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Blunted Blood Pressure Dipping During Night Shift Work: Does It Matter? Can We Intervene?

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ABSTRACT

Cardiovascular disease (CVD) is the leading cause of adult death in the United States. Numerous studies show that night shift workers face a disproportionately higher risk of CVD compared to non-shift workers. Despite these data, the scientific and medical communities have not identified the physiological mechanisms that contribute to increased CVD risks for night shift workers. We propose that repetitive exposure to blunted blood pressure (BP) dipping associated with sleep loss during night shift work is an important, clinically meaningful, understudied, and modifiable contributor to increased risk of CVD. Blunted BP dipping occurs when BP fails to decrease or "dip" 10%–20% during nighttime hours (typically while sleeping) relative to daytime hours (typically while awake). Blunted BP dipping is widely considered a clinically meaningful indicator of poor cardiovascular health. Previous research suggests it is a common consequence of night shift work and occurs during sleep before and immediately after night shifts. Relatively few studies of shift work and CVD have focused on blunted BP dipping as a mechanism of CVD risk. Recent experimental research shows that restoration of normal BP patterns—during night shift work—is achievable with strategic napping and may reduce the risk of CVD. We present a series of important mechanistic-related questions and next steps for future research focused on blunted BP dipping and night shift work.

1 | Background

Cardiovascular disease (CVD) is the leading cause of adult death in the United States [1]. Numerous studies show that shift workers, in particular night shift workers, face a disproportionately higher risk of CVD compared to non-shift workers and persons who do not regularly work night shifts [2–4]. Night shift work involves working beyond midnight and is often associated with irregular sleep, poor sleep quality, and a number of sleep health-related disorders [5–10]. The incidence of hypertension (HTN) over a 5-to-10-year period, for example, is higher among night shift workers compared to traditional day workers [11, 12]. The risk of myocardial infarction is 23% higher (risk ratio 1.23, 95% CI 1.15, 1.31) for shift workers versus non-shift workers, and the risk of coronary heart disease is 37% higher (hazard ratio 1.37, 95% CI 1.20, 1.58) for individuals with ≥ 10 years of night shift work compared to no night shift work [4, 13]. Compared to other work schedules, the risk of hospital admission due to any coronary event is greatest among night shift workers (risk ratio 1.41, 95% CI 1.13, 1.76) [4]. Despite these data, the scientific and medical communities have not identified the physiological mechanisms that contribute to increased CVD risks for night shift workers. Thus there is a compelling need to explore novel and inadequately investigated pathways to CVD. In addition, bold efforts are needed to test the effectiveness of diverse mitigation strategies that are appealing and practical for night shift workers and their employers.

We propose that repetitive exposure to blunted blood pressure (BP) dipping associated with sleep loss during night shift work is a clinically meaningful, understudied, and modifiable contributor to increased risk of CVD (Figure 1). Blunted BP dipping is abnormal and occurs when nighttime or sleep-related BP averages for systolic, diastolic, or both fail to decrease by 10%−20% relative to daylight or wake BP averages [14]. A normal 24 h pattern in BP is characterized by higher values during waking (typically daylight) hours followed by lower values during sleep (typically nighttime) hours [15]. This decrease that occurs during nighttime and sleep is commonly referred to as "BP dipping" or the "dip." [15] Dipping is more common during nighttime hours, yet it is not isolated to night time hours and can occur during daylight-related sleep [16]. This dip in BP is thus independently related to both sleep and circadian patterns.

Blunted BP dipping is widely considered a clinically meaningful indicator of poor cardiovascular health [17–20]. It is associated with subclinical atherosclerosis (e.g., coronary artery calcification), left ventricular hypertrophy, progressive renal damage, stroke, and cardiovascular mortality [14, 20–26]. One prospective cohort study of 316 young adults (mean age 30 years ±3.7) showed that blunted BP dipping detected at a younger age is associated with the presence of coronary atherosclerosis 10−15 years later [21]. Conditions commonly associated with blunted BP dipping include hormonal and metabolic disorders (e.g., abnormally high sympathetic activation, thyroid dysfunction, Cushing's syndrome), dietary factors (e.g., high sodium intake), chronic diseases (e.g., metabolic syndrome, diabetic autonomic neuropathy, chronic kidney disease), and sleep disorders (e.g., sleep apnea) [19].

2 | Is Blunted BP Dipping Important for Night Shift Workers? Does It Matter?

