wall. Smoking, hypertension, diabetes, and genetic alterations are common sources of these injuries to the arterial wall. When an injury occurs to the arterial walls, monocytes and T-lymphocytes are attracted to the endothelial cells of the intima at the site of the injury. Monocytes mature into macrophages and ingest local lipids, eventually becoming foam cells. These foam cells often migrate into the media layer of the blood vessel where they can accumulate smooth muscle cells (SMCs). The SMCs secrete fibrous elements causing these plaques to become fibrous and grow in size towards the adventitia

which can lead to an expansion of the blood vessel known as “remodeling.” Eventually, the growth outward reaches a critical point and the growth expands inward narrowing the lumen. These plaque expansions have a fibrous cap made up of SMCs. The plaques can eventually become calcified, permanently narrowing the lumen and reducing or restricting blood flow; however, the real danger is a rupture of the fibrous caps causing the formation of a thrombus or clot and eventually a myocardial infarction (MI) or stroke. The formation of fibrous lesions have been found to occur even in the first decade of life and are not always fatal, but the chronic accumulation can lead to MI or stroke (Lusis, 2000; Ross, 1993).

More recently, researchers have come to recognize CVD as an inflammatory disease in which inflammatory mediators play a vital role. Increased inflammatory mediators have been associated with the process of atherosclerosis, MI, and stroke (Pai et al, 2004). The stress and accumulation of lipids from atherosclerosis have been found to increase expression of adhesion molecules and inflammatory genes in the endothelial cells (Hansson, 2005). T-cells and macrophages accumulated during injuries to the endothelial layer of blood vessels promote activation of inflammatory mediators, most notably interleukins (IL-1β, IL-4, IL-6, TNF-α) and C - reactive protein (CRP). These inflammatory mediators contribute to the inflammatory process and can promote the atherosclerotic process (Sarwar et al, 2009). In addition, inflammatory mediators are believed to contribute to atherothrombosis (Ridker, 2004).

CRP, produced in smooth muscle cells, is one of the most prominent of the inflammatory mediators. Studies have shown CRP to directly affect gene expression of adhesion molecules, which contributes to the attraction and binding of leukocytes occurring during the early stages of atherosclerotic plaque accumulation. CRP can also affect fibrinolysis

and alter endothelial dysfunction. Studies suggest CRP to be a predictor of MI, stroke, and sudden cardiac death (Ridker, 2004; Koenig, 1999; Pai et al, 2004).

Pai and coworkers (2004) conducted a study involving a large cohort of registered female nurses with a baseline age range of 30-55 and a large cohort of male health professionals with a baseline age range of 40-75, all of whom were free from any CVD at the baseline. Subjects provided a baseline blood sample from 1989-1995. The sample included 239 women and 265 men who had a non-fatal MI or fatal CVD. The blood samples of those who developed CHD were compared to a control group and measured for a number of inflammatory mediators. Both men and women who developed CHD had significantly higher levels of CRP and IL-6 at baseline, even when controlling for other conventional risk factors (Pai et al, 2004). The results in this study are similar to findings in several other studies (Ridker et al 2000; Koenig et al 1999; Wang et al, 2006).

IL-6 is another interleukin found to be associated with CVD risk. IL-1β and TNF-α can stimulate the production of IL-6 from endothelial cells and smooth muscle cells of the vascular wall. IL-6 is also a stimulant for CRP production (Hansson, 2001). A study by Ridker and colleagues (2000) found an association between CVD and IL-6. Blood samples were collected from 202 apparently healthy male subjects (ages 40-84) at baseline and following a CVD event. The subjects were paired with control subjects showing no CVD. Quartiles of higher and lower elevations of IL-6 were compared at baseline. Subjects in the highest quartile had a 2.3 times greater risk for CVD; evidence supporting IL-6 as a possible indicator for CVD (Ridker et al, 2000). Obesity, smoking, and physical inactivity have been attributed to higher levels of inflammatory mediators, particularly CRP (Ridker, 2004). Along with the aforementioned

potential causes of inflammation, sleep health has been suggested to profoundly impact on many aspects of health, including increased systemic inflammation. This last point brings the need to further elaborate the relationship between sleep and inflammation.

Sleep, Health, and Inflammation

Sleep is well-established as one of the most crucial life-processes. Sleep plays a critical role in brain health and cellular repair. "Restorative sleep" is a term that health professionals attribute to sleep of adequate duration and quality to allow these important processes to take place. Individuals lacking restorative sleep show functional declines in processes such as memory and cognition. Lack of "restorative sleep" is associated with many negative pathophysiological health consequences including hypertension, obesity, diabetes mellitus, dyslipidemia, CVD and overall mortality risk. It is interesting to note the integrative nature of biological processes, as hypertension, obesity, dyslipidemia and diabetes mellitus are all well-established risk factors for CVD and are found on individuals with chronic sleep issues. In additional to traditional CVD risk factors, sleep deprivation also decreases immunity, and immune function is a mechanism of interest specific to this study (Aldabal et al, 2011).

