Shift Work at Young Age Is Associated with Elevated Long-Term Cortisol Levels and Body Mass Index

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Background: The incidence of obesity and other features of the metabolic syndrome is increased in shift workers. This may be due to a misalignment between the internal circadian rhythm and the behavioral rhythm. The stress hormone cortisol could play a role in this phenomenon because it is secreted in a circadian rhythm, and long-term elevated cortisol leads to components of the metabolic syndrome. We compared cortisol levels in scalp hair of shift and day workers to study changes in long-term cortisol due to shift work.

Methods: Hair samples were collected from 33 shift workers and 89 day workers. Cortisol was extracted from the hair samples with methanol, and cortisol levels were measured using ELISA. Height and weight were measured, and body mass index (BMI) was calculated.

Results: Shift workers had higher hair cortisol levels than day workers: 47.32 pg/mg hair [95% confidence interval (CI) = 38.37–58.21] *vs.* 29.72 pg/mg hair (95% CI = 26.18–33.73) ($P < 0.001$). When divided in age groups based on the median age, elevated cortisol levels were present only in younger shift workers: 48.53 pg/mg hair (95% CI = 36.56–64.29) *vs.* 26.42 pg/mg hair (95% CI = 22.91–30.55) ($P < 0.001$). BMI was increased in younger shift workers as well: 27.2 (95% CI = 25.5–28.8) *vs.* 23.7 (95% CI = 22.8–24.7) in young day workers ($P = 0.001$). Hair cortisol and BMI were positively correlated ($\beta = 0.262$; $P = 0.005$).

Conclusion: Shift work at a young adult age is associated with elevated long-term cortisol levels and increased BMI. Elevated cortisol levels and BMI may contribute to the increased cardiovascular risk found in shift workers. **(*J Clin Endocrinol Metab* 96: E1862–E1865, 2011)**

Shift work, defined as work performed primarily outside standard working hours, has been associated with increased incidences of obesity and other features of the metabolic syndrome, such as hypertension, hyperlipidemia, and insulin resistance, ultimately leading to an increased incidence of cardiovascular disease (1–3). It is hypothesized that these health problems in shift workers are caused by misalignment between the endogenous circadian system and the behavioral cycles (4, 5). One of the factors that could play a role in the development of the metabolic syndrome in shift workers is the stress hormone cortisol. Cortisol is secreted in a circadian rhythm with high levels in the early morning and low levels in the evening and night. Pathologically high levels of cortisol are associated with abdominal obesity, insulin resistance, hypertension, and dyslipidemia, all features of the metabolic syndrome (6, 7). Changes in behavioral cycles due to shift work could result in disruption of the circadian rhythm of cortisol secretion, resulting in hyperactivity of the hypothalamic-pituitary-adrenal axis, leading to long-term elevated cortisol levels. Several studies have investigated cortisol rhythms in shift workers and found that the cortisol awakening response is decreased and evening cortisol levels are increased during shift work (8–10). Whether these

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Abbreviations: BMI, Body mass index; CI, confidence interval.

changes in the cortisol secretion result in long-term changes in cortisol exposure has not been studied, probably because there was no suitable method to measure long-term cortisol levels. Recently, a novel method was developed to measure long-term cortisol levels in scalp hair, with 1 cm of hair representing a period of approximately 1 month (11–13). This method is very suitable to evaluate changes in cortisol levels in shift workers over a prolonged period of time. Our aim was to investigate long-term hair cortisol levels in shift workers in comparison with individuals working only during the day. In addition, we hypothesized that body mass index (BMI) is higher in shift workers and is correlated to long-term cortisol levels.

TABLE 1. Group characteristics

	Day workers (n = 89)	Shift workers (n = 33)
Age (yr)	33 (19–63)	41 (27–62)[a]
Caucasian ethnicity	83 (94.3%)	25 (75.8%)[b]
Frequency of hair wash		
≤2 times/wk	22 (25%)	2 (6.3%)[a]
≥3 times/wk	66 (75%)	30 (93.8%)[a]
Use of hair products	47 (52.8%)	13 (40.6%)
BMI (kg/m^2)	24.6 (18.4–34.6)	27.0 (19.2–33.9)[b]
Duration of shift work (yr)		7 (2–42)

Data are shown as median (range) or number (percentage).