Blunted BP dipping is more prevalent among persons with existing CVD and among those with conditions that compound risk for CVD like metabolic disease [27]. Most often, these individuals are older adults [28]. Thus, it is not unreasonable to assume that blunted BP dipping is a result/sequelae of older age or chronic disease and is of little significance for night shift workers, especially younger and generally healthy night shift workers. We believe a different perspective is warranted and hypothesize that long-term exposure to blunted BP dipping associated with night shift work contributes to an increased risk of CVD.

To support our hypothesis, we searched for relevant studies indexed in the PubMed database using "blunted BP dipping," "shift work," and related terms (i.e., night shift) for keyword searches. We searched the results of two recent systematic reviews that focused on shift work and BP [16, 29]. We also searched the bibliographies of papers selected for inclusion. We identified six studies [30–35]. The findings from one observational field study demonstrated that 100% of 56 healthy, young (mean age 26.5 years ±7.5) paramedics, Emergency Medical Technicians, and nurses experienced blunted BP dipping during night shift work without an on-shift nap opportunity [30]. In addition, 49.1% of these night shift workers experienced blunted BP dipping during daytime sleep that occurred immediately before or immediately after a night shift [30]. Data from two recent randomized crossover trials of healthy young (mean age < 25 years) shift workers also reported a blunted BP dipping pattern during simulated night shifts without nap opportunities and attenuated BP dipping during daytime recovery sleep post-night shift [31, 32]. A 2017 study by Yang et al. examined blunted BP dipping in response to repeated episodes of shortened sleep (approximately 4 h per night) [33], which is a sleep pattern similar to that which many public safety shift workers experience on a regular basis [36]. Their study showed repetitive exposure to shortened sleep—within days—was associated with a blunted BP dipping pattern [33]. A more recent observational study by McHill et al. investigated blunted BP dipping among new early morning shift workers [34]. This study found that 93% of workers going from no shift work to a new shift work schedule exhibited blunted BP dipping at 90 days. Torun et al. compared BP patterns assessed every 2 h over 48 continuous hours among young night shift healthcare workers (mean age 27.2 years ±2.2) [35]. Assessments occurred during a 16 h night shift during a non-workday, and among a comparison group of daylight workers (mean age 31.3 years ±7.2), during daylight work and a non-workday [35]. The night shift worker's BP dipping pattern was blunted and significantly different from that of daylight workers [35]. The above-summarized findings are subject to limitations and bias

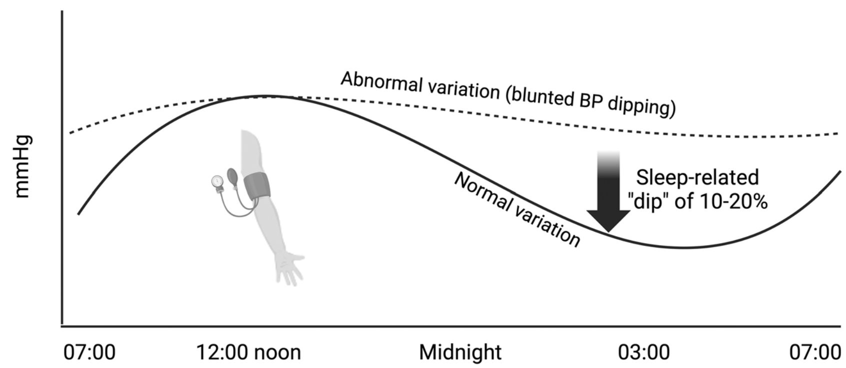

FIGURE 1 | Illustration of normal versus blunted BP dipping.

associated with non-systematic literature reviews. In particular, there may be additional research indexed in other databases or published as grey literature that were not included in our review, and thus may alter our findings.

The data outlined above confirm that blunted BP dipping is common among night shift workers and present among young healthy adults rather than isolated to those with existing disease or older adults. These data also imply that, among night shift workers, blunted BP dipping is not a condition that manifests slowly over time with ongoing exposure to night shift work. Rather, blunted BP dipping is a phenomenon that occurs immediately upon initial exposure to night shift work conditions (sleep loss/irregular sleep). This is confirmed by and consistently detected in observational and experimental studies [30–35]. In addition, these data show that blunted BP dipping affects all night shift workers and is not isolated to a select group with select characteristics. Despite these data, the relatively brief follow-up of participants in these studies raises questions about the biologic plausibility of blunted BP dipping during night shift work as a mechanism in a pathway that contributes to CVD.