One study demonstrated the acute sleep-restriction can lead to increased systemic inflammation. In 2009, van Leeuwen and colleagues demonstrated this in 19 male subjects with healthy, regular sleep habits. In this study, the participants were divided into two groups: a control group sleeping for eight hours each night and an experimental group in which sleep was restricted. The control group kept sleeping for eight hours per night throughout the duration of the study, and the experimental group slept for eight hours for the first two nights

followed by five nights in which they were restricted to four hours of sleep and again with two nights of eight-hour recovery sleep. Heart rate, CRP, IL-6, IL-β, and IL-17 were all significantly increased in the sleep-restricted subjects (van Leeuwen et al, 2009).

Irwin's lab (2006) reported similar findings in another study examining sleep and inflammation. In this study, 30 healthy volunteers performed three nights of baseline measures in which the subjects slept for eight hours uninterrupted from 11:00 p.m. to 7 a.m. After baseline, subjects underwent one night of sleep disruption in which their sleep was restricted from 3:00 a.m. to 7:00 a.m. Cytokine measures were taking during the baseline and sleep-disrupted periods. Following the sleep disruption, Irwin and colleagues reported significant increases in IL-6 and TNF-α. Significant increases in IL-6 messenger RNA (mRNA) and TNF-α mRNA were also reported indicating that inflammatory production may have been increased at the genomic level as a result of the sleep-restriction. A similar study by Irwin and colleagues (2008) examined the effects of sleep disruption on the levels of nuclear factor kβ (NF-kβ). NF-kβ is a transcriptional factor which has been found to play a critical role in the molecular signaling of inflammatory gene expression. Thirty healthy-sleeping subjects slept for eight hours per night for two weeks followed by one night in which their sleep was restricted from 11:00 p.m. to 3:00 a.m. The overall sample demonstrated a significant increase in NF-kβ levels following the restricted sleep protocol. Interestingly, only the female samples demonstrated a significant increase in NF-kβ when the data was cross-analyzed by sex. Nevertheless, increased molecular signaling of the inflammatory pathway during sleep deprivation may play a role increased inflammation in poor sleep patterns (Irwin et al, 2008).

Inflammatory mediators in response to shiftwork

The previous section highlighted studies that suggest poor sleep quality and duration may impact systemic inflammation. Less understood is the relationship between working shiftwork schedules and inflammation. Shiftwork refers to rotating, varied schedule work hours, or working at constant, unusual hours such as afternoon or night shifts. For example, an employee with a shiftwork schedule may work four work days, followed by four work nights, three rest days, two work nights, three rest days, four work nights and etc. This varied scheduling can cause disruptions in circadian rhythm, fatigue, and sleep disturbances (Aschoff et al, 1975; Knutsson, 2003). Furthermore, shiftwork schedules are common among LEO. There is some evidence to support shiftwork to show increased risk of CVD, as well as increased levels of inflammatory mediators.

Studies suggest sleep deprivation can cause increase stimulation of the autonomic nervous system and increased catecholamines which can lead to the production of inflammatory mediators. Sleep deprivation has also been associated with elevated blood pressure, increasing the stress on the endothelial layer of blood vessels and thus resulting in the production of inflammatory mediators such as IL-6 and adhesion molecules (Mullington, 2009). King's team of scientists (2009) used computerized tomography to determine coronary artery calcification over a 5-year period with a cohort of subjects. Longer sleep duration was associated with less coronary artery calcification. King and coworkers suggested inflammatory mediators to be a mechanism of coronary artery calcification in this study as well, although no measures of inflammatory mediators were taken.

Hoevenaar-Blom's lab (2011) examined sleep duration and sleep quality with a cohort of 20,432 Dutch men and women with no CVD at baseline. During 10-15 years of follow-up, 1,486 CVD and 1,148 CHD events occurred. Subjects with the shortest sleep duration (≤ 6 hours) had a higher incidence of CVD (HR: 1.15; 95%CI: 1.00-1.32) and CHD (HR: 1.23; 95% CI: 1.04-1.45) compared to normal sleepers (≥ 7 hours). Furthermore, short sleepers with poor sleep quality had an even higher prevalence of CVD (OR: 1.63; 95% CI: 1.21-2.19) and CHD (OR: 1.79; 95% CI: 1.24-2.58) compared with normal sleepers with good sleep quality, even after adjusting for common CVD risk factors. In a meta-analysis, Cappuccio and colleagues (2011) suggested a relationship between sleep duration and heart disease. Cappuccio and colleagues analyzed 15 studies and found short duration of sleep associated with a greater risk of developing or dying of CHD (OR 1.48, 95% CI 1.22–1.80, $P < 0.0001$).

The literature relating bioinflammatory markers to sleep and, more specifically, shiftwork have yielded mixed results. Sookoian and colleagues (2007) investigated the impact of shiftwork on biomarkers of inflammation. In this study, 877 day workers and 474 rotating shiftworkers participated in health examinations assessing conventional CVD risk factors such as cholesterol, triglycerides, BMI, and waist to hip circumference and also leucocyte count. The rotating shift workers were found to have elevated cholesterol, triglycerides, BMI, and waist to hip ratio. Shift workers also showed an elevated leucocyte count even after controlling for the other CVD risk factors. In another study, Okun and coworkers (2009) found poor sleep quality to be associated with increased CRP in women (age 28±5.2) years when measuring inflammatory mediators and sleep quality via the Pittsburg Sleep Quality Index (PSQI). However, there was not a strong association between IL-6 or TNF-α levels and poor sleep

quality. Nishitani and co-workers also found results to support inflammatory response in shiftworkers in another study (2007). In this study, a cohort of 208 factory workers were assessed on a number of factors including smoking, poor sleep, shift work, age, BMI, exercise, sleeping hours, and overtime work and the effect on white blood cell count (WBC). Nishitani et al (2007) found shift workers to have higher WBC compared to daytime workers. Smoking, poor sleep, BMI and age were independent risk factors. Shiftwork itself was not an independent risk factor. However, shiftworkers demonstrated higher complaints of poor sleep quality (Nishitani et al, 2007).

