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# Shiftwork and Metabolic Dysfunction

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Many of the health problems that are more prevalent among shiftworkers are thought to be linked to their heightened susceptibility to metabolic syndrome, i.e., the association of even moderate degrees of visceral obesity, dyslipidemia, abnormal blood pressure, and serum glucose levels in the same individual. Although previous studies have identified associations between shiftwork and metabolic syndrome, there is relatively little evidence to date of how the risk of developing it varies as a function of exposure to shiftwork. The current study seeks to confirm earlier findings of an association between shiftwork exposure and metabolic dysfunction, and to examine the impact of exposure duration, while adjusting for a number of covariates in the analyses. The analyses were based on data from VISAT, a study involving the measurement of physiological, behavioral, and subjective outcomes from 1757 participants, 989 being current or former shiftworkers. The sample comprised employed and retired wage earners, male and female, who were 32, 42, 52, and 62 yrs old. The first analysis sought to confirm previous findings of an association between exposure to shiftwork and the risk of developing metabolic syndrome. It indicated that participants who were or who had previously been shiftworkers (i.e., working schedules that involved rotating shifts; not being able to go to bed before midnight; having to get up before 05:00 h; or being prevented from sleeping during the night) were more likely to exhibit symptoms of metabolic syndrome, after adjusting for age, sex, socioeconomic status, smoking, alcohol intake, perceived stress, and sleep difficulty (odds ratio [OR] 1.78; 95% confidence interval [CI] 1.03–3.08). The results suggest the association between shiftwork and metabolic syndrome cannot be fully accounted for by either higher levels of strain or increased sleep difficulty among shiftworkers, although it remains a possibility that either one or both of these factors may have played a contributing role. The second analysis addressed the issue of duration of exposure to shiftwork. Participants with >10 yrs' experience of working rotating shifts were more likely to exhibit symptoms of metabolic syndrome than participants without exposure to shiftwork, i.e., dayworkers, even after adjusting for age and sex (OR 1.96; 95% CI 1.03–3.75). Thus, the current study confirms the association between shiftwork exposure and metabolic syndrome. It also provides new information regarding the time course of the development of the illness as function of exposure duration, although this was only examined in relation to rotating shiftwork. It is concluded that those responsible for monitoring workers' health should pay particular attention to indices of metabolic dysfunction in workers who have been exposed to shiftwork for >10 yrs. (Author correspondence: p.t.tucker@swansea.ac.uk)

**Keywords:** Health, Metabolic syndrome, Shiftwork, Sleep, Stress

## INTRODUCTION

Shift workers have up to 40% higher risk of developing cardiovascular disease (CVD) than comparable dayworkers (see reviews by Bøggild & Knutsson, 1999; Frost et al., 2009; Kristensen, 1989). They are also more likely to suffer obesity, peptic ulcers, gastrointestinal problems, and failure to control their blood sugar levels (Knutsson, 2003). Recent reviews (Esquirol et al., 2011; Lowden et al., 2010) have noted that many of these health problems are thought to be linked to heightened susceptibility of shiftworkers to metabolic syndrome, i.e., the association of even moderate degrees of visceral obesity, dyslipidemia, abnormal blood pressure, and serum glucose levels in the same individual, compared to dayworkers. Metabolic syndrome is associated with an almost 2-fold increase in risk for coronary heart disease (Guize et al., 2008), a 2- to 3-fold increase in risk for ischemic stroke (Kurl et al., 2006), and an even greater risk of diabetes (Hanley et al., 2005).

