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Influences of early shift work on the diurnal cortisol rhythm, mood and sleep: Within-subject variation in male airline pilots

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Summary We aimed to investigate how early and late work shifts influenced the diurnal cortisol rhythm using a within-subjects study design. Participants were 30 healthy male non-smoking pilots, mean age 39.4, employed by a short-haul airline. The standard rotating shift pattern consisted of 5 early shifts (starting before 0600 h), followed by 3 rest days, 5 late shifts (starting after 1200 h) and 4 rest days. Pilots sampled saliva and completed subjective mood ratings in a logbook 6 times over the day on two consecutive early shift days, two late days and two rest days. Sampling was scheduled at waking, waking + 30 m, waking + 2.5 h, waking + 8 h, waking + 12 h and bedtime. Waking time, sleep duration, sleep quality and working hours were also recorded. Cortisol responses were analysed with repeated measures analysis of variance with shift condition (early, late, rest) and sample time (1—6) as within-subject factors. Early shifts were associated with a higher cortisol increase in response to awakening (CAR_i), a greater total cortisol output over the day (AUC_G) and a slower rate of decline over the day than late shifts or rest days. Early shifts were also associated with shorter sleep duration but co-varying for sleep duration did not alter the effects of shift on the cortisol rhythm. Both types of work shift were associated with more stress, tiredness and lower happiness than rest days, but statistical adjustment for mood ratings did not alter the findings. Early shift days were associated with significantly higher levels of circulating cortisol during waking hours than late shifts or rest days.

1. Introduction

In industrialised countries, almost one in five workers participates in shift work, in which different groups of workers replace each other in the same role (ILO, 2004). The most common shift pattern in the UK is a two-shift double-day system, consisting of early and late day shifts (such as 6 am—2 pm and 2 pm—10 pm), with workers alternating on a routine basis (Steel, 2011). Large-scale prospective cohort studies have found that rotating shift work is associated with increased risks of weight gain (Suwazono et al., 2008), diabetes (Pan et al., 2011), heart disease (Fujino et al., 2006), stroke (Brown et al., 2009) and some cancers (Kubo et al., 2006). Adverse health consequences are thought to

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arise as a result of chronic misalignment between endogenous circadian timing systems and behavioural sleep/wake and feeding cycles (Ruger and Scheer, 2009). Controlled laboratory studies, designed to mimic shift work sleep/wake disruption, have demonstrated disruptions to the normal 24-h cycle of a number of metabolic, autonomic and endocrine system indicators (Griefahn and Robens, 2010; Ribeiro et al., 1998; Scheer et al., 2009).

The influence of shift work on the hypothalamic—pituitary—adrenal (HPA) axis has been identified as a potential mechanism through which circadian desynchrony may lead to ill-health (Nader et al., 2010). Circulating cortisol levels naturally follow a circadian rhythm. Cortisol peaks in response to morning waking, declines gradually over the day, falls further after the onset of sleep and rises gradually in the early hours of the morning before waking (Spath-Schwalbe et al., 1992; Wilhelm et al., 2007). The HPA axis also reacts to physical or perceived stressors, leading to temporary increases in circulating cortisol. The awakening response or CAR is thought to be a discrete phenomenon superimposed on the circadian cycle of cortisol release, and is a phasic response to the sleep-wake transition (Kudielka et al., 2012). Total cortisol output over the day or area under the curve (AUC) and the slope or rate of decline over the day are also frequently studied as indicators of HPA axis function (Adam and Kumari, 2009). For example, the magnitude of the awakening response was positively correlated with job stress in a recent meta-analysis (Chida and Steptoe, 2009); increased cortisol secretion over the day was predictive of depression (Stetler and Miller, 2011) and a flatter diurnal slope predicted cardiovascular mortality in over 4000 community-dwelling adults (Kumari et al., 2011).

