Individual differences in shift work tolerance
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Citation for published version (APA):
“There is a time for many words, and there is a time for sleep”

Homer (Odyssey)
7th century BC
Chapter 1

General introduction
Chapter 1

Case report

I squint and see the silhouette of my daughter by the window: ‘Daddy, it’s already noon, please wake up!’ I mutter and she disappears downstairs cheerfully. My body is hurting and my throat is sore. The fourth night shift hasn’t done my body much good.

My wife says ‘You look horrible!’ while I drop down onto the couch, heavy-headed. I’m never sick, but now my legs are stiff and I feel nauseous. My coffee is getting cold and I try to turn myself around while lying on the couch. My other daughter sits next to me and touches my head saying: ‘Is daddy ill?’

After the mandatory and minimal ATW rest days, I drag myself back to the police station. Barely recovered, but aware of the tightness in the work schedules, I grab my coat and walk to the Touran for the next shift. My partner looks at me and says: ‘Jeez Vince, do you feel all right?

After a few days of hard work and days off, I take a look at my work schedule. The most regular thing about my work schedule is the irregularity. I laugh quietly, but feel like I could cry. When I show this work schedule to a medical doctor, he will predict that I get burned out within a few months! But we don’t burn out, we continue smoldering. If you think I start feeling depressed, no worries:

‘cause we are the national police force and everything will change for the better!’ The crooks will shiver by the thought of this new, solid police system.

My fingers touch the ‘blue’ and ‘red’ light switches. The sirens make their noise and the flashing lights color the streets. The patrol car drives smoothly through heavy traffic. My partner sings cheerful: ‘The police is here to rescue you!’

Upon arrival at the traffic accident, we do the best we can. The hectic situation makes me feel perfectly healthy. Still I feel sick.

Sickly in love with the greatest job in the world!

Source: Blog of Vincent, a police officer.
Shift work

Shift work is a signature feature of our contemporary 24-hour society, with work teams alternating their duty periods to sustain around-the-clock operations (Tucker & Folkard, 2012). The term ‘shift work’ is not well defined but is commonly understood to include working hours that differ from the standard diurnal working hours of 8 am to 5 pm. As such, it is synonymous to “irregular or odd working hours” (Costa, 2003). Using this as a definition, shift work includes morning shifts, evening shifts, night shifts, irregular schedules during the week and working on weekends. It can involve permanent (fixed) or rotating shifts, in several configurations of direction and speed; backward (night-evening-morning), forward (morning-evening-night) and with quick or slow returns. Moreover, shifts may differ in duration as well as in start and end times.

Besides shift timing and duration, there may be differences in mental and physical workload between shifts and by different occupations. For instance, the work of police officers is more demanding and stressful at night. The level of stressors during the night shift is much higher compared to the level of stressors during the day shifts (Ma et al., 2015). In contrast, for nurses the physical workload is much higher during day shifts compared to night shifts (Nicoletti et al., 2014).

Despite all these differences in schedules and occupations, on an individual level we see systematic differences between workers in tolerance for shift work. The above case report describes this issue by presenting Vincent’s perception of irregular working hours.

Shift work schedules are most commonly found in the law enforcement, emergency response, and the military (police officers, fire-fighters, etc.), and in food and entertainment, health care, and transportation (McMenamin, 2007).

Over the last few decades, shift work has increased substantially to meet the demands of industrialization and globalization. Depending on the classification of work hours used, the incidence rate of shift work ranges between European countries from 8% to 23% (Parent-Thirion et al., 2007). Reports of the prevalence of shift work within the Netherlands vary from 17% to 22% of the working population (Kerkhof, 2015 in preparation; Koppes et al., 2013).
The circadian timing system

The biological clock
Under normal conditions humans are synchronized to the natural 24 h cycle of day and night caused by the rotation of our Earth. This synchronization is driven by 24 h environmental oscillations of which the light/dark cycle is the primary time cue (“zeitgeber”) for our endogenous circadian (‘circa’: around, ‘dies’: day) timing system. This system consists of a master clock in our brain (circadian pacemaker) and subordinate clocks located in peripheral tissues in the body (Mohawk et al., 2012). These peripheral clocks are under direct control of the master clock (the circadian pacemaker) which is located in the suprachiasmatic nuclei (SCN) of the hypothalamus.