One of the earlier studies to examine the link between shiftwork and metabolic syndrome was a population-based (N = 27 485) cross-sectional one conducted in Sweden by Karlsson et al. (2001). These investigators

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identified associations between shiftworking (broadly defined) and certain symptoms of metabolic syndrome, namely obesity, high triglycerides, and low high-density lipoprotein (HDL) cholesterol. Karlsson et al. (2003) subsequently replicated these findings in another cross-sectional study, this time involving a sample of rotating shiftworkers of the Swedish paper industry. More recently, Biggi et al. (2008) identified links between permanent night work and certain symptoms of metabolic syndrome, i.e., higher triglycerides and total cholesterol, in a retrospective longitudinal study of municipal workers in Italy. However, this study found no differences in levels of hypertension or glucose intolerance between night and dayworkers. De Bacquer et al. (2009) reported a population-based prospective study of employees of several large Belgian companies, in which rotating shiftwork was found to be associated with increased risk of developing metabolic syndrome over a median of 6.6-yr follow-up period. Pietroiusti et al. (2010) conducted a prospective study in which they followed a large sample of Italian health workers over a 4-yr period and found that the risk of developing metabolic syndrome was strongly associated with working nights. Most recently, Li et al. (2011) conducted a large-scale longitudinal study over 3 yrs in Japan, where they found that shiftworkers had a significantly higher risk (odds ratio [OR] 1.87; 95% confidence interval [CI], 1.13-3.08) than dayworkers of developing metabolic syndrome.

Several hypotheses have been proposed to explain the link between shiftwork and CVD (Puttonen et al., 2010). Sleep disturbance has been suggested as an important factor, although evidence for this remains somewhat limited. Supportive evidence was provided by Violanti et al. (2009), who conducted a small-scale study of US police officers; those working midnight shifts in combination with either short sleep or overtime were identified as being at increased risk of having metabolic syndrome. It also remains to be clearly established how the duration of exposure to shiftwork impacts on the risk of developing metabolic syndrome. This is a key issue, as identifying the time course of the development of illness is important for determining appropriate follow-up procedures for exposed workers and for the development of prevention strategies.

The current study seeks to determine whether there is an association between shiftwork experience and incidence of metabolic syndrome, while adjusting for a number of covariates, including sleep disturbance and work-related stress. The first analysis will compare incidence rates of metabolic syndrome among dayworkers, i.e., those with no experience of shiftwork, and those who are either current or former shiftworkers. The second analysis will build on the findings of previous studies by examining, for the first time, how the risk of developing metabolic syndrome varies as a function of duration of exposure to shiftwork. It will seek to determine whether risk increases in relation to the duration of exposure by comparing three groups, defined in terms of how much experience they have in years of working shifts.

## METHODS

The data were taken from the first phase of the VISAT study (for further details on the methods and aims of this study, see Marquié et al., 2002). The initial sample was composed of 3232 present and former wage earners born in 1964, 1954, 1944, or 1934. At the time of study they were 32, 42, 52, or 62 yrs old. Eighty three percent of the participants born in 1934 were retirees. Participants were randomly drawn from the client list of 94 occupational physicians, who volunteered for VISAT, in three southern regions of France. The data were obtained during the participants' mandatory annual check-up (retirees were invited to attend specifically for the purposes of taking part in the study). The participation rate was 76%. Data were collected during the yearly medical examination, which formed part of the health screening program that took place within the employing organization. Questionnaires were self-administered but validated by a face-to-face interview. Retired workers, who were no longer monitored by the occupational physicians, were invited specially for the purpose of the study. The VISAT project was approved by the French National Committee for Computer Data and Individual Liberties, and all procedures were compatible with international standards pertaining to human research (Portaluppi et al., 2010).

The participants were asked four questions to determine whether they were on some form of shift system for >50 d/yr). The questions were (i) whether they were rotating shiftworkers; (ii) whether their work schedule did not allow them to go to bed before midnight; (iii) whether their work schedule resulted in their having to get up before 05:00 h; and (iv) whether their work schedule prevented them sleeping during the night. There were three possible responses for each question, namely, "yes, currently" (now), "not now, but yes in the past" (past), or "never" (never). In the present paper those who answered "yes currently" or "in the past" to any of these four questions were considered to be working, or to have previously been working, on some form of shift system and are referred to as "shiftworkers" from hereon. Those with no experience of shiftwork are defined as "dayworkers." For each of the four questions, participants were also asked for how many years in total they had worked such a schedule. For the purposes of the second analysis (see below), participants were classified with respect to the number of years they had worked rotating shifts (never worked rotating shifts or any of the other three forms of shiftwork described above, i.e., only ever a dayworker; 1–10 yrs; >10 yrs).

