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Hypothesis: A perfect day conveys internal time

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ABSTRACT

In 2007 the International Agency for Research on Cancer [IARC] concluded "shift work that involves circadian disruption is probably carcinogenic to humans" (Group 2A). To investigate the "probable" causal link, information on individual chronobiology is needed to specify exposures to circadian disruption associated with shift work. In epidemiological studies this information is usually assessed by questionnaire. The most widely used Morningness-Eveningness-Questionnaire (MEQ) and MunichChronoTypeQuestionnaire (MCTQ) reveal information on circadian type (MEQ) and actual sleep behaviour (MCTQ). As a further option we suggest to obtain preferred sleep times by using what we call the perfect day (PD) approach. We hypothesize that a PD – as a day of completely preferred sleep behaviour – captures pristine internal time. We argue that the PD approach may measure internal time more accurately than the MEQ and MCTQ which convey influences by work and social time pressures. The PD approach may therefore reduce misclassifications of internal time and reveal circadian disruption caused by different shift systems.

Introduction

In 2007 the International Agency for Research on Cancer (IARC) concluded that shift work involving circadian disruption is probably carcinogenic to humans (Group 2A) [1]. Since then, several studies have examined associations between shift work and cancer. Surprisingly, most investigations have been based on the assumption that working at the civil night has the same biological effect on all humans. However, this assumes that internal time [2] and external time [3] (see Table 1 with glossary) are equivalent. Importantly, humans' internal times vary inter-individually (e.g. morning persons have an earlier cycle, evening persons have a later cycle) and intra-individually (e.g. changes by season or age). This means that ignoring chronobiological diversity can bias effect estimates of the same work shifts on chronobiologically different individuals, leading to under- or overestimations of possibly associated risks. Hence, an accurate assessment of exposures to – or doses of – chronodisruption (operationalized as the split physiological nexus of internal and external times [4]), is needed to explore the nature of associations between shift work and cancer. To this end, accurate information on the individual internal time is a *conditio sine qua non*.

The key question is: How can we assess individuals' internal time in epidemiological studies? To this end, we offer a novel approach via the following steps:

1. We explain why measuring internal time is a principal challenge.
2. We summarize how the widely used Morningness-Eveningness-Questionnaire [MEQ] and MunichChronoTypeQuestionnaire [MCTQ] have been employed to assess internal time in epidemiological studies.
3. We identify limitations of using either the MEQ or the MCTQ.
4. To assess pristine internal time we hypothesize that "A perfect day conveys internal time". We describe how the perfect day [PD] approach uses preferred sleep behaviour to approximate internal time and explain advantages and limitations.
5. Conclusions with perspective considerations close the paper.

Measuring internal time is a principal challenge

To estimate internal time (IT) is demanding as it depends on the individual chronotype which (co-)determines an individual biological day – with the propensity of activity – and an individual *biological night* – with the propensity to be asleep [2]. However, actual wake/sleep behaviour is influenced by various external factors which act as *zeitgebers*. These external influences complicate deriving an individual's pristine internal time, i.e., the internal time

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Table 1
Glossary.

Variables	Definitions
Biological Day	Individuals' propensity to be awake; see chronotype and internal time
Biological night	Individuals' propensity to be asleep; see chronotype and internal time
Chronotype	Genetically (co-)determined [13,14] "temporal phenotype of an organism" [15]; see internal time [6]
External Time	Environmental time determined by sun, occupational and social times [3]
Free Day Shift System	Predominantly determined by individuals (such as family and friends), social events (such as cultural events) or private duties (such as house work) in addition to natural and occupational zeitgebers
Internal Time	Biological time as individuals' genetically (co-) determined [13,14] propensity to be asleep (biological night) and awake (biological day); see chronotype
Natural Shift System	Determined by natural, environmental zeitgebers only (such as sun light, temperature or natural noises)
Perfect day	A day with preferred sleep times within two weeks entirely for oneself
Pristine Internal Time	Internal time without external influences such as work during an individual's biological night
Work Day Shift System	Predominantly determined by the work schedule, and furthermore influenced by natural and social zeitgebers
Zeitgeber	External factors that synchronize the individual's biological rhythm with the environment; first defined by Aschoff [5] there are different zeitgebers that can be grouped by meteorological (such as sunlight and darkness, temperature or humidity) or ecological/social (such as other species' individual rhythms, noise or food availability)