The molecular biological basis of our circadian time keeping lies in gene-transcriptional feedback loops comprised of a set of clock genes (Archer & Oster, 2015; Mohawk et al., 2012). The circadian pacemaker generates endogenous circadian rhythms throughout the body. The output of the circadian system is sent to other parts of the brain and body via endocrine and neural pathways, to preserve internal synchronization as well as synchronization with the external world (Boivin & Boudreau, 2014). For instance, the hypothalamic-pituitary-adrenal (HPA) axis including cortisol is under circadian control, as well as the propensity to sleep (Morris et al., 2012a). Circadian synchronization has a positive effect on overall health and well-being (Boivin & Boudreau, 2014).

The light/dark cycle being the most prominent time cue, light exposure is projected directly to the SCN via the retinohypothalamic and geniculohypothalamic tracts, through photoreceptors in the retinae and extra intergeniculate leaflet from the optic tract (Do & Yau, 2010). Dependent on the time of exposure, light can either advance or delay the circadian phase.

Sleep
Humans spend approximately one third of their lives sleeping, a necessity of life. Two neurobiological processes regulate the daily alternation of sleep and wakefulness (Borbély, 1982). Next to the circadian process, which promotes wakefulness during the day and sleep at night, there is a homeostatic drive, which builds up a sleep pressure with time awake and
dissipates while sleeping (Daan et al., 1984). When wakefulness and sleep correspond to the natural day-night alterations, the homeostatic and circadian drives are aligned, for details see figure 1 adopted with permission from Van Dongen, 2006.

**Figure 1.** Schematic representation of the changes over time in the homeostatic pressure for sleep, the circadian pressure for wakefulness, and the resulting sleepiness during the day, under normal circumstances with waking and sleeping placed during the day and night, respectively. Gray areas indicate sleep periods. The dashed line depicts the homeostatic pressure for sleep. The thin solid line depicts the circadian pressure for wakefulness, inverted such that down corresponds to greater pressure for wakefulness. The thick solid line displays sleepiness during the waking periods. Conceptually, this is equivalent to the net drive for sleep, computed by adding up the curves of the homeostatic pressure for sleep and the (inverted) circadian pressure for wakefulness (published with permission of Van Dongen, 2006).

**Sleep & shift work**

When working in shifts, the temporal variations of the homeostatic and circadian pressure are desynchronized, resulting in sleep debt and increased sleepiness (Van Dongen, 2006). Both the duration and the structure of sleep are affected by shifted timing of sleep periods
(Åkerstedt et al., 1991; Kerkhof & Lancel, 1991). The misaligned sleep-wake pattern feeds back on to the core processes of the circadian system, thereby disrupting the biological clock (Archer et al., 2014).

Sleep-wake disturbances are among the most pertinent and challenging problems of shift work (Åkerstedt, 2003; Åkerstedt & Wright, 2009; Wright et al., 2013). Daytime sleep after night shifts is shortened, due to trying to fall asleep ‘at the wrong time’; i.e. the circadian process promotes wakefulness during the day (Åkerstedt et al., 2010).

**Health & shift work**

The desynchronization between external zeitgebers, the circadian system and the sleep-wake cycle gives rise to the negative health consequences of shift work (Morris et al., 2012a; Puttonen et al., 2010; Rajaratnam et al., 2013).