Clinical measures obtained during the medical examination included blood pressure, heart rate, weight, and height. Information was also obtained on a range of medical parameters, including all past and present diseases. This information was used to classify participants in terms of being either very likely or very unlikely, to be suffering from metabolic syndrome. Classification

was based on the criteria specified by the International Diabetes Federation (2006), namely, central obesity plus any two of the following: raised triglycerides; reduced HDL cholesterol; raised blood pressure; raised fasting plasma glucose. The current data set lacked measures of HDL cholesterol. Hence, participants were classified as being highly likely sufferers of metabolic syndrome if they had a body mass index (BMI) >30, and if, in addition, they met any two of the following criteria: (i) a diagnosis of dyslipidemia either now or in the past (triglycerides >2.0 g/L); (ii) systolic blood pressure >130 mm Hg, or diastolic blood pressure >85 mm Hg, or a diagnosis of hypertension now or in the past; (iii) a diagnosis of type 2 diabetes either now or in the past. Conversely, participants were classified as being highly unlikely sufferers of metabolic syndrome if they had a BMI ≤30 and met all of the following criteria: (i) no diagnosis of dyslipidemia neither now nor in the past; (ii) systolic blood pressure ≤130 mm Hg, diastolic blood pressure ≤85 mm Hg, and no diagnosis hypertension neither now nor in the past; (iii) no diagnosis of type 2 diabetes neither now nor in the past. Participants who could not be classified according to these criteria were excluded from the analyses that follow, which resulted in a final sample of 1757 participants. Table 1 provides a cross-tabulation of shiftwork experience (current or former shiftworkers vs. dayworkers and current or former rotating shiftworkers with 1–10 yrs experience of rotating shifts vs. current or former rotating shiftworkers with >10 years experience of rotating shifts vs. dayworkers) and metabolic syndrome status.

Sleep quality was assessed by asking the participants to rate on a 4-point scale (never, seldom, sometimes, often) the frequency in the last month of five symptoms associated with sleep problems: (1) difficulty falling asleep, (2) difficulty maintaining sleep, (3) difficulty getting back to sleep, (4) premature awakening, (5) hypnotic medication use. These items were the same as those used in previous sleep-related VISAT studies (e.g., Marquié & Foret, 1999) and the same or quite similar to numerous earlier studies on perceived sleep problems (e.g., Kecklund & Åkerstedt, 1992). A sleep difficulty score was computed by summing the ratings (range: 5–20, with 20 indicating greatest sleep difficulties; Cronbach's $\alpha = .74$). Perceived stress was assessed by means of the short version of the perceived-stress scale of Cohen et al. (1983). Scores range from 4 to 20, with 20 indicating maximum stress (Cronbach's $\alpha = .70$). Participants were also asked a range of questions regarding general biographical information, their work situation, and health behaviors, e.g., alcohol and tobacco intake.

Two analyses of the data were conducted using the multiple logistic regression procedure in SPSS (version 19; SPSS, Chicago, IL, USA). Both analyses incorporated

TABLE 1. Cross-tabulation of shiftwork experience and metabolic syndrome status

| | | Metabolic syndrome | | |
|---|---|---|---|---|
| | | Yes | No | Total |
| Current or former shiftworker | No (i.e., only ever a dayworker) | 28 | 961 | 989 |
| | Currently or in past | 40 | 728 | 768 |
| | Total | 68 | 1689 | 1757 |
| Rotating shiftwork experience | Never (i.e., only ever a dayworker) | 28 | 960 | 988 |
| | 1–10 yrs | 10 | 300 | 310 |
| | >10 yrs | 17 | 260 | 277 |
| | Missing values | 13 | 169 | 182 |
| | Total | 68 | 1689 | 1757 |