without external influences such as work during an individual's biological night, from the actual sleeping behaviour: On work days, humans' sleep behaviour is often obviously influenced by the work schedule. But furthermore, various social *zeitgeber* pressures affect the sleep timing on work days and work-free days (hereinafter referred to as "free days"), e.g. the partner's chronotype, TV-events at particular points of time or social duties. The relevance of social *zeitgebers* was initially recognized by Aschoff in 1954, when he described the evening activity of salmons that was associated with the circadian preference of insects as their favorite food. Moreover, Aschoff reported that male rats adapt to female rats' activity rhythms when raised next to each other [5]. Arilie Hochschild described a Second Shift covering work outside the official working hours including housework and childcare. For women in the 1960s and 1970s she described an extra month of twenty-four-hour days (per year) working in this Second Shift in addition to the regular First Shift at the contracted workplace [6]. Taken together, social influences are highly relevant for the individual sleep behaviour.

Various, often co-existing *zeitgebers*, bond to different shift systems: On work days occupational zeitgebers, like the work schedules, have a main influence on activity and sleep behaviour (*Work Day Shift System*) whereas on free days (*Free Day Shift System*) social life requirements will have major impacts as *zeitgebers*. In principle, separating free days and work days could be a feasible approach to assess work's impact on activity and sleep behaviour. But it may be misleading to derive the internal time from the Free Day Shift System. In addition to the social life requirements a worker's sleep behaviour on a free day likely remains affected e.g. by the work schedule of previous days. How much work schedules influence a worker's sleep behaviour will depend on shift details or individual preferences. Empirically, it takes our bodies time to overcome time-zone travel-associated jetlag. Similarly, workers will need time to adjust temporal wake-sleep habits to free day obligations or liberties. Hence, depending on shift and chronobiological details, the time span of a week-end away from work may be too short to wash out effects on their chronobiology accumulated over preceding work days. In summary, a variety of external influences may make it difficult to assess an individual's pristine internal time simply from his behaviour on, for instance, two free days. By way of contrast, isolating an individual from the influences of both work and social life would leave only exposures to natural *zeitgebers* – such as sunlight or natural temperature. This situation could be conceptualized as the *Natural Shift System*. This Natural Shift System may mirror pristine internal time as it includes natural *zeitgeber* information only (Fig. 1).

The MEQ and MCTQ in epidemiological studies

Epidemiologists regularly use various questionnaires to reveal chronobiological information. Amongst these, the Morningness Eveningness Questionnaire and the Munich Chronotype Questionnaire are the two "most widely used tools in epidemiological research to assess circadian preferences" [7].

The Morningness Eveningness Questionnaire (MEQ)

In 1976, Horne and Östberg proposed the Morningness Eveningness Questionnaire (MEQ) [8]. It is described as a validated tool and considered as the gold standard measure of morningness [9]:

The MEQ contains 19 questions on individual preferences for physical or mental activity, sleep timing, morning alertness, appetite or tiredness at specific times of the day and self-assessing circadian preference. Horne and Östberg chose different scenarios for their questions: 9 questions investigate hypothetical situations (e.g. days to be planned entirely free), 9 further questions focus on real experiences (e.g. feeling best at time of day) and in one question a comparison with others (self-assessing the diurnal preference) is used. The questionnaire consists of multiple choice questions and ordinal scales with responses being matched to different scores. The cumulative result of these scores is classified into one of five categories from definitively evening type to definitively morning type. Different definite cutoff points for the circadian preferences' categories are discussed in the literature [9]. Overall, the MEQ provides a cumulative result that enables to assess circadian preference as categorical variable.

The Munich Chronotype Questionnaire (MCTQ)

The MCTQ, first described by Roenneberg et al. in 2003, is a questionnaire to assess information on individual circadian timing [3]. In its current form, the questionnaire includes 14 questions [10] that focus on individual sleep behaviour specified for work and free days – with free days being defined as normal circumstances on free days without partying. Hence, the MCTQ collects information on current real life situations. It can be used to show quantitative differences in sleep behaviour between work and free days. One outcome, the Social Jet-Lag as the absolute difference between mid-sleep time on work and free days [11], can be calculated in fractions of hours. The mid sleep time on free days is furthermore used to assess individual chronotypes. Assuming a normal distribution of chronotypes, different categories of chronotypes are assigned by splitting the continuous results obtained from the investigated population according to quartiles