Numerous studies present results that imply that frequently shifting the periods of sleep and wakefulness poses a serious threat to the shift worker’s physical, mental and psychosocial health (for review see Boivin & Boudreau, 2014). In the short term, shift workers suffer from insomnia and/or excessive sleepiness, performance decrements, and mood swings (Drake et al., 2004; Ohayon et al., 2010; Rajaratnam et al., 2013). In the long term, workers may develop shift work disorder, including complaints of either insomnia or excessive sleepiness, and a variety of other physical and mental health-related problems (Roth, 2012; Wright et al., 2013). Higher incidence rates of metabolic syndrome, cardiovascular disease, mood disorders and increase risk for cancer among shift workers have been well documented (Hansen & Stevens, 2012; Matheson et al., 2014; Puttonen et al., 2010; Vogel et al., 2012; Wang et al., 2011).

**Shift work tolerance**

Enduring sleep deficiencies are considered to be a major component of shift work intolerance (Costa, 2003; Reinberg & Ashkenazi, 2008). Even in retirement, shift workers report more sleep problems than day workers (Monk et al., 2013). The concept of shift work tolerance was first described by Andlauer and colleagues in 1978 as the ability to adapt to shift work without adverse consequences, in terms of sleep alterations, digestive problems, persisting fatigue and nervousness (Andlauer et al., 1978).
Over the years, a wide spectrum of indices of shift work (in)tolerance has been used, ranging from subjective ratings of health, quality of sleep, fatigue, and satisfaction with work schedule to objective measures of sleep, neurocognitive performance, obesity, and mortality. This has resulted in a scattered picture of the concept of tolerance (Härmä, 1993; Nachreiner, 1998; Saksvik et al., 2011). There is a pressing need for a better conceptualization of shift work tolerance (Saksvik-Lehouillier et al., 2015).

**Individual differences in shift work tolerance**

One of the major issues related to the adverse consequences of shift work concerns the impact of inter-individual differences. Some workers tolerate shift work well, whereas others develop symptoms of chronic illness. Härmä stated that the percentage of workers failing adaptation to shift work is usually between 10 to 20 percent (Härmä, 2006). This inter-individual variability seemed to be present in the development as well as in the severity of shift work intolerance (Härmä, 1993; Härmä et al., 2006; Saksvik et al., 2011).

A 1978 study reported that about 20 to 30 percent of shift workers were forced to leave shift work in the first 2-3 years due to chronic medical problems (Harrington, 1978). Even after only 6 months on a nocturnal work schedule, some workers show serious disturbances, whereas others show no signs of health complaints after more than 30 years of shift work (Ashkenazi et al., 1997; Reinberg et al., 1984). A recent study showed that 23 percent of the shift workers met the criteria of shift work disorder (Waage et al., 2009). Shift work intolerance has adverse financial and social consequences for both the individual shift worker as well as their company and society overall, due to increased medical expenses and/or inability to work (Culpepper, 2010). It would be beneficial in terms of productivity and well-being if it were possible to recognize symptoms of shift work intolerance early on in those who are most vulnerable.

**Factors associated with shift work tolerance**

Several studies have been conducted in order to identify factors associated with shift work tolerance. A wide range of exogenous factors of shift work tolerance have been considered, varying from work hours (such as schedules), working conditions (workload), home
environment (domestic duties) and social conditions (social support) (Costa, 2003; Monk, 1988).

Recently, there has been increasing awareness that person-specific characteristics, i.e. endogenous factors, play a crucial role in shift work tolerance (Van Dongen et al., 2006). Given the central role of sleep deficiencies in shift work, it has been proposed that person-specific characteristics of sleep/wake regulation may be involved in inter-individual differences in shift work tolerance. Trait vulnerability to sleep loss, circadian phase position (chronotype), and flexibility of sleep timing (natural ability to sleep and work at unusual times of day) have been put forward, but conclusive evidence has not yet been presented (Kantermann et al., 2010; Kerkhof, 1985; Van Dongen, 2006; Van Dongen & Belenky, 2009).

The extant literature on this topic is limited and mainly cross-sectional. In most studies to date, subjects were experienced shift workers, so that symptoms of intolerance had already developed in those who were vulnerable (De Raeve et al., 2009). Moreover, selection effects could have already removed the most intolerant individuals from the population, i.e. ‘the healthy worker effect’ (Knutsson & Åkerstedt, 1992).