Other studies have found shiftwork to be unassociated with inflammatory mediators. Taheri and coworkers (2007) found no association between CRP levels and sleep duration or sleep disordered breathing. One weakness to this study is that only sleep duration and sleep disordered breathing was measured, but sleep quality was not taken into account. Dowd and colleagues (2011) examined the relationship between inflammatory mediators, sleep duration, and sleep quality in a survey of Taiwainese adults. The subjects were assessed via the PSQI, and blood samples were taken in a fasting state to examine inflammatory biomarkers including CRP, IL-6, fibrinogen, and WBC. Dowd et al (2011) found no association between inflammatory biomarkers and sleep quality. Short sleep duration was also unassociated with inflammatory biomarkers. Oddly, longer sleep duration (> 8 hours) showed a statistically significant association ($P < 0.05$) with elevated levels of CRP, IL-6, fibrinogen, and WBC (Dowd et al, 2011).

The total number of studies examining the relationship between shiftwork, sleep quality or duration, and inflammatory mediators is relatively sparse. The results of the literature are inconclusive as some studies suggest a relationship between shiftwork and elevated

inflammatory mediators (Sookoian et al, 2007; Okun et al, 2009; Nishitani et al 2007), while other studies found no association between shiftwork and elevated inflammatory mediators (Taheri et al, 2007; Dowd et al, 2011). Further research is needed to better understand the association between shiftwork and inflammatory mediators.

Association between shiftwork, sleep and inflammatory mediators in LEO

The evidence evaluating shiftwork and inflammatory mediators is inconclusive. In addition, few studies have investigated shiftwork and health specifically in the Law Enforcement profession. Charles and colleagues (2007) investigated shiftwork and sleep in the Buffalo Police health study. A randomly selected group of 111 Buffalo-area LEO responded to surveys about sleep quality and duration. Charles and co-workers found night shift work to be independently and significantly associated ($P < 0.05$) with snoring and decreased sleep duration. The findings in the study by Charles's lab(2007) provides evidence that LEO with shiftwork schedules may be susceptible to sleep disorders. No measures of inflammatory mediators were conducted in this study, however.

Yoo and colleagues (2013) examined the relationship between sleep habits and mental stress on metabolic syndrome (MetS) in LEO. Sleep quality, sleep duration, and mental stress were compared in a cohort of 106 LEO. Sleep quality was found to have no association with MetS in this study, whereas longer sleep duration (>8 hours) was associated with MetS (OR = 4.89). However, poor sleep quality was associated with more mental stress, burnout, and depression. Violante and colleagues found similar results in a study published in 2009. Violante and coworkers (2009) found MetS in LEO to be significantly associated with sleep duration and

overtime hours. Once again, inflammatory mediators were not measured in these studies. However, the studies provide more evidence to the link between sleep and the health of LEO.

In a review article, Zimmerman (2012) identified shiftwork as a possible occupation-specific risk factor for CVD among LEO. Shiftwork was identified as a risk factor for many of the aforementioned reasons including a high association with atherosclerosis, MI, and traditional CVD risk factors such as hypertension, obesity. Franke's lab (2010) attempted to link elevated inflammatory mediators and work-related stress in a cohort of LEO. Franke and colleagues demonstrated inflammatory mediators to be elevated in LEO compared to the general population; however stress was not strongly associated with elevated levels of inflammatory mediators. Interestingly, 77% of LEO reported working shiftwork or irregular work hours compared to 27% in the general population, but sleep disorders were not assessed in this study (Franke et al, 2010).

Conclusion

An extensive list of studies suggests high CVD morbidity and mortality in the law enforcement profession (Calvert et al, 1999, Dubrow et al, 1988; Sardinas et al, 1986; Franke et al, 1998). Studies have tried to identify the specific mechanisms behind CVD and the law enforcement profession, but traditional risk factors have not been able to fully explain this phenomenon (Franke et al, 1998; Ramey et al, 2009). CVD is becoming increasingly recognized as an inflammatory disease, and many studies have associated elevated levels of inflammatory mediators with CVD (Ridker et al 2000; Koenig et al 1999; Wang et al, 2006; Pai, 2004). Studies have linked shiftwork to increased levels of inflammatory mediators (Sookoian et al, 2007;

Okun et al, 2009; Nishitani et al 2007), but these studies have not been conducted with the law enforcement population. One study by Franke et al (2010) found significantly elevated levels of inflammatory mediators in LEO, but job stress could not be attributed to the elevated levels of inflammatory mediators as hypothesized. Other studies have found associations between short sleep duration and poor sleep quality to be associated with health issues among LEO, but inflammatory biomarkers were not measured in these studies (Yoo, 2013; Violante, 2009) Thus, a need for a study examining the relationship between shiftwork, inflammatory mediators, and LEO is warranted.