Biologic plausibility refers to current knowledge of a disease/outcome and our current understanding of the detailed steps in the chain of events (etiology) that lead to a disease/outcome [37]. Biologic plausibility is a core component of Sir Austin Bradford Hill's aspects of association, a framework of nine criteria guiding investigations of causal inference since the 1960s [38, 39]. These criteria have helped researchers address the "black box" of exposure-to-disease relationship, consider alternative mechanisms and pathways to disease, and encouraged the use of diverse information to establish causality [38].

We hypothesize that repetitive exposure to blunted BP dipping is one of multiple mechanisms (part of a pathway) that increases the risk of CVD among night shift workers. The following evidence, we believe, supports this hypothesis. Systematic reviews and meta-analyses show that circadian misalignment created by night shift work and rotating shift work is associated with abnormal patterns in BP like blunted BP dipping and higher average 24 h BP [16, 40, 41]. Second, the best available direct evidence described above shows that blunted BP dipping is detectable during actual night shift work and during simulated night shift work when sleep and circadian patterns are misaligned [30–35]. These findings are consistent across multiple studies. Third, longitudinal data show that as little as 3 years of rotating shift work is associated with a significantly greater increase in arterial stiffness than that observed in non-shift worker controls after the same 3 years follow-up [42]. Blunted BP dipping is independently associated with increased arterial stiffness and endothelial dysfunction [43–45], two known subclinical indicators of CVD [46, 47]. Fourth, recent data show that the removal of night shift work (and likely the repeated exposure to blunted BP dipping) reverses arterial stiffening [48].

These observations support a biologically plausible model: Blunted BP dipping is a physiological response detectable immediately when exposed to night shift work and precedes a cascade of biological responses to exposure to night shift work conditions that culminate in CVD. When BP fails to dip normally in a 24 h period, it is often accompanied by increased 24 h sympathetic activity and reduced parasympathetic activity [49]. Increased sympathetic activity through norepinephrine release is associated with cytokine production and inflammatory response [50]. The immune response includes elevated levels of monocytes, changes in IL-6 secretion, and measurable changes in endothelial function [51–54], all of which have been linked to poor cardiovascular health and disease severity [55, 56]. Most of these changes become detectable and clinically meaningful after repeated episodes of night shift work—as few as three-night shifts in a row for some workers or after several weeks of night shift work for others [51–54]. A single episode of night shift work may not lead to a clinically meaningful change in some of these indicators [57]; however, blunted BP dipping is detectable early with first exposure to night shift conditions [31, 32]. Blunted BP dipping may, therefore, be thought of as one of potentially several factors detected early and often in the pathway to increased risk of CVD.

Finally, the scientific and medical communities have not isolated the dominant or all the likely physiological mechanisms that contribute to increased risk of CVD for night shift workers. Blunted BP dipping fits logically into the exposure-to-disease relationship which is core to the biologic plausibility paradigm [38, 39]. Blunted BP dipping is associated with existing CVD; it is associated with known subclinical indicators of CVD (i.e., arterial stiffness); and it is easily detected in healthy young individuals, likely well before significant abnormal changes are detected in other subclinical CVD indicators, like arterial stiffening and endothelial dysfunction [32]. To be clear, we do not assert that blunted BP dipping is the sole or only factor of significance in the pathway to CVD. Rather, blunted BP dipping is likely one of multiple factors that, in combination, raise the risk of CVD for night shift workers. Acute and infrequent exposure to blunted BP dipping (i.e., occasional episodes) is likely not harmful. Repeated exposure, however, is potentially harmful. We therefore believe it is biologically plausible that repeated exposure to blunted BP dipping contributes to a greater risk of CVD among night shift workers. The total duration of repeated exposure that results in increased risk, however, is not known.

3 | Blunted BP Dipping Is Understudied in Relation to Night Shift Work

Blunted BP dipping related to workplace conditions has not received much attention from investigators in occupational medicine or among those concerned with cardiovascular health and wellness in workplaces that involve night shift work. This is evidenced by a systematic review and meta-analysis of studies that assessed the impact of shift work on BP: none of 44 studies published between 1980 and 2018 reported blunted BP dipping as an outcome [16]. A separate systematic review of studies published between 1980 and 2016 determined that, of the 100 studies that compared the effects of one shift duration to another on outcomes (including health outcomes), none reported on blunted BP dipping as an outcome of interest [29]. Of the six studies identified in our literature review, only one was published before 2021 (the Yang et al. study) [33]. This study did not involve shift workers, and is at best, considered indirect evidence. The current best available evidence, as outlined previously, is from two observational studies [30, 34] and four experimental studies [31–33, 35]. All studies have small sample sizes, not all samples involve actual night shift workers (thus, some data are indirect), and there is wide variation in protocols tested.