To overcome these challenges, more longitudinal field studies are required to provide insight into inter-individual variability in response to shift work over time. A recent review by Saksvik and colleagues, covering the period 1998-2009, reported 60 studies on individual differences in shift work tolerance with only 10 longitudinal studies (Saksvik et al., 2011). Yet none of these longitudinal studies included baseline data, i.e. measurements taken prior to commencing shift work.

To identify person-specific characteristics as potential predictors for shift work tolerance, longitudinal studies including baseline measurements are needed. Studies of this kind are scarce. To our knowledge, there are only 11 longitudinal field studies with baseline data (including ours) over the last 40 years within this research area; for details see table 1. These studies show associations between individual factors and shift work tolerance at an early stage of shift work exposure. Comparison of these studies is complicated mostly by heterogeneity in occupational conditions and shift work tolerance criteria used.

These studies were based predominantly on self-report, through surveys on aspects of health and well-being, where response bias may have played a role (Podsakoff et al., 2003).
One study objectively measured gastrin blood levels after only 3 weeks of night shifts (Åkerstedt & Theorell, 1976). Studies with objective measures are important, in view of possible dissociations between objective results and subjective reports. Subjective measurements may not show the complete picture; when subjective measures are not confirmed objectively, challenges arise with the interpretation of the results.

To conclude, several factors should be taken into account to investigate individual differences in shift work tolerance. A longitudinal field study is needed, using both subjective and objective measurements for an integrative approach to the development of shift work tolerance. Furthermore, baseline (prior to shift work exposure) data is needed to investigate causal pathways between person-specific predictors and outcome variables over time. In this dissertation these factors have been addressed.

**Aim and scope of this thesis**

The aim of this thesis was to investigate the facets of shift work tolerance – the inter-individual variability in response to shift work and the search for potential baseline predictors – using both cross-sectional and longitudinal data.

In the first part we used an exploratory approach to the concept of shift work tolerance with 2 cross-sectional studies. In chapter 2, a large survey was set out within the Dutch police force to investigate subjective shift work tolerance in relation to variables in the domains of sleep, health and work-life balance, and to examine inter-individual differences in the nature of this relation. In chapter 3, we aimed to investigate individual factors in relation to subjective health and sleep variables in another group of shift workers; the croupiers in Dutch casinos.

In the second part, a prospective field study was set up with novice police officers. Due to the nature of their job, police officers work mainly full time in rotating shift work (Vila, 2006). Subjects were assessed at baseline, prior to commencing shift work, and re-assessed during three follow-up sessions within the first 2 years of shift work exposure after approximately 4, 12 and 20 months of rotating shift work. Inter-individual differences in shift work tolerance were operationalized by objective and subjective assessments on sleep, fatigue and stress responses (see Chapters 4, 5 and 6).
In Chapter 4, we aimed to examine prospectively whether individual sleep characteristics at baseline were related to diurnal sleep parameters after commencing shift work, using preliminary results of baseline and the first two follow-up sessions in a subgroup of subjects.

In Chapter 5, our goal was to evaluate the development of individual stress responses to commencing shift work. Inter-individual differences were measured by repeated assessments of morning cortisol in saliva (cortisol awakening response, CAR), as a prime index of shift work tolerance.

In Chapter 6, we examined inter-individual differences in sleep responses within the first two years of shift work exposure (all three follow-up sessions), and sought to identify baseline predictors; i.e. person-specific characteristics.
## Results

The decrease in gastrin over the night shifts was associated with an increase in psychosomatic symptoms, mainly among subjects with a higher score on neuroticism at baseline.

Health decreased after 6 months of SW. After 4 yrs, the remaining shift workers showed higher health decrements as the leavers. Main reasons for leavers were disturbances of subjective well-being and disruption of social relations.

Night workers showed more psychological symptoms than day workers. Neuroticism and work/non-work conflict predicted these symptoms after 6 months of SW. Night work, morningness and social support predicted symptoms at 15 months of SW.