CHAPTER THREE: METHODOLOGY

The objectives of the present study are to (1) determine the association between sleep hygiene and biomarkers for atherogenesis (specifically inflammatory mediators) in a cohort of law enforcement officers and (2) to determine the extent to which sleep hygiene and inflammatory mediators are associated with shift work disorder in law enforcement officers. The primary measures of the present study are sleep hygiene, shiftwork, and inflammatory mediators. However, a number of confounding variables can significantly affect the variables of interest such as personal or work-related stress, depression, social support, and common CVD risk factors such as smoking, obesity, and high blood-pressure. Therefore, the aforementioned confounding variables must also be addressed by the present study to control for these factors.

Participants

Participants in the LEO group are volunteers from the Iowa Department of Public Safety, already undergoing an annual medical examination at Iowa State University. The sample included 133 officers with a mean age of 41.2±8.4 years old. The sample was 95% male. Exclusion criteria include using large doses of anti-inflammatory medication or glucocorticoids, or a history of auto-immune disease (Franke et al, 2010).

Data Collection Procedures

CVD Risk Assessment

All subjects were evaluated for conventional risk factors of CVD including age, gender, obesity, total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), blood triglycerides, diabetes or pre-diabetes, and smoking status. The measurement of risk factors were used to determine 10-year risk for CVD via the Framingham Risk Score (Wilson et al, 1998). Obesity was inferred using the body mass index (BMI). BMI was calculated from height and weight obtained at the time of the health examination. Approximately 30 ml of blood was drawn via venipuncture from each subject. Half of the blood draw (15 ml) was used to determine blood levels of TC, LDL, HDL, triglycerides, and diabetes risk from blood glucose levels. Metabolic Syndrome markers were determined from BMI ≥ 30, triglycerides ≥150, HDL<40, blood glucose ≥100, and systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 (Grundy et al, 2005; WHO: 1999). The remaining 15 ml of blood was utilized for analysis of inflammatory mediators in the blood. Physical activity was measured via the International Physical Activity Questionnaire (IPAQ) short format (Craig et al, 2003). The IPAQ consists of a few short questions regarding time spent performing vigorous, moderate, and light physical activity. The IPAQ short format has been validated with pooled r value of .76.

Physiological Measures

Blood samples were obtained from the officers agreeing to participate in this study. Inflammatory mediators were evaluated by analyzing a sample of blood obtained from each subject at the health examination. The sample was allowed to clot and then the serum was extracted and frozen at -80° C. Measurement of circulating inflammatory cytokines

was conducted using a MILLIPLEX MAP human cytokine and chemokine multiplex assay (Millipore). Briefly, plates were washed and 25ul's of standards, controls and samples in duplicate were added to appropriate wells. Magnetic beads were added to all wells and plates were sealed and allowed to incubate on a plate shaker overnight at 4° C. After incubation, plates were gently washed two times and 25ul's of detection antibodies were added to all wells. The plate was sealed and incubated on a plate shaker for one hour at room temperature. After incubation 25ul's of Streptavidin-Phycoerythrin was added to all wells and incubated on a plate shaker for 30 minutes at room temperature. The plate was washed three times and 150ul of sheath fluid was added to all wells. Samples were read on a Bio-plex system (Biorad). Sample readings were compared to standards to give final concentrations. In addition to blood sampling, blood pressure was assessed via auscultation after five minutes of quiet, seated rest. Two measures of blood pressure were taken 5 minutes apart and then averaged (Franke et al, 2010; Ramey et al 2011). Subjects also were measured for height (cm) and weight (kg).

Sleep Hygiene

Sleep hygiene was determined using the Pittsburg Sleep Quality Index Questionnaire (PSQI). The PSQI is a user-friendly tool with high validity to assess sleep quality and disorders (Buysse et al, 1988). The PSQI consists of a series of questions related to sleeping habits of the previous month. The PSQI utilizes survey questions with inquiry about the subjects' overall duration of sleep, difficulties of sleep, and signs of sleep apnea. Subjects received an overall sleep quality score upon completion of the PSQI. Individual questions of the PSQI are scored from "0" (better) to "3" (worse). An overall PSQI scored was totaled from all sections with the minimum score being "0" (better) and the maximum score being "21" (worst). A PSQI score of

5 or less is interpreted as reflecting good sleep quality, while a score of 6 or more is associated with poor sleep quality. The PSQI has an alpha score of .83 in terms of validity. Subjects completed the questionnaire at the time of the health evaluation.

Shift Work

Shift work disorder was assessed using the Shiftwork Disorder Screening Questionnaire (Barger et al, 2012). The Shiftwork Disorder Screening Questionnaire consists of 4 item questions relating to daytime sleepiness, impaired well-being, insomnia complaints and the recurrence of sleepiness following non-work days. The questions were validated against a medical diagnosis of shift work disorder and have a sensitivity of .74 and a specificity of .82 for correctly identifying subjects with shift work disorder.

Work-related stressors

Work-related stressors were determined using the Operational and Organizational Police Stress Questionnaires (McCreary and Thompson, 2006). These instruments each consist of 20 questions related to common organizational or operational stressors of the police occupation. Each questionnaire has high internal consistency ($\alpha = .92$).