[a] $P < 0.05$.

[b] $P < 0.01$.

Subjects and Methods

Subjects

Fifty male shift workers from a textile factory in The Netherlands were asked to participate in this study. Seventeen of them were excluded due to glucocorticoid use or insufficient hair growth at the posterior vertex. All 33 remaining participants worked in the same factory and were working in a fast-forward rotating shift schedule. The morning shift started at 0600 h and continued to 1400 h, the afternoon shift started at 1400 until 2230 h, and the night shift started at 2230 until 0600 h. All participants worked continuously 2 d on the morning shift, 2 d on the evening shift, and 2 d on the night shift with 4 d of rest after the night shift. After the rest days, they started again with 2 d of day shift, *etc.* Age at the start of working in shifts and the number of years in shift work were documented.

As a control group, we used the 89 healthy men from our previous study (13). All subjects worked only during the day and did not use glucocorticoids. From both shift and day workers, height and weight were measured and BMI was calculated. This study was approved by the Medical Ethical Committee, and all participants gave written informed consent.

Hair collection, preparation, and analysis

A detailed description of the methods used to measure cortisol in scalp hair can be found elsewhere (12, 13). In brief, hair samples were cut from the posterior vertex of the scalp, as close to the scalp as possible. The most proximal 3 cm of the hair strands were used, corresponding roughly to a period of 3 months. Cortisol was extracted from the hair samples by overnight incubation in methanol. After incubation, methanol was evaporated under a stream of nitrogen, and the samples were dissolved in PBS (pH 8.0). Cortisol was measured using a salivary ELISA cortisol kit (DRG Instruments GmbH, Marburg, Germany).

Statistical analysis

Statistical analyses were performed with SPSS version 17.0 and GraphPad Prism version 5.0. Mann-Whitney *U* tests and χ^2 tests were used to determine differences in group characteristics. Cortisol levels were log transformed to obtain a normal distribution. Analysis of covariance was used to investigate differences in cortisol levels between shift workers and day workers. Linear regression was used to determine correlations between cortisol and BMI.

Results

Group characteristics are shown in Table 1. Shift workers were significantly older, washed their hair more frequently, and had a higher BMI than day workers. Mean hair cortisol levels were significantly higher in the shift workers than in the day workers: 47.32 pg/mg hair [95% confidence interval (CI) = 38.37–58.21] *vs.* 29.72 pg/mg hair (95% CI = 26.18–33.73) ($P < 0.001$). After adjustment for age, BMI, and frequency of hair washing, this difference remained significant ($P = 0.01$). Because the age of shift workers and day workers was significantly different, we divided both groups into two subgroups based on the median age (41 yr) of the shift workers. With no individuals aged 40, the subgroups were under 40 yr of age and over 40 yr of age. In the group under 40 yr of age, hair cortisol levels were significantly higher in the shift workers (n = 14) than in the day workers (n = 54) [48.53 pg/mg hair (95% CI = 36.56–64.29) *vs.* 26.42 pg/mg hair (95% CI = 22.91–30.55), $P < 0.001$], also after adjustment for age, BMI, and frequency of hair wash ($P = 0.004$). However, in the older group, there were no significant differences in hair cortisol levels between shift workers (n = 19) and day workers (n = 35) ($P = 0.171$ unadjusted) (Fig. 1). We found no correlations between cortisol and age at the start of working in shifts ($P = 0.376$) and duration of working in shifts ($P = 0.476$).

BMI was significantly higher in the shift workers compared with day workers. When divided into age subgroups, this difference was present only in the younger group. Young shift workers had a mean BMI of 27.2 kg/m^2 (95% CI = 25.5–28.8), whereas young day workers had a mean BMI of 23.7 kg/m^2 (95% CI = 22.8–24.7) ($P = 0.001$). At an older age, there was no difference in

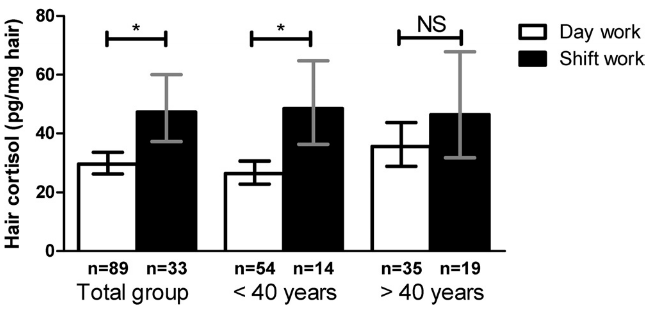

FIG. 1. Long-term cortisol levels in shift workers and day workers in total and divided into age groups, based on the median age of shift workers. *, $P < 0.001$ (unadjusted). NS, Not significant. Data are shown as geometric mean with 95% CI.

