Rotating night shift work and disparate hypertension risk in African–Americans

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Objective **Hypertension disproportionally affects black compared with white Americans, even after accounting for known risk factors. Circadian disruption as encountered by rotating night shift workers has been associated with an increased risk for hypertension. Because blood pressure responds differently to sleep alterations in blacks compared with whites, we hypothesized that rotating night shift work may be a stronger risk factor for hypertension among blacks.**

Methods **We prospectively examined the association between rotating night shift work and the risk of hypertension in 1510 black and 94 142 white female participants of the Nurses' Health Study II who were nonhypertensive at baseline in 1991. We used Cox proportional hazards models to control for potential confounders.**

Results **During 16 years of follow-up (1991–2007), we identified 580 incident cases of hypertension in blacks and 23 360 cases in whites. In blacks, the multivariable hazard ratio for incident hypertension among women who worked rotating night shift for more than 12 months in the previous 2 years was 1.81 [95% confidence interval (CI) 1.14–2.87], compared with those working none. By contrast, in whites, we observed no increase in risk (hazard ratio 0.99, 95% CI 0.93–1.06). The association between shift work and hypertension varied significantly by race (*P* interaction = 0.01). In secondary analyses, the multivariable hazard ratio for incident hypertension in black women who ever performed rotating night shift work was 1.46 (95% CI 1.07–1.99), compared with those never working rotating night shifts. In whites, there was no increase in risk (hazard ratio 0.97, 95% CI 0.93–1.01) (*P* interaction < 0.01).**

Conclusion **Rotating night shift work is independently associated with an increased risk of hypertension in blacks but not in whites. *J Hypertens* 30:61–66 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Keywords: hypertension, race, risk factors, shift work

Abbreviations: DASH, dietary approaches to stop hypertension; METs, metabolic equivalent task scores; NHS II, Nurses' Health Study II

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Introduction

Hypertension disproportionately affects blacks. In the USA, the prevalence of hypertension is 60% higher in the non-Hispanic black population than the non-Hispanic white population after adjusting for traditional risk factors [1]. Hypertension accounts for up to 25% of all deaths among black adults, primarily from cardiovascular and cerebrovascular causes [2,3].

The reasons for this disparity in hypertension risk are not well understood, but physiologic studies suggest that blacks have a more activated sympathetic nervous system, greater endothelial dysfunction, more arterial stiffness, and different renal sodium handling compared with whites [4–12]. It is likely that there are currently unknown environmental factors that influence these physiologic processes, thereby contributing to the hypertension disparity.

Rotating night shift work, presumably by disrupting circadian rhythms, alters sympathetic output (i.e., catecholamines), and the secretion of other hormones such as cortisol, which, in turn, may increase blood pressure [13–15]. Several studies have found associations between rotating night shift work with coronary heart disease and stroke [16–19]. Investigations in Japanese men and in Scandinavian men and women have provided conflicting findings on the association of night shift work and risk of hypertension [20,21]. None of these studies included black individuals. As circadian phase shifting exhibits racial differences [22], we investigated whether the association between rotating night shift work and risk of incident hypertension differed between black and white nurses participating in the Nurses' Health Study II (NHS II).

Methods

Study population

The derivation of the study population for the current analysis is summarized in Fig. 1. The NHS II is a prospective cohort study of 116 430 female registered

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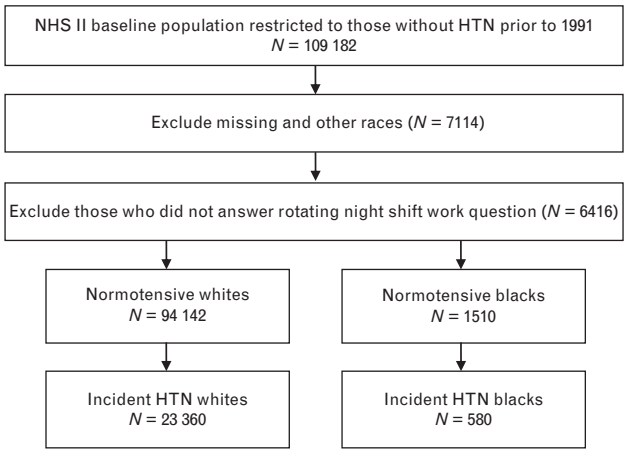
Fig. 1



Assembly of the study population. HTN, hypertension.

nurses who were 25–42 years old when they returned an initial questionnaire in 1989. Subsequent questionnaires have been mailed every 2 years to update information on health related behaviors and medical events. Participants with hypertension at baseline in 1991 were excluded from the analysis. We also excluded women who did not answer the questions about whether or not they performed rotating night shifts. Furthermore, women reporting their race as other than black or white were excluded. After these exclusions, the final study population included a total of 95 652 women, of whom 1510 were black and 94 142 white. In a secondary analysis, we redefined the baseline year as 1989, excluding participants with prevalent hypertension at that time. In this secondary analysis, the study population included 1895 blacks and 100 446 whites. The institutional review board at Brigham and Women's Hospital approved this study. Participants provided implied consent by virtue of voluntarily returning the mailed questionnaires.