TABLE 2. Demographic details of the comparison groups

| | Current or former shiftworker No (only ever dayworker) | Current or former shiftworker Yes | Rotating shiftwork experience Never | Rotating shiftwork experience 1–10 yrs | Rotating shift work experience >10 yrs | Metabolic syndrome Yes | Metabolic syndrome No |
|---|---|---|---|---|---|---|---|
| Age, yrs (SD) | 41.7 (9.5) | 41.9 (9.0) | 41.7 (9.6) | 39.6 (8.4) | 44.7 (8.2) | 52.1 (8.7) | 41.3 (9.0) |
| Sex, % female | 62.0 | 50.8 | 62.0 | 50.3 | 60.6 | 32.4 | 58.1 |
| Socioeconomic status, % executive | 44.3 | 37.2 | 44.3 | 35.9 | 36.5 | 29.9 | 41.7 |
| Alcohol intake, % every day | 79.2 | 77.6 | 79.2 | 81.0 | 77.3 | 61.8 | 79.2 |
| Smoking, % currently or in the past | 55.9 | 62.5 | 55.9 | 64.8 | 60.6 | 66.2 | 58.5 |
| Perceived stress (SD) | 8.4 (3.0) | 8.5 (3.0) | 8.4 (3.0) | 8.4 (3.0) | 8.6 (2.8) | 8.4 (2.9) | 8.4 (2.9) |
| Sleep difficulty (SD) | 10.5 (3.2) | 11.2 (3.5) | 10.5 (3.2) | 11.1 (3.3) | 11.5 (3.5) | 10.8 (3.3) | 10.8 (3.3) |

TABLE 3. Odds ratio (OR) of metabolic syndrome associated with shiftwork (reference group = dayworkers)

| Predictor | OR | 95% CI |
|---|---|---|
| Shiftwork[a] | 1.89* | 1.15–3.09 |
| Shiftwork[b] | 2.06** | 1.24–3.44 |
| Shiftwork[c] | 1.90* | 1.13–3.19 |
| Shiftwork[d] | 1.74* | 1.02–2.98 |
| Shiftwork[e] | 1.74* | 1.01–2.98 |
| Shiftwork[f] | 1.81* | 1.05–3.12 |
| Shiftwork[g] | 1.78* | 1.03–3.08 |

[a]Crude OR; [b]OR adjusted for age; [c]OR adjusted for age and sex; [d]OR adjusted for age, sex, and socioeconomic status; [e]OR adjusted for age, sex, socioeconomic status, smoking, and alcohol; [f]OR adjusted for age, sex, socioeconomic status, smoking, alcohol, and stress; [g]OR adjusted for age, sex, socioeconomic status, smoking, alcohol, stress, and sleep difficulty.
*$p < .05$; **$p < .01$.

TABLE 4. Odds ratio (OR) of metabolic syndrome associated with exposure to rotating shiftwork (reference group = dayworkers)

| | 1–10 yrs | | >10 yrs | |
|---|---|---|---|---|
| Predictor | OR | 95% CI | OR | 95% CI |
| Shiftwork exposure[a] | 1.14 | .55–2.38 | 2.24* | 1.21–4.16 |
| Shiftwork exposure[b] | 1.62 | .76–3.48 | 1.94* | 1.02–3.66 |
| Shiftwork exposure[c] | 1.38 | .64–3.00 | 1.96* | 1.03–3.75 |
| Shiftwork exposure[d] | 1.29 | .59–2.83 | 1.82 | .94–3.55 |
| Shiftwork exposure[e] | 1.27 | .58–2.81 | 1.81 | .93–3.53 |
| Shiftwork exposure[f] | 1.32 | .60–2.91 | 1.86 | .95–3.63 |
| Shiftwork exposure[g] | 1.30 | .59–2.90 | 1.83 | .93–3.59 |

[a]Crude OR; [b]OR adjusted for age; [c]OR adjusted for age and sex; [d]OR adjusted for age, sex, and socioeconomic status; [e]OR adjusted for age, sex, socioeconomic status, smoking, and alcohol; [f]OR adjusted for age, sex, socioeconomic status, smoking, alcohol, and stress; [g]OR adjusted for age, sex, socioeconomic status, smoking, alcohol, stress, and sleep difficulty.
*$p < .05$.