Personal stress

Personal stress was assessed using the Perceived Stress Scale (Cohen et al, 1983). This survey consists of 10 questions related to how a person responds to unpredictable or uncontrollable events in their lives. In other words, the scale measures the degree to which a personal perceives a situation as stressful, but not the cause of that stress. The Perceived Stress Scale has a reliability of .75.

Depression

Depression was assessed using the CES-D scale (Radloff, 1977). The CES-D scale is a short questionnaire widely used in epidemiologic research of depression on the general population. The questionnaire consists of 20 questions relating to depressive symptomology. The CES-D scale has high internal consistency with both the general population ($\alpha = .85$) and for clinical populations ($\alpha = .90$).

Social Support

Social support was assessed using the Social Provisions Scale (Cutrona and Russell, 1987). Social supports need to be assessed in the present study since it may strongly affect sleep hygiene. The social provision scale assesses the presence or absence of support from friends, family members, co-workers, community members and etc. in regards to attachment, social integration, guidance, alliance, and reassurance of worth. The scale consists of 24 item-questions. The social provisions scale has been found to be very reliable ($\alpha = .85$).

Statistical Analysis

The subjects were divided into three groups based on their PSQI score: group 1 contained officers with a PSQI score of 3 or less indicating "good" sleep quality (GOOD; n = 40), group 2 contained "borderline" sleepers with a PSQI total score of 4 or 5 (BRDL; n = 42), and group 3 contained officers with a PSQI score of 6 or more, reflecting poor sleep quality (POOR; n = 51). ANOVA tests were conducted to determine statistically significant differences between groups across all variables of interest. Post hoc multiple comparison Tukey tests were conducted to locate statistically significant differences between the individual groups for each variable ($P < 0.05$). All data are reported as mean $\pm$ sd.

CHAPTER FOUR: RESULTS

General Subject Information

General subject information is summarized in Table 1. No significant differences existed between the three groups in general demographics, age, BMI, duration as a LEO, or duration working the current shift schedule.

Table 1. Subject Information

	LEO Groups		
Variable	**Good**	**Borderline**	**Poor**
N	40	42	51
Age (y)	40.3 ± 9.0	42.2 ± 8.4	41.1 ± 8.0
BMI ($kg \bullet m^{-2}$)	27.7 ± 3.1	28.9 ±3.00	28.9 ± 3.4
Duration as LEO (yrs)	17.4 ± 8.2	17.9 ± 8.7	18.1 ± 8.5
Duration of current schedule (yrs)	11.7 ± 7.6	11.1 ± 7.2	11.3 ± 9.1
Overtime/Unexpected work hours (%)	18.5 ± 23.2	17.7 ± 19.2	18.3 ± 21.8

Sleep Hygiene

POOR was significantly worse in PSQI scores for sleep duration, sleep disturbance, sleep latency, sleep day dysfunction, sleep efficiency, overall sleep quality, and needing medication to sleep than GOOD ($P < 0.05$ for all measures). POOR was significantly different ($P < 0.05$) from BRDL in all categories except sleep day dysfunction. POOR also differed significantly from GOOD and BRDR in shiftwork disorder prevalence and days per month in which they did not get enough sleep ($P < 0.05$). Sleep measures are summarized on Table 2.

Table 2. Sleep Measures			
		LEO Groups	
Variable (Possible Range)	**Good**	**Borderline**	**Poor**
PSQI Total (0-21)	2.4 ± 0.8	4.6 ± 0.5 *	8.6 ± 2.6 *†
PSQI Sleep Duration (0-3)	0.2 ± 0.4	0.5 ± 0.6	1.1 ± 1.0 *†
PSQI Sleep Disturbance (0-3)	1.0 ± 0.3	1.1 ± 0.4	1.7 ± 0.6 *†
PSQI Sleep Latency (0-3)	0.3 ± 0.5	0.7 ± 0.6	1.9 ± 1.0 *†
PSQI Sleep Day Dysfunction (0-3)	0.3 ± 0.5	1.0 ± 0.6 *	1.0 ± 0.7 *
PSQI Sleep Efficiency(0-3)	0.0 ± 0.2	0.1 ± 0.4	0.7 ± 0.9 *†
PSQI Overall Quality (0-3)	0.6 ± 0.5	1.1 ± 0.3 *	1.4 ± 0.6 *†
PSQI Need Meds to Sleep (0-3)	0 ± 0	0 ± 0	0.8 ± 1.1 *†
Shiftwork Disorder Risk (%)	8 ± 3	18 ± 4	43 ± 5 *†

* P < 0.05 from Control; † P < 0.05 from Borderline

CVD Risk

No significant differences existed between any of the groups on all traditional CVD risk factors including age, BMI, total cholesterol, LDL and HDL cholesterol, triglycerides, glucose, or systolic and diastolic blood pressure. No significant differences were found in Framingham 10-year CVD risk or metabolic syndrome risk between the three groups. No significant differences were found in meeting the minimum weekly physical activity requirements among groups. CVD risk results are summarized in Table 3.