BMI between both groups ($P = 0.508$). Because we found a similar pattern for BMI and hair cortisol, with the main difference between young day and shift workers, we investigated whether there was an association between hair cortisol and BMI in this group. We found a significant positive correlation between cortisol and BMI with $\beta = 0.262$ ($P = 0.005$ unadjusted, and $P = 0.01$ after adjustment for age). Furthermore, when the total group was divided into groups based on BMI classification with normal individuals having a BMI under 25 kg/m^2, overweight individuals with a BMI of 25–30 kg/m^2, and obese individuals with a BMI over 30 kg/m^2, we found that cortisol increased significantly through the groups, with a mean cortisol level of 31.26 pg/mg hair (95% CI = 26.79–36.48) in individuals with a normal BMI, a cortisol of 36.06 pg/mg hair (95% CI = 30.48–42.76) in overweight individuals, and 60.95 pg/mg hair (95% CI = 43.95–84.72) in obese individuals ($P = 0.002$).

Discussion

The main finding of our study is that long-term cortisol levels, measured in scalp hair, are significantly increased in individuals working in shifts, especially in the group younger than 40 yr of age. At an older age, there is no difference in hair cortisol levels between shift and day workers. The same pattern was found for BMI, with higher BMI in young shift workers compared with young day workers and no difference in BMI at an older age. Hair cortisol levels and BMI were positively correlated.

Our results indicate that the previously documented changes in circadian rhythm of cortisol secretion in shift workers (8–10) result in a long-term elevation of cortisol levels. This appears to be especially the case in the younger group of shift workers, which may be important, because long-term elevated cortisol levels and obesity at a younger age can contribute significantly to increased cardiovascular risk at an older age. Hair cortisol levels in shift and day workers at an older age were similar, suggesting that older individuals working in shifts suffer less from stress or adjust better to shift work than younger individuals, resulting in a habituation to the alterations in the hypothalamic-pituitary-adrenal axis. This contrasts with the general hypothesis that the tolerance to shift work decreases with age. Several studies investigating this issue report inconclusive results. Some studies found no effect of age on the tolerance to shift work (14, 15), and other studies have shown a decreased tolerance in older shift workers (16, 17). These contrasting findings may be caused by the differences in study population and outcome measurements used in these studies. In our study, we measured long-term cortisol levels, a biological marker for chronic stress, and we did not find differences between older day workers and shift workers. This may theoretically be explained by selection of individuals who have a higher tolerance for shift work and therefore still work in shifts at an older age, whereas individuals who cannot adjust to shift work already stopped working in shifts at a younger age. A negative correlation between hair cortisol and number of years working in shifts would support this hypothesis. However, we did not see this in our study group. Another explanation for the lack of increased cortisol levels in older shift workers could be that the impact of shift work on the circadian rhythm is not as strong in older individuals as in younger individuals, because the circadian rhythm and sleep pattern change during aging.

Our finding of increased long-term hair cortisol levels in shift workers is of particular importance, because cortisol may contribute to the increased prevalence of obesity and cardiovascular risk that is found in shift workers. This finding is supported by our observation of an increased BMI in shift workers and the positive correlation between hair cortisol and BMI. Interestingly, our shift workers all worked in a fast-forward shift schedule, which is supposed to be less deleterious than backward shift schedules (18, 19). The changes in long-term cortisol might be even more abundant in shift workers working in other schedules.

Unraveling the role of cortisol in the health problems found in shift workers could result in new approaches to prevent cardiovascular damage in this specific group. However, our study was limited by a relatively small number of shift workers and lack of data concerning diet, exercise, education level, social economic status, perceived stress, and different shift schedules. Nevertheless, the differences found between day workers and shift workers may be of significance, and more research is needed to truly reveal the role of cortisol and its potential negative effects in shift workers.

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