Ascertainment of rotating night shift work and race

Detailed information on total years during which the nurse had worked on rotating night shifts was available from the 1989 questionnaire. Between 1991 and 2005, subsequent questionnaires asked women to report how many months they worked rotating night shifts during each 2 year interval: 1989–1991, 1991–1993, and so on. Rotating night shift work was defined as working least three nights per month in addition to days or evenings in that month. The prespecified categories were 'none, 1–4 months, 5–9, 10–14, 15–19, and 20 months or more'. Rotating night shift work was categorized into the following categories: none, between 1 and 11 months during the previous two years, and 12 and 24 months during the previous 2 years. As a secondary analysis, we examined the association between ever working rotating night shift work and hypertension and never working rotating night shift work and hypertension. Additionally, we analyzed cumulative years of rotating night shift work comparing none and each of the following categories: 0 years, 1–4, 5–9, 10–14, and 15 or more years.

Race was ascertained on the 1989 questionnaire. Those who classified their ancestry as 'south European/Mediterranean', 'Scandinavian', or 'other Caucasian' were categorized as white. Those who classified themselves as 'African–American' were categorized as black. Hispanic, Asian, and other ancestry were excluded from the analysis.

Assessment of other factors

Age, BMI (weight in kilograms divided by height in meters squared) in six categories (<21, 21–22, 23–24, 25–29, 30–31, 32+), smoking history (never, past use, current use), physical activity (metabolic equivalent task scores, METs, which are the caloric need per kilogram of body weight per hour of activity divided by caloric need per kilogram of body weight per hour at rest, in quintiles), alcohol intake (grams per day, divided into six categories), a score reflecting dietary adherence to the dietary approaches to stop hypertension (DASH) diet (in quintiles) [23], average number of hours of sleep per 24 h (continuous), menopausal status (categorized into premenopausal and postmenopausal), oral contraceptive use status (never, past use, current use), analgesic use including aspirin, NSAIDs, and acetaminophen (<two times per week, two or more times per week), folate supplementation (percentage using), and history of hypertension in a first-degree relative were considered as potential confounders. Except for family history of hypertension, hours of sleep in 24 h (asked once in 2001), folate supplementation (updated every 4 years), and DASH score (updated every 4 years), information on these confounders was updated with each questionnaire cycle to reflect the most recent available values. DASH scores, which have previously been linked to hypertension, were calculated based on high intake of fruits, vegetables, nuts and legumes, low-fat dairy products, and whole grains, with low intake of sodium, sweetened beverages, and red and processed meats [24,25]). Self-reports of BMI, physical activity, alcohol intake, folate use, and dietary information provided by the food frequency questionnaire were all previously validated [26–31].

Ascertainment of hypertension

The 1989 and biennial follow-up questionnaires inquired about physician diagnosed hypertension and the year of diagnosis. Self-reported diagnosis of hypertension was validated in a randomly selected subset of 147 women in NHS II, among whom 94% had their diagnosis confirmed upon review of medical records [32].

Participants who reported a diagnosis of hypertension on the baseline (1991) questionnaire were considered to

have prevalent hypertension and were, thus, excluded in the primary analysis. Incident cases of hypertension included those who first reported hypertension on subsequent questionnaires, and whose date of diagnosis was after the baseline questionnaire and before 1 June 2007 (the end of follow-up).

Statistical analysis

Covariates except family history of hypertension, hours of sleep in 24 h (asked once), DASH score (updated every 4 years), and supplemental folate use (updated every 4 years) were updated with each questionnaire cycle to reflect the most recent information on rotating night shift work status. For each participant, person-months of follow-up were counted from the date of return of the baseline questionnaire in 1991 (1989 for secondary analysis) to the date of hypertension diagnosis, or among noncases, the date of return of the last questionnaire, and allocated according to exposure status. Participants were censored at the date of death or June 2007, whichever came first. If they did not return the subsequent questionnaires, they were censored at the date the subsequent questionnaire was mailed.