Table 3. CVD Risk			
	LEO Groups		
Variable	**Good**	**Borderline**	**Poor**
CVD Risk Factors			
Age (y)	40.3 ± 9.0	42.2 ± 8.4	41.1 ± 8.0
BMI (kg • m^{-2})	27.7 ± 3.1	28.9 ± 3.0	28.9 ± 3.4
Total Cholesterol (mg • dl_{-1})	189.7 ± 33.6	187.2 ± 30.5	187.6 ± 35.1
LDL Cholesterol (mg • dl_{-1})	113.8 ± 30.2	113.5 ± 24.8	113.3 ± 29.1
HDL Cholesterol (mg • dl_{-1})	52.0 ± 16.5	49.7 ± 12.6	49.4 ± 11.5
Triglycerides (mg • dl_{-1})	125.5 ± 84.8	134.9 ± 133.6	137.6 ± 87.2
Glucose (mg • dl_{-1})	93.9 ± 19.3	92.2 ± 8.5	94.1 ± 19.6
Systolic Blood Pressure (mmHg)	124.6 ± 8.6	124.6 ± 8.3	123.1 ± 7.9
Diastolic Blood Pressure (mmHg)	85.1 ± 7.3	85.7 ± 7.2	84.7 ± 7.0
Weekly PA participation met (%)	75 ± 44	57 ± 50	63 ± 49
10-year CVD Risk %	6.4 ± 6.2	6.6 ± 4.2	7.1 ± 6.2
Referenced to "normal" risk for age	1.0 $\pm$ 1.4	1.0 $\pm$ 1.4	1.1 $\pm$ 1.5
Metabolic Syndrome (%)	23 ± 42	17 ± 38	28 ± 45
Metabolic Syndrome Markers (n)	1.5 ± 1.4	1.5 ± 1.2	1.6 ± 1.4

Inflammatory Biomarkers

The results of the inflammatory biomarker analysis are summarized in Table 4. No significant differences existed between the groups in any of the inflammatory biomarkers analyzed

Table 4. Cytokine Profiles

	LEO Groups		
Variable	**Good**	**Borderline**	**Bad**
EGF (pg • ml^{-1})	37.1 ± 43.4	47.5 ± 58.4	38.0 ± 43.2
FGF-2 (pg • ml^{-1})	98.2 ± 92.7	76.5 ± 56.5	92.7 ± 94.8
Eotaxin (pg • ml^{-1})	420.7 ± 213.2	446.1 ± 247.4	411.8 ± 182.2
TGF-α (pg • ml^{-1})	19.8 ± 33.9	17.3 ± 27.6	18.2 ± 24.5
GCSF (pg • ml^{-1})	41.8 ± 40.0	54.1 ± 65.2	58.3 ± 76.0
Fit3L (pg • ml^{-1})	49.6 ± 59.6	110.4 ± 169.1	99.5 ± 127.1
GMCSF (pg • ml^{-1})	23.8 ± 27.1	20.1 ± 32.8	31.8 ± 44.3
Fractalkine (pg • ml^{-1})	333.0 ± 470.1	325.4 ± 421.3	373.3 ± 620.2
IFNα-2 (pg • ml^{-1})	162.8 ± 181.4	113.8 ± 145.5	145.2 ± 159.7
IFNy (pg • ml^{-1})	48.9 ± 91.6	80.9 ± 178.7	105.0 ± 172.9
GRO (pg • ml^{-1})	545.1 ± 238.1	607.2 ± 235.7	510.6 ± 205.8
IL-10 (pg • ml^{-1})	16.0 ± 18.8	15.3 ± 15.9	14.1 ± 20.6
MCP-3 (pg • ml^{-1})	51.8 ± 61.0	50.4 ± 66.0	53.6 ± 65.3
IL-12P40 (pg • ml^{-1})	91.3 ± 69.5	80.6 ± 79.1	78.4 ± 68.4
MDC (pg • ml^{-1})	1319.2 ± 690.1	1458.7 ± 862.7	1494.0 ± 1056.8
IL-12P70 (pg • ml^{-1})	53.8 ± 96.6	59.3 ± 92.0	71.5 ± 124.5
IL-13 (pg • ml^{-1})	77.0 ± 91.5	82.8 ± 108.4	79.3 ± 109.3
IL-15 (pg • ml^{-1})	28.7 ± 26.9	24.1 ± 21.2	29.8 ± 23.8
sCD40L (pg • ml^{-1})	4433.6 ± 2374.8	5174.5 ± 2953.1	4052.1 ± 2708.6
IL-17A (pg • ml^{-1})	24.9 ± 45.1	39.2 ± 86.1	72.3 ± 143.9
IL-1RA (pg • ml^{-1})	140.9 ± 182.1	99.8 ± 145.8	113.07 ± 151.9
IL-1a (pg • ml^{-1})	311.5 ± 361.6	381.2 ± 408.4	319.1 ± 307.6
IL-09 (pg • ml^{-1})	10.1 ± 13.1	5.1 ± 4.3	8.5 ± 15.0
IL-1B (pg • ml^{-1})	18.9 ± 18.1	14.0 ± 13.77	16.2 ± 20.4
IL-2 (pg • ml^{-1})	27.4 ± 21.7	25.5 ± 19.8	33.0 ± 30.4
IL-3 (pg • ml^{-1})	6.1 ± 5.6	3.3 ± 3.9	5.3 ± 6.5
IL-4 (pg • ml^{-1})	111.7 ± 60.6	88.7 ± 90.3	99.3 ± 92.3
IL-5 (pg • ml^{-1})	13.0 ± 14.3	7.1 ± 3.7	13.7 ± 14.7
IL-6 (pg • ml^{-1})	60.6 ± 61.1	56.4 ± 54.9	69.7 ± 70.6
IL-7 (pg • ml^{-1})	14.5 ± 13.3	18.5 ± 13.4	14.8 ± 13.3
IL-8 (pg • ml^{-1})	25.0 ± 27.5	30.2 ± 51.4	35.5 ± 52.7
IP-10 (pg • ml^{-1})	545.3 ± 264.2	756.6 ± 526.3	677.1 ± 433.6
MCP-1 (pg • ml^{-1})	471.7 ± 177.3	544.8 ± 208.1	540.9 ± 188.8
MIP-1a (pg • ml^{-1})	14.7 ± 10.9	13.6 ± 15.0	16.1 ± 15.5
MIP-1B (pg • ml^{-1})	84.3 ± 89.4	86.5 ± 87.8	85.0 ± 86.5
TNF-α (pg • ml^{-1})	8.1 ± 10.2	11.9 ± 13.0	8.6 ± 10.5
TNF-β (pg • ml^{-1})	83.0 ± 103.3	58.9 ± 80.8	119.9 ± 151.3
VEGF (pg • ml^{-1})	456.2 ± 471.8	435.1 ± 510.4	495.1 ± 591.2