a range of potential covariates that were identified from previous research that has examined the association between shiftworking and metabolic dysfunction (Biggi et al., 2008; Karlsson et al., 2001, 2003; Pietroiusti et al., 2010). The covariates identified for inclusion in the current analyses were age, sex, socioeconomic status (executive vs. nonexecutive), smoking (current or in the past vs. never), alcohol intake (every day vs. not every day), perceived stress, and sleep difficulty. The first analysis examined the association between shiftwork status and risk of metabolic syndrome, whereas the second examined the association between length of exposure to rotating shiftwork (in years) and risk of metabolic syndrome. Regarding the latter, it should be noted that although data were available on the number of years that participants had been exposed to each of the four forms of shiftwork described above, it was not possible to calculate the *total* exposure by summing the exposures to each. This was because, in many cases, the periods of exposure to the various forms of shiftwork would have overlapped by an unspecified amount. Hence, the second analysis only examined the impact of exposure to a single form of shiftwork, namely rotating shiftwork. Table 2 provides details of the comparison groups in terms of the covariates that were included in the analyses.

## RESULTS

The results of the first analysis indicated that the presence of metabolic syndrome was predicted by having current or past experience of shiftwork. This was the case both in the unadjusted analysis and also after statistically adjusting for age, sex, socioeconomic status, smoking, alcohol usage, stress, and sleep difficulty (see Table 3).

The second analysis indicated a higher prevalence of metabolic syndrome among participants with >10 yrs of exposure to shiftwork, when compared to participants with no exposure to shiftwork (i.e., dayworkers). This was the case both in the unadjusted analysis and also after adjusting for age and sex (see Table 4). Further adjustment for socioeconomic status, smoking, alcohol, and stress, however, made the effect of exposure no longer significant. There was no evidence of significantly

higher prevalence rates among participants with 1–10 yrs of exposure to shiftwork.

## DISCUSSION

Participants with current or prior experience of shiftwork were more likely than dayworkers to be classified as being highly likely sufferers of metabolic syndrome. This finding is consistent with previous research (Biggi et al., 2008; Esquirol et al., 2009; Karlsson et al., 2001, 2003; Li et al., 2011; Pietroiusti et al., 2010; Tanaka et al., 2010; Violanti et al., 2009). Furthermore, the current study builds on previous findings by providing an indication of the time course of the development of metabolic syndrome in shiftworkers. There was a clear indication in the current study that participants with >10 yrs of exposure to rotating shiftwork were more likely to be suffering metabolic syndrome than those with less exposure (or none), even after adjusting for age and sex.

Several factors have been identified as potentially playing a role in the relationship between shiftwork and metabolic syndrome, including stress, sleep debt, altered health behaviors, and disrupted circadian rhythms. Regarding stress, there is a reasonably consistent literature showing that abnormal work schedules, and especially those involving night work, may result in increased levels of anxiety and depression (e.g., Bara & Arber, 2009; Bohle & Tilley, 1989; Driesen et al., 2010). At the same time, a number of studies have identified links between work stress and incidence of metabolic syndrome (Chandola et al., 2006; Kang et al., 2004), although there was no suggestion in these studies that the participants were shiftworkers. In the current study, the association between shiftwork and metabolic syndrome remained significant after adjusting for perceived stress. This suggests that the higher stress that is commonly experienced by shiftworkers cannot entirely account for their increased susceptibility to metabolic syndrome, in this instance. However, it may also be that the current measure of stress was insufficiently sensitive to measure shiftwork-related stress.

