

In Body-Clock Genes Working Nights for Years is Linked to Changes

Researchers examined peripheral circadian gene expression and transcriptional network changes associated with night-shift exposure among female [healthcare workers](#) (HCWs).



Study

The cross-sectional study enrolled 93 female HCWs aged 37-66 years, including 47 day-shift workers (DSWs) with no previous night-shift history and 46 [night-shift workers](#) (NSWs). Participants followed the same shift schedule for at least 6 months.

Night work included ≥ 3 hours between midnight and 5:00 a.m. Among NSWs, duration, cumulative shifts, and recent activity were recorded. Participants underwent occupational and clinical assessments, including reproductive history, lifestyle factors, sleep characteristics, and [body mass index](#) (BMI).

Ribonucleic acid (RNA) was extracted from morning fasting blood samples. In these samples, the expression of clock circadian regulator (CLOCK), thyrotrophic embryonic factor (TEF), period circadian clock 1 (PER1), period circadian clock 3 (PER3), and YY1 transcription factor (YY1) was quantified using reverse transcription-quantitative [polymerase chain reaction](#) (RT-qPCR).

[Cycle threshold](#) (Ct) values were analyzed using comparative Ct analysis with actin beta (ACTB) as the housekeeping gene, and results were expressed as log2 fold change (log2FC). A Clock Gene Expression Score (CGES) combined CLOCK, PER1, PER3, and TEF values. Group comparisons, regression, receiver operating characteristic (ROC) analyses, correlation testing, principal component analysis (PCA), and hierarchical clustering were performed; multiple testing used Benjamini-Hochberg false discovery rate (FDR) correction.

Results

Age and [BMI distributions](#) were similar between DSWs and NSWs. Among NSWs, 54% had 13-35 years of night-shift exposure and 57% had accumulated at least 1,000 lifetime night shifts.

About 43% of NSWs reported recent night-shift activity. Poor or very poor sleep satisfaction was more common among NSWs (54% vs. 40%), while [sleep duration](#) was slightly lower, with a borderline difference between groups.

[Peripheral expression](#) of CLOCK, TEF, and PER1 was significantly lower in NSWs than DSWs, whereas PER3 did not differ. The CGES was also lower in NSWs. Multivariable analyses indicated that the measured clinical and lifestyle factors explained only a limited proportion of variation in gene expression, with stronger evidence for associations involving TEF and PER1 than CLOCK or PER3.

[Alcohol consumption](#) was negatively associated with TEF, while BMI and smoking were positively associated with PER1. Other examined covariates were not significantly associated with gene expression.

Among the individual genes, TEF most clearly distinguished night-shift workers from day-shift workers, followed by PER1 and CLOCK, while PER3 showed little discriminatory ability. Hierarchical clustering placed CLOCK, TEF, and PER1 in one [gene cluster](#), with PER3 on a separate branch.

PCA showed partial separation between groups, driven mainly by PER1, TEF, and CLOCK. Combining the four [genes](#) improved the ability to distinguish between the two groups.

TEF correlated strongly with PER1, while PER1, TEF, and CLOCK were strongly associated with CGES. Sleep duration correlated positively with TEF and CGES, whereas [sleep dissatisfaction](#) correlated negatively with both.

Correlation structures differed between DSWs and NSWs, with weaker overall connectivity among several gene pairs in NSWs, particularly involving CLOCK. Longer night-shift duration was associated with lower CLOCK and TEF expression, while high cumulative exposure was associated with lower [TEF expression](#).

Recent [night-shift activity](#) was not associated with significant differences in individual gene expression.

[YY1 expression](#) was significantly lower in NSWs than DSWs and was also lower among workers with long-term or high cumulative exposure. YY1 alone showed modest ability to distinguish night-shift workers from day-shift workers, while combining it with TEF improved discrimination.

An exploratory model incorporating all five genes performed particularly well at distinguishing the groups, but it was developed and evaluated in the same cohort and not independently validated. In an exploratory analysis of five NSWs with previous [breast cancer](#), the night-shift-associated expression pattern was largely preserved. Still, the small subgroup prevented firm conclusions about breast cancer-related differences.

Conclusion

Chronic night shift work among female HCWs was associated with altered peripheral expression of several [circadian genes](#), including CLOCK, TEF, PER1, and YY1. PER3 expression did not differ significantly between groups, but its relationships within the transcriptional network appeared altered.

TEF and YY1 showed particularly strong relationships with longer-term and cumulative night-shift exposure. Network analyses also indicated altered coordination among [circadian transcripts](#) in NSWs.

The cross-sectional design prevents conclusions about causality or the timing of these changes. The lack of direct measures of circadian phase, the relatively [small sample size](#), and the absence of independent validation also limit the findings' generalizability.

Importantly, peripheral blood gene expression provides an incomplete measure of systemic circadian regulation and may not reflect changes in other tissues. Because the researchers did not measure internal circadian phase, they could not distinguish persistent transcriptional changes from differences related to the biological timing of [blood collection](#).

The classification analyses were exploratory and were not designed to predict future disease or other clinical outcomes. The researchers also could not determine whether the transcriptional changes reflected harmful disruption or a compensatory response to repeated circadian stress. Longitudinal and mechanistic studies are necessary to determine whether these changes in gene expression are persistent, reversible, or relevant for future [health outcomes](#).

Source:

<https://www.news-medical.net/news/20261005/Working-nights-for-years-is-linked-to-changes-in-body-clock-genes.aspx>