Mental Health

POOR had significantly worse depressive symptomology compared to GOOD ($p < 0.05$). POOR was also significantly worse on mental stress, operational and organizational police stress compared to GOOD ($p < 0.05$)BRDL was significantly worse than GOOD only in organizational police stress. In terms of health related quality of life, there was a graded increase in the number of "not enough sleep days" across the three groups ($p<0.05$) and a trend ($P=0.072$) for group differences in the number of healthy and unhealthy days. Mental health measures are summarized in Table 5.

Table 5. Mental Health

	LEO Groups Based on PSQI Score		
Variable (Possible Range)	**Good**	**Borderline**	**Poor**
Depression (0-60)	4.6 ± 4.6	7.1 ± 6.1	10.1 ± 7.3 *
Stress – PSS-10 (0-40)	8.5 ± 4.8	10.6 ± 4.7	11.8 ± 5.0 *
Operational police stress (1-7)	2.1 ± .9	2.6 ± .8	3.3 ± 1.2 *
Organizational police stress (1-7)	2.4 ± 1.1	3.1 ± 1.1 *	3.4 ± 1.4 *
Social Support (24-96)	83.6 ± 10.2	83.3 ± 9.0	82.7 ± 9.6
Health Related Quality of Life			
Not Enough Sleep Days (0-30)	1.8 ± 2.9	4.3 ± 4.9	12.3 ± 9.9 *†
Total Unhealthy Days (0-30)	1.5 ± 4.8	3.9 ± 7.4	4.3 ± 5.5 §
Total Healthy Days (0-30)	28.4 ± 4.8	26.1 ± 7.4	25.7 ± 5.5 §

* $P < 0.05$ vs. Control; §$P = 0.077$ vs. Control; † $P < 0.05$ vs. Borderline

CHAPTER FIVE: DISCUSSION

The intent of this study was to assess the extent to which sleep affects the risk of CVD in the law enforcement population via an increased systemic inflammation. In other words, does poor sleep lead to increased inflammation which can lead to increased CVD risk beyond traditionally established risk factors? First, the results of this study suggests that poor sleep hygiene is an issue among LEO. The results of this study are supported by another study conducted by Rajaratnam and colleagues in 2011. Rajaratnam's laboratory sampled 4957 LEO in North America and found 40.4% of the LEO reported having at least one sleep disorder. Thirty-three percent of the sample reported sleep apnea. Rajaratnam and colleauges also found sleep disorders were correlated with depression, increased risk of adverse work-related events, increased risk of burnout, and decreased work productivity. This is consistent with the findings from Franke and colleagues (2010) in which 77% of the LEO cohort reported shiftwork compared to only 27% of civilians. One point to highlight is that officers in the POOR group, who were getting significantly worse sleep compared to the GOOD group, also had a significantly higher prevalence of shiftwork disorder. This result supports our hypothesis that shiftwork schedules are affecting the sleep patterns of the LEO population. This result is consistent with other studies which have reported shiftworking schedules to cause health and sleep issues among LEO cohorts (Charles et al, 2007; Violante et al, 2009; Yoo et al; 2013).

One finding worth noting is the relationship with sleep and mental health. The POOR reported significantly higher depression and stress levels than did the GOOD or BRDL groups. Other studies have also found poor sleep hygiene to be associated with mental health issues. As previously mentioned, the study by Rajaratnam and coworkers found sleep disorders to be

correlated with depression in LEO (OR 2.20; 95% CI, 1.52-3.19). In another study, Lin and coworkers (2012) found nurses on rotating shifts to have worse mental health scores on the Chinese Health Questionnaire-12 when compared to day shift nurses. Sleep may also play a role in major psychiatric disorders such as major depressive disorder, Alzheimer's disease, Parkinson's disease, dementia and even schizophrenia (Anderson et al, 2013). This finding is not to be taken lightly. Reducing the risk of mental illnesses and neurodegenerative diseases gives reason to find an alternative way to schedule shiftworking LEO. Future research should investigate the prevalence of neurodegenerative diseases in LEO of different sleep and shiftwork patterns.