Associations between rotating night shift work [recent (number of months in the last 2 years), ever/never, and cumulative years working rotating night shift] and incident hypertension in blacks and whites were analyzed using Cox proportional hazards regression. Hazard ratios and 95% confidence intervals (95% CI) were calculated. Our final multivariable models included the following potential confounders: age (continuous), BMI (in 6 categories), smoking status (never, past, current), physical activity (METs, in quintiles), alcohol intake (g/day, in 6 categories), DASH diet (quintiles), use of nonnarcotic analgesics (yes/no), supplemental folate supplementation (percentage using), family history of hypertension (yes/no), menopausal status (premenopausal/postmenopausal), oral contraceptive use (never, past, current), and average hours of sleep per day (continuous).

Associations between rotating night shift work and incident hypertension were analyzed separately for blacks and whites. Effect modification between race and rotating night shift work was tested by creating a multiplicative interaction term between race and rotating night shift status and using the likelihood ratio test comparing models with and without the interaction term.

Results

Baseline characteristics

Baseline characteristics of the cohort according to race and rotating night shift work status are reported in Table 1. The prevalence of rotating night shift work in 1991 was higher in black participants (33%) compared with white participants (23%). Blacks also slept fewer hours, had higher BMI values, had lower physical activity scores, and a higher proportion had a family history of hypertension. Whites had higher alcohol intakes, used more analgesics, and smoked more than blacks. Those who worked greater than 12 months of rotating night shifts in the previous 2 years had greater physical activity scores than those working none.

Rotating night shift work and risk of hypertension

In this 16 year prospective study, there were a total of 1510 black females contributing 16 546 person-years for analysis with 580 incident cases of hypertension reported.

Table 1 Baseline characteristics of normotensive women in 1991

	Black women ($n=1510$)			White women ($n=94\,142$)		
Characteristic	0 months[a] 67[b]	>0–12 months[a] 19[b]	>12–24 months[a] 14[b]	0 months[a] 77[b]	>0–12 months[a] 14[b]	>12–24 months[a] 9[b]
Age (years)	37 (4)	36 (5)	36 (5)	36 (5)	35 (5)	35 (5)
Sleep (hours/day)	6 (1)	6 (1)	6 (1)	7 (1)	7 (1)	7 (1)
BMI (kg/m^2)	26 (5)	27 (6)	28 (7)	24 (5)	25 (5)	25 (6)
Alcohol (g/day)	2 (6)	2 (4)	2 (3)	3 (6)	3 (6)	3 (6)
Physical activity (METs/week)	19 (27)	18 (27)	25 (38)	21 (26)	22 (28)	24 (32)
DASH score [8–40]	23 (5)	22 (5)	24 (5)	24 (5)	24 (5)	23 (5)
Family history of hypertension (%)	65	65	61	50	50	50
Folate supplementation use (%)	46	41	48	42	45	43
Postmenopausal (%)	5	4	6	3	3	4
Oral contraceptive use						
Never (%)	15	10	11	15	14	14
Past (%)	75	79	77	75	73	74
Current (%)	10	11	12	10	13	12
Analgesic use						
Aspirin $\geq$ 2 days/week (%)	7	4	6	11	12	12
Acetaminophen $\geq$ 2 days/week (%)	17	14	18	20	24	25
NSAIDs $\geq$ 2 days/week (%)	14	11	11	18	22	22
Smoking status						
Never (%)	71	73	73	66	63	63
Past use (%)	16	11	14	23	22	21
Current use (%)	13	16	13	11	16	16

Data are presented as mean (standard deviation) or percentages. DASH, dietary approaches to stop hypertension; METs, metabolic equivalent task scores. [a] Rotating night shift work in prior 2 years. [b] Percentage in each category.

There were 94 142 white females contributing a total of 1 280 010 person-years with 23 360 incident cases of hypertension reported.

Associations between categories of recent rotating night shift work and hypertension risk are displayed by race in Table 2. White women who worked greater than 12 months rotating night shifts in the previous 24 months had a moderately increased risk of incident hypertension compared with white women who never worked rotating night shifts in age-adjusted models (hazard ratio 1.11, 95% CI 1.05–1.17). However, this association was no longer present after controlling for standard hypertension risk factors (hazard ratio 0.99, 95% CI 0.93–1.06). In whites, the strongest (positive) confounder was BMI.