Lowden et al. (2010) discussed a range of possible dietary mechanisms that may underlie the link between shiftwork and the symptoms of metabolic syndrome. They noted that several studies have shown associations between shiftwork and obesity (e.g., Chen et al., 2010; Gangwisch et al., 2005; Vorona et al., 2005), although not all findings have supported such a link. The causal factors underlying the association are not well established, although restricted sleep that is common among shiftworkers has been identified as a potentially important issue (Lowden et al., 2010). For example, laboratory studies have shown that partial sleep deprivation causes changes in two of the hormones involved in the regulation of food intake, namely ghrelin (increased after sleep deprivation) and leptin (decreased after sleep deprivation), prompting an increase in subjective appetite (Spiegel et al., 2004). Sleep deprivation has also been linked to a number of other symptoms of metabolic syndrome, namely decreases in glucose tolerance (Spiegel et al., 1999) and insulin sensitivity (Gonzalez-Ortiz et al., 2000), as well as increased blood pressure (Gangwisch et al., 2006). The current analysis indicated that the association between shiftwork and metabolic syndrome remained significant after adjusting for sleep difficulty. Thus, we cannot fully explain shiftworkers' increased risk of developing metabolic syndrome in terms of greater levels of sleep disruption, in this instance. However, it is notable that sleep difficulty is not necessarily the same as sleep duration, which was not measured, and so we cannot completely rule out the role of sleep deprivation in the association.

Lowden et al. (2010) also identified a number of other possible factors linking shiftwork to increased prevalence of metabolic syndrome, although these factors were not examined in the current study. They included the lifestyle and health behaviors that are more common among shiftworkers, and also desynchrony between shiftworkers' behavioral and circadian rhythms. For example, Geliebter et al. (2000) compared the activity habits of day and night workers. They found that those working late or night shifts reported greater weight gain in the previous 2 yrs, and that this was associated with decreased exercise, more napping, and a consequent reduction in total estimated energy expenditure. It also seems likely that the altered timing of shiftworkers' food intake may play an important role. Shiftworkers show a lowered tolerance to glucose and lipids following a change from day work to night work (Hampton et al., 1996; Lund et al., 2001; Riberio et al., 1998). This is thought to reflect disruption of normal human circadian patterns of metabolism, which ordinarily promote glucose metabolism and fat storage during the daytime (when humans normally eat) and glucose sparing and fat metabolism at night (when people normally fast). Thus, for example, a study of permanent night workers indicated that even after 2 yrs of regular night work, glucose and insulin secretions were only partially adjusted to night work (Morgan et al., 2003). The authors suggested that the cumulative postprandial effects of meals consumed at night, during the phase of maximal insulin insensitivity, may predispose individuals to the abnormalities of metabolic syndrome.

The main strengths of the current study were that it was based on a broad range of objective and subjective measures, obtained from large a sample of workers from a broad range of occupational settings. The primary limitations were the cross-sectional nature of the data and the absence of data relating to the full set of criteria for diagnosing metabolic syndrome. Hence, it is not possible to determine what, if any, causal relationship exists in the association between shiftwork and metabolic syndrome. Moreover, although the classification of participants into highly likely sufferers of metabolic syndrome and highly unlikely sufferers may be considered reliable, nearly half the original sample

(46%) could not be classified and were, therefore, excluded from the analyses. It is very likely that some of those who were excluded from the analysis might have been suffering metabolic syndrome, but could not be identified as such due to inadequate data. The fact that only a relatively small number of participants could be classified as highly likely suffers of metabolic syndrome might have diminished the reliability of the results, particularly in the second analysis where the numbers of suffers in the shiftworking groups were especially low. Statistical power might have been further reduced by the inclusion of several covariates. This may have contributed to the lack of significance in the later stages of the second analysis, after the addition of several covariates. Nonetheless, the current results confirm those of previous studies that have identified an association between shiftwork and metabolic syndrome. Additionally, in this instance, metabolic syndrome was found to be associated primarily with prolonged exposure (>10 yrs) to rotating shiftwork. This suggests that medical surveillance (e.g., check-ups) should pay particular attention to indices of metabolic dysfunction, especially in individuals with >10 yrs of exposure to shiftwork. Those identified as being at highest risk should then be provided with appropriate advice for ameliorating the condition, e.g., changing work schedule, modifying diet, increasing physical exercise, and improving sleep hygiene. Further research is needed in order to examine the time course of the development of metabolic syndrome in other forms of shiftwork, e.g., permanent night shifts, and also to more clearly identify the mechanisms underlying the link between shiftwork and metabolic dysfunction.



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