However, the results of this study do not suggest that poor sleep has impacted the systemic inflammatory levels of this cohort. No significant differences existed between GOOD, BRDL, or POOR in inflammatory biomarker levels. This result is different than other research studies in which sleep did influence systemic inflammatory biomarkers (Sookoian et al, 2007; Okun et al, 2009; Nishitani et al 2007). There are some key differences between the studies. Sookoian et al (2007) and Nishitani et al (2007) utilized a factory-working population of different ethnicity than this study. Okun et al (2009) examined women in their study. On the contrary, the results of this study are consistent with other studies in which poor sleep hygiene was not associated with increased systemic inflammation (Taheri et al., 2007; Dowd et al, 2011). The literature is still not clear on the relationship between sleep and systemic inflammation. Further research is needed to address this issue.

There are several limitations to address in this study. One is the lack of dietary measures in this study. Hardman summarized an extensive list of dietary products and the

respective impact on inflammation in a 2014 review article. Hardman suggests that dietary fruits, nuts, vegetables, and whole grains can have anti-inflammatory effects, while dietary intake of hydrogenated oils, saturated fats, and refined sugars can have pro-inflammatory effects. Regrettably, no measures of diet analysis were made in this study. Also, officers were not excluded from this study if they were currently taking lipid lowering or blood pressure lowering medications. This oversight could be artificially lowering their CVD risk independently of any behavioral or lifestyle factors. Measurement in tobacco usage is another limitation in this study. The officers sampled were questioned about smoking status and were not included in the final analysis if they were a smoker. However, the usage of smokeless tobacco was not assessed . It is possible that officers were using smokeless tobacco, but did not screen positive for smoking. This study did assess alcohol usage by self-reported weekly number of drinks consumed by the sample, but no significant trends were found. Underreporting alcohol consumption could have confounded the results as well.

Methodological limitations exist in the analysis of inflammation as well. The current study utilized blood serum and low-sensitivity assay kits to analyze cytokine and chemokine concentrations. Dowd's lab (2011) utilized blood serum to analyze inflammation in their study, and another study conducted by Ramey and colleagues (2012) utilized blood serum to analyze CRP. This study and the two aforementioned studies found no significant differences in inflammatory measures. On the contrary, Irwin's lab (REF) utilized peripheral blood mononuclear cells to detect transcriptional levels of inflammatory mRNA in both 2006 and 2008 studies looking at sleep restriction and inflammation. Nishitani and coworkers were examining white blood cell count from venous blood (2007). Sookoian's lab examined leukocytes by

"standard lab techniques." The variance in methods of measuring inflammation could be partially causing the discrepancy of sleep and inflammation in the literature. It is possible that utilizing blood mononuclear cells to investigate inflammation would have yielded different results. Future research should carefully consider methodological procedures when measuring cytokine and chemokine profiles.

Self-reporting is also limiting in this study. All measures of sleep, mental health, physical activity, tobacco, and alcohol usage utilized self-reporting surveys. Self-reporting is inherently at risk for over and under reporting all conditions. One should be careful not to overgeneralize from self-reporting. Studies with larger sample sizes can reduce the error of self-reporting, but no study can eliminate self-reporting errors.

Finally, the results of this study found no significant difference in CVD risk for GOOD, BRDL, or POOR. Another limitation to address is the lack of a civilian or non-LEO control group. The results of this study show no significant difference in CVD risk among LEO regardless of sleep hygiene. However, this does not address the issue that the entirety of our officer sample could have elevated CVD risk when compared to an otherwise similar civilian control. However, this study reported the relative risk of poor sleeping compared to other officers without sleep issues which gives us a measure of comparison for normalized risk. Regrettably, this study did not have a civilian sample to utilize in the analysis. In the future, the sample in this study could be compared to a non-LEO control group to determine differences in sleep, inflammation, and CVD risk to further investigate this relationship. Studies have found increased CVD risk in the law enforcement population when compared to civilians, but measures of sleep and inflammation were not taken into account (Calvert et al, 1999, Dubrow et al, 1988; Sardinas et

al, 1986; Franke et al, 1998; Franke et al, 2002; Ramey et al, 2009). However, it is important to report the "relative risk" of what is expected in a civilian cohort. LEO with poor sleep and shiftwork disorder may still be at higher relative risk for CVD and other health ailments independently of tradition CVD risk factors. Thus it is possible that while CVD risk is increased in LEO it may be from a different pathway than inflammation.

In conclusion, there was a clear discrepancy between healthy sleeping and non-healthy sleeping LEO which was attributed to shiftwork disorder. LEO with poor sleep hygiene also reported higher incidence of depression and stress than their good-sleeping counterparts. No significant differences exist between groups in inflammatory biomarkers, suggesting that a different biological mechanism may be playing a role in the increased CVD risk associated with the law enforcement profession. Inflammation and sleep studies have been inconclusive, and further research in the area needs to be done to further investigate the mechanism of CVD prevalence in the law enforcement profession, and, ultimately improve the health outcome of our emergency responders and shiftworking professionals alike.

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