Studies which have examined the association between waking time and the CAR have found contrasting results. In the series of studies which first characterised the awakening response, Pruessner et al. (1997) reported that the cortisol increase after waking showed moderate intra-individual stability (r = 0.39—0.70, $p < 0.001$) and, importantly, was independent of time of waking. This latter finding has been replicated by a number of other studies (e.g. Born et al., 1999; Kunz-Ebrecht et al., 2004; Wust et al., 2000a,b). In direct contrast, two small studies in shift workers (Federenko et al., 2004; Williams et al., 2005) and two studies in community-dwelling adults reported that earlier waking was associated with a significantly heightened cortisol increase on awakening (Edwards et al., 2001; Kudielka and Kirschbaum, 2003). A recent case study measured the CAR on 50 occasions in one student and reported a wide range of values for the waking increase (3.6—39.0 nmol/l). In this individual, waking cortisol, but not the mean increase, was significantly associated with waking time (Stalder et al., 2009).

Salivary cortisol is increasingly used as an indicator of HPA function in epidemiological studies (Adam and Kumari, 2009). Clarification of time of waking effects is important not only for interpreting shift work effects but also for the design and interpretation of future studies. It is possible that between-subjects differences in the CAR attributed to early waking above (Edwards et al., 2001; Kudielka and Kirschbaum, 2003) were confounded by unmeasured individual trait characteristics such as coping style (O'Donnell et al., 2008) or preferred 'morningness' chronotype (Kudielka et al., 2006). To remove potential for systematic differences between groups of early and late 'awakeners', within-subject comparisons may be most appropriate design for understanding time of waking effects. Kudielka and Kirschbaum (2003) used a within-subjects design but did not account for time-varying factors such as sleep duration (Kumari et al., 2009), exercise (Scheen et al., 1998), positive affect or negative affective states on the day of testing (Jacobs et al., 2007; Steptoe et al., 2005). A previous study from our group showed that the same workers waking for an early shift (mean waking time 0400 h $\pm$ 41 m) had a higher CAR than on later day shifts (waking time 0739 h $\pm$ 94 m) or rest days (waking time 0804 h $\pm$ 78 m) (Williams et al., 2005). Shift differences in the CAR were no longer significant after controlling statistically for perceived stress and lower sleep quality on early shift mornings.

The CAR is thought to be controlled independently of cortisol output over the remainder of the day so waking for an early shift may have different implications for other aspects of the cortisol rhythm (Schmidt-Reinwald et al., 1999; Wust et al., 2000a). Edwards et al. (2001) reported that earlier waking was followed by prolonged elevation of cortisol for several hours. A recent study comparing waking and evening cortisol samples in two groups of bus drivers suggested that there was less decline over the day in early shift workers than afternoon shift workers, but the samples were not timed in relation to waking (Diez et al., 2011).

We aimed to investigate how early and late shift patterns influenced the CAR, the rate of diurnal decline and total cortisol output over the day using a within-subjects study design. We recruited UK-based airline pilots working a rotating two-shift pattern consisting of 5 early shifts (starting before 0600 h), 3 rest days, 5 late shifts (starting after 1200 h) and 4 rest days. To reduce variability in the cortisol responses, we included only healthy non-smoking men (Kudielka and Kirschbaum, 2003; Steptoe and Ussher, 2006). Pilots' work hours are regulated and therefore accurate records of work-related hours were available. We considered the influence of a range of potential confounding factors including work demands, stress and happiness over the day, sleep duration and sleep quality, alcohol and exercise.

2. Methods

2.1. Participants

Participants were healthy male non-smoking pilots employed by one short-haul passenger airline based in the United Kingdom. An invitation to participate in a research study to explore work fatigue was emailed to trade union members. To be eligible, participants had to work full-time on the standardised shift pattern, consisting of 5 early shifts, followed by 3 rest (non-working) days, 5 late shifts and 4 rest days (5-3-5-4 pattern). Early shifts required the pilot to start work before 0600 h and late shifts after 1200 h, followed by 7—12 h on duty. Pilots typically flew 2 or 4 flights per day, of between 45 m and 5 h in length, returning home overnight. Approximately 85% of pilots fulfilled these criteria, according to a prior workforce survey. Pilots routinely taking steroid medication were excluded. During the 4 weeks allocated for