In black women, greater than 12 months compared with no rotating night shift work in the previous 2 years showed an increased risk of incident hypertension (hazard ratio 1.40, 95% CI 1.01–1.93) after adjusting for age. After controlling for known risk factors for hypertension, there was a significant and independent association between working rotating night shifts and hypertension (hazard ratio 1.81, 95% CI 1.14–2.87) comparing those working greater than 12 months with those working none in the previous 2 years. In blacks, the strongest (negative) confounder was hours of sleep. Effect modification by race was statistically significant (P interaction = 0.01).

Our secondary analysis (Table 3) examining the association between ever working rotating night shifts showed an independent association in blacks but not in whites. The hazard ratio in multivariable models comparing black women who ever worked rotating night shifts with black women who never worked rotating night shifts was 1.46 (95% CI 1.07–1.99). There was no association in whites (P interaction < 0.01). When we analyzed cumulative rotating night shift work (starting in 1989) in categories (never, 1–4, 5–9, 10–14, and 15 or greater years), the P trend was near statistical significance at 0.07 in blacks with no association observed in whites.

Table 3 Ever compared to never rotating night shift work[a] and hypertension risk by race

Rotating night shift work	Never	Ever
Black (n = 1895)		
Person-years	13 730	6112
Cases (655)	469	186
Age-adjusted HR (95% CI)	1.0 (reference)	1.16 (0.93, 1.44)
MV-adjusted[b] (95% CI)	1.0 (reference)	1.46 (1.07, 1.99)
White (n = 100 446)		
Person-years	1 150 355	301 785
Cases (24 399)	20 504	3895
Age-adjusted HR (95% CI)	1.0 (reference)	1.08 (1.04, 1.12)
MV-adjusted[b] HR (95% CI)	1.0 (reference)	0.97 (0.93, 1.01)

CI, confidence interval; HR, hazard ratio. [a]Rotating night shift work assessed starting 1989. [b]Multivariable adjusted for age, BMI, alcohol intake, physical activity, family history of hypertension, DASH score, hours of sleep per day, menopausal status, oral contraceptive use, analgesic use, folate supplementation, and smoking status.

Discussion

Over 16 years of prospective follow-up, we found that working rotating night shifts and the risk of hypertension among black nurses, but not among white nurses. To our knowledge, this is the first study to examine racial differences in the association between rotating night shift work and long-term incident hypertension risk.

Shift work has been implicated as an independent risk factor for cardiovascular disease [17,19,33,34]. The literature dealing with shift work and hypertension, however, is conflicting. Studies of Japanese men showed positive associations between rotating night shift work and hypertension risk [21,35]. For example, in a cohort of 5 338 steel workers, there was a modestly elevated risk of hypertension in rotating shift workers [relative risk (RR) 1.10, 95% CI 1.01–1.20], whereas in a study of 1 551 manual factory laborers, a higher risk of hypertension among shift workers was present only in the youngest compared with the oldest group (RR 3.60, 95% CI 1.41–9.10 vs. RR 1.20, 95% CI 0.55–2.70). In contrast, a large prospective Finnish study showed no association between shift work and hypertension [20]. In this Finnish study, shift work was ascertained in 1975 and 1981, whereas the ascertainment of hypertension occurred

Table 2 Rotating night shift work in previous 2 years and hypertension risk by race

Rotating night shift work in prior 2 years	0 months	1–11 months	12–24 months
Black (n = 1510)			
Person-years	12 714	2303	1529
Cases (580)	450	67	63
Age-adjusted HR (95% CI)	1.0 (reference)	0.94 (0.68, 1.29)	1.40 (1.01, 1.93)
MV-adjusted[a] HR (95% CI)	1.0 (reference)	1.20 (0.79, 1.82)	1.81 (1.14, 2.87)
White (n = 94 142)			
Person-years	1 083 909	112 347	83 754
Cases (23 360)	20 097	1820	1443
Age-adjusted HR (95% CI)	1.0 (reference)	1.07 (1.02, 1.13)	1.11 (1.05, 1.17)
MV-adjusted[a] HR (95% CI)	1.0 (reference)	0.97 (0.92, 1.02)	0.99 (0.93, 1.06)

CI, confidence interval; DASH, dietary approaches to stop hypertension; HR, hazard ratio; MV, multivariable. [a]Multivariable adjusted for age, BMI, alcohol intake, physical activity, family history of hypertension, DASH score, hours of sleep per day, menopausal status, oral contraceptive use, analgesic use, folate supplementation, and smoking status.

much later in 2003, possibly introducing bias into the analysis. Additionally, this study queried workers as to whether their jobs involved shift work *per se*, but did not specify whether the shift work required rotating nights and days; only the latter would putatively disrupt circadian rhythms and, hence, exposure misclassification might be another explanation for their null finding.