Workers with a higher mesor of positive moods and a lower mesor of negative moods and fatigue at baseline, tended to tolerate shift work better. Baseline early heart rate acrophase was related to higher sleep quality in SW. Workers with small amplitudes of temperature, negative mood and fatigue at baseline tended to show better night-shift tolerance.

First exposure to night was work associated with acute difficulties, increase in minor complaints and loss of energy and interest. A subdivision was made in complainers versus non-complainers.

Workers who at baseline had higher scores on speed and impatience, rigidity in sleeping habits, neuroticism and low scores on relaxedness and efficiency showed higher health complaints after 1 year of SW. After 3 years, rigidity of sleeping habits and vigorousness were the main predictors.

Sleep duration decreased over the first 5 years of SW while subjective sleep quality (SSQ) did not change. A positive correlation was found between SSQ at baseline and SSQ in general after 5.5 years of SW.

## Study methods

- **Blood specimens and questionnaires at baseline and after 3 weeks of night shifts.**
- **Questionnaires at baseline, after 6 months and 4 years of shift work (SW).**
- **Questionnaires at baseline, after 6 months and 15 months of SW.**
- **At baseline; 24 h oral temperature, mood and heart rate measures. Questionnaires after 16 and 39 months SW.**
- **Questionnaires at baseline and after 8 weeks of SW.**
- **Questionnaires at baseline, after 1 year and 3 years of SW.**
- **Questionnaires at baseline and after 1.5, 3.5 and 5.5 years of SW.**

## Sample

- 17 railway workers
- 95 wire mill workers, stayers/leavers
- 60 trainee nurses, dayworkers vs. night workers
- 153 Oil refinery workers
- 37 trainee nurses
- 185 Oil refinery workers
- 101 oil refinery workers

## Authors

- Åkerstedt & Theorell, 1976
- Meers et al., 1978
- Bohle & Tilley, 1989
- Vidaček et al., 1993
- Minors et al., 1994
- Kaliterna et al., 1995
- Radoševic-Vidaček et al., 1995

## Table 1. Longitudinal studies on individual differences in shift work tolerance with baseline (before commencing shift work) data.

<table>
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<td>185 Oil refinery workers</td>
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<td>Workers who at baseline had higher scores on speed and impatience, rigidity in sleeping habits, neuroticism and low scores on relaxedness and efficiency showed higher health complaints after 1 year of SW. After 3 years, rigidity of sleeping habits and vigorousness were the main predictors.</td>
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<td>Radoševic-Vidaček et al., 1995</td>
<td>101 oil refinery workers</td>
<td>Questionnaires at baseline and after 1.5, 3.5 and 5.5 years of SW.</td>
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<td>Florida-James et al., 1996</td>
<td>23 student nurses</td>
<td>Questionnaires during a 12 wk period, including 8 weeks of night shifts.</td>
<td>The POMS dimensions showed phase shifts in their circadian rhythms when alternated between diurnal and nocturnal living patterns.</td>
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<td>Bohle &amp; Tilley, 1998</td>
<td>130 student nurses</td>
<td>Questionnaires at baseline, after 6 and 15 months of SW.</td>
<td>Work/non-work conflict was the strongest predictor for dissatisfaction. Weaker associations were found for vigoroussness, psychological symptoms and social support from co-workers/family and dissatisfaction levels.</td>
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<td>West et al., 2007</td>
<td>37 trainee nurses</td>
<td>Questionnaires at baseline, after 6 and 12 months of SW.</td>
<td>Flexibility of sleeping habits showed a negative correlation with subjective sleep disturbance associated with night shift after 6 months of SW. This relationship disappeared after 12 months of SW.</td>
</tr>
<tr>
<td>Lammers-van der Holst et al., 2006</td>
<td>26 novice police officers</td>
<td>Actigraphy and questionnaires at baseline, 4 and 12 months of SW.</td>
<td>Systematic inter-individual differences were found for daytime total sleep time and subjective sleep quality. The subjective quality of night time sleep at baseline predicted the subjective quality of daytime sleep in shift work.</td>
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