Measuring blunted BP dipping does not require invasive devices or procedures [58]. However, the noninvasive ambulatory devices often used to measure BP in field studies and in laboratory-based research are not inexpensive. Device costs may be $2000 or more each. Thus, costs associated with measurement may be a barrier for many. Recruitment of participants may also be a barrier. Protocols will often require participants to continuously wear an ambulatory BP device, including during sleep. For many potential participants, this may be too intrusive with sleep disturbance as a commonly reported adverse effect with these devices [59, 60]. A lack of previous research, specifically longitudinal research, linking blunted BP dipping in shift work settings to CVD outcomes may have led many investigators to focus on other known exposures and outcomes that require a shorter period of follow-up.

4 | Can We Intervene?

Yang et al., who detected blunted BP dipping during repetitive exposure to shortened sleep in the lab, identified blunted BP dipping as one mechanism that may lead to an increased risk of CVD [33]. Recent data show us that restoration of a "normal-like" BP dipping pattern with a 10%–20% dip in BP during night shift work is achievable. In a randomized crossover trial testing the effect of three nap conditions, 58% of subjects achieved a $\geq$ 10% dip in SBP or DBP during a 30 min nap opportunity while completing a simulated 12 h night shift [31]. Most (84%) achieved a normal dip in BP during a 2 h nap opportunity. A separate crossover trial involved simulated night shift work and showed that 67% of participants achieved a normal dip in SBP or DBP during a 45 min nap opportunity [32]. These data show us that short nap opportunities during night shifts may help attenuate the negative effects on BP and help restore, if only briefly, normal BP dipping patterns.

Limiting periods with irregular sleep is another opportunity for intervention that may reduce exposure to blunted BP dipping. Night shift work schedules contribute to irregular sleep and increased exposure to blunted BP dipping. Data shown in Figure 1 of a separate publication illustrates just how irregular sleep can be for some night shift workers [36]. In this example, the shift worker slept an average of 3.4 h per sleep episode for a total of 16 episodes over 7 days [36]. By comparison, a day worker slept an average of 7.5 h per sleep episode also over 7 days [36]. Analyses of ambulatory BP data from these individuals show that blunted BP dipping was detected in 56% of all sleep episodes for the shift worker ($n = 9$ sleep episodes) versus 28% for the day worker ($n = 2$ sleep episodes). These data are limited to just two individuals and not representative of all night shift workers. However, many night shift workers, especially those with multiple jobs, like those who work in public safety [61–63], likely experience irregular sleep patterns and concurrent blunted BP dipping like the shift worker referenced here [36]. The more irregular a person's sleep patterns is, the greater the risk of major adverse cardiovascular events like fatal or nonfatal myocardial infarction, heart failure, and stroke [64]. Eliminating irregular sleep for night shift workers is not realistic. However, an opportunity for intervention is to target the weekly sleep patterns of night shift workers and introduce as much regularity as possible, which may reduce exposure to blunted BP dipping.

5 | Essential Next Steps

Despite years of research that consistently shows a relationship between exposure to night shift work and increased risk of CVD [2–4, 11, 12, 65], important questions remain regarding the mechanisms and pathways that underlie this risk. We propose that repetitive exposure to blunted BP dipping as a consequence of night shift work per se, and not as a result of underlying disease, is a clinically meaningful, yet modifiable risk factor for night shift workers. Important questions to address include: How common is exposure to blunted BP dipping for night shift workers? Do different work schedules that include night shifts and different duration night shifts affect BP dipping differently? What interventions can mitigate blunted BP dipping while allowing night shift workers to maintain their night shift schedules?

Answers to many of these questions could come from prospective, longitudinal observational designs that include night shift workers as participants and that aim to quantify the incidence of exposure to blunted BP dipping long-term. Ideal targets for enrollment include novice night shift workers with limited prior exposure and workers with a long-term (multiple years) exposure history. Targeting both groups would address, in part, the connection between initial exposure, a dose of exposure, and the likelihood of incident-blunted BP dipping. Investigators should also measure individual, work-related, and environmental factors that may confound the relationship between night shift work and incident-blunted BP dipping. Individual-level factors might include body mass index and health diagnoses (such as sleep apnea) [66], work-related factors to consider include workload and rest/nap opportunities on duty [16], and environmental factors that could affect BP include ambient temperature, time of day, and seasonal variation [67].