Normal sleep decreases sympathetic nerve activity, blood pressure, and heart rate [36]. Rotating night shift work alters the circadian biology of blood pressure that can potentially lead to hypertension in susceptible individuals. Although the mechanisms whereby circadian disruption may increase blood pressure are not thoroughly elucidated, several possible mechanisms have been proposed. First, circadian disruption increases sympathetic output. In a sleep deprivation study, both mean 24-h blood pressure and heart rate were higher during the following day compared with routine days not preceded by sleep deprivation; in addition, urinary excretion of norepinephrine increased significantly at night during sleep deprivation [37]. Second, circadian disruption leads to reduced melatonin production [38,39], and low melatonin levels have been associated with an increased risk of hypertension [40]. Third, disruption of circadian rhythms may alter the renin–angiotensin–aldosterone axis. For example, mice lacking the *Cry-1* and *Cry-2* genes develop salt-sensitive hypertension due to the abnormal production of aldosterone [41]. The *Cry* gene encodes a transcription factor that is integrally related to circadian periodicity [42], and *Cry* disruption also leads to circadian disorders such as inhibition of negative feedback to circadian genes that regulate gluconeogenesis [43,44]. *Cry*-null mice were found to have elevated levels of an enzyme (type VI β-hydroxyl-steroid dehydrogenase, or Hsd3b6) that is exclusively expressed in aldosterone-producing cells and is under transcriptional control of the circadian clock. The enhanced enzymatic activity of Hsd3b6 subsequently led to increased aldosterone production. Taken together, altering circadian rhythms via rotating night shift work may increase blood pressure via enhanced sympathetic output, decreased melatonin production, and/or enhanced mineralocorticoid activity.

We found that the association between rotating night shift work and incident hypertension varied significantly by race. Racial differences in the circadian biology of blood pressure may account for these findings. It is well established that blood pressure exhibits a circadian variation, with a nighttime dip in blood pressure and subsequent rise in the morning hours [45]. Several studies have found that nocturnal dipping is blunted in blacks [46–50], and that this phenomenon is not explained by racial differences in dietary patterns [50]. One study showed that blacks have a decreased baroreceptor response during sleep compared with whites [51]. Not only do blacks have different circadian blood pressure changes compared with whites, their blood pressure patterns also appear to respond more adversely to disruptive stimuli. For example, in the Work Site Blood Pressure study, rotating night shift work blunted nocturnal dipping to a greater degree (by 6 mmHg systolic) in blacks compared with whites, indicating blunted nocturnal inhibition of the sympathetic nervous system in blacks [52]. Blacks may, thus, represent a population particularly vulnerable to shift work-associated alterations in blood pressure.

Our study has limitations. Hypertension was self-reported and direct blood pressure measurements were not taken. This may have led to misclassification of a few truly hypertensive individuals as being classified as normotensive; however, this misclassification is likely nondifferential in nature and would, thus, tend to diminish the magnitude of the hazard ratio in both blacks and whites. Additionally, all of our participants were nurses and hypertension has been validated in our cohort [32]. Rotating night shift work was also self-reported and subject to misclassification. Again, the resulting misclassification would likely diminish the hazard ratio in both racial groups and our findings may, thus, be an underestimate of the true association. Third, socioeconomic factors may play a role in the disparate hypertension risk in blacks [53,54], and we did not directly adjust for socioeconomic status; however, our cohort consists of nurses who have similar educational backgrounds and, presumably, income. Fourth, we are unable to comment on whether the risk of rotating night shift work on hypertension is reversible once stopping rotating night shift work. Additionally, we were not able to examine changes in metabolic biomarkers (i.e., blood glucose, serum aldosterone, serum norepinephrine). Further studies on measured biomarkers would be helpful to demonstrate potential mechanistic pathways between rotating night shift work and hypertension. Finally, the participants in our cohort (female nurses) do not represent a random sample of the US population, so the findings may, thus, not be generalizable to the entire population. The findings also cannot be extrapolated to all black and all white persons.

Strengths of our study include its large size, prospective information on all important covariates, and close to complete follow-up.

In conclusion, rotating night shift work is associated with an increased risk for hypertension incidence in blacks but not in whites. Potential mechanisms should be elucidated with physiologic studies. Circadian disruption may be a novel risk factor contributing to the disparity in hypertension prevalence between the two racial groups.

Acknowledgement

Conflicts of interest

There are no conflicts of interest.

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