Well-designed prospective studies can also explore questions related to dose–response based on shift schedule, explore questions about the magnitude and severity of blunted BP dipping, and control for individual, work-related, and environmental factors that can alter BP. Simultaneously, experimental studies can simulate night shift work conditions, reduce the presence of potential confounders (e.g., dietary patterns and caffeine consumption), and determine if certain patterns of sleep and if different night shift schedules affect BP dipping differently.

Investigators will need to address how and how often BP is measured. Most field studies of shift workers and BP have used ambulatory BP devices programmed to measure BP every 30–60 min [16]. Shorter intervals during waking hours (e.g., every 15 min) have been used in select investigations as have longer intervals during sleep (e.g., every 2 h) [16]. Devices that measure BP at the brachial site are most common and feasible for field-based research [30]. However, these devices may disrupt sleep, which in turn can affect the number of sleep-based measurements captured and disturb the investigator's ability to quantify sleep-related BP changes including incident-blunted BP dipping. Some investigators have addressed this concern by using continuous, beat-to-beat BP monitoring devices that use small cuffs placed on one or more fingers [33]. While studies of non-shift workers show us that these devices can provide valid BP measurements [68–70], their utility in field-based studies is uncertain. Newer devices for continuous BP measurements are under development [71] and may prove useful for BP assessment of night shift workers. Regardless of which device is used, investigators should aim to capture a minimum of 24 h of BP data and use a threshold for the number of valid measurements of 70% or greater, as these are widely accepted and prescribed benchmarks for ambulatory measurement of BP [72].

Experimental laboratory-based studies, like those referenced above [31–33], are also needed. In particular, Phase II trials would provide much-needed data. Phase II trials are often used to determine whether an intervention is sufficiently promising to warrant further investigation and often used to address questions related to dose and safety [73]. In the context of blunted BP dipping in shift work, Phase II trials would include strategic napping of different durations during night shifts; 24 h BP measurements as primary outcome; markers of subclinical CVD as secondary efficacy outcomes; and measurements of performance and post-nap sleep inertia as secondary safety outcomes. Well-controlled, randomized trials testing different duration naps and their effect on BP [31, 32, 74] would be an important first step. If such phase II studies are positive, large pragmatic trials (i.e., Phase III trials) in actual shift work settings could follow [73].

The hypothesized relationship between night shift work and blunted BP dipping could be modeled much like the relationship between other workplace exposures that occur over years of work and have previously been linked to poor health outcomes [75–78]. For example, repetitive exposure to loud noise or pesticides in the workplace are recognized as important precursors to disease and morbidity [75–78]. Notably, hearing loss and cancer are not equivalent diseases to CVD. There is great potential to eliminate or mitigate some CVDs, such as hypertension, with treatment or changes in lifestyle habits. In contrast, hearing loss related to workplace exposure may not be reversible, and cancer also related to workplace exposure may not be curable for many. However, much like repetitive exposure to loud noise or pesticides in the workplace, repetitive exposure to blunted BP dipping due to night shift work may contribute in a clinically meaningful way to increased risk of CVD. Thus, mitigating exposure could reduce risk and lead to improved health.

6 | Conclusion

Night shift work is not going away. It is engrained in today's 24 h society, at least for healthcare and public safety workers fundamental to public welfare. Research focused on exposure to blunted BP dipping is necessary to both better understand and intervene upon the mechanisms that underlie increased risk of CVD for night shift workers. With this knowledge, the likelihood of developing pragmatic and effective interventions is increased, and so too is the possibility of improving the health of night shift workers.

Author Contributions

P.D.P. conceived of the work and led acquisition of the literature (data). P.D.P., D.H., M.F.M., D.J.B., and S.E.R. collaborated to analyze and interpret the data for this work, assisted with drafting and revising the manuscript, and approved the version to be published. All authors agree to be accountable for all aspects of this work.

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The authors have nothing to report.

Ethics Statement

Review and approval by an institutional review board was not applicable for this work given the data acquired was existing published literature.

Conflicts of Interest

The authors declare no conflicts of interest.

Disclosure by AJIM Editor of Record

John Meyer declares that he has no conflict of interest in the review and publication decision regarding this article.

Data Availability Statement

The authors have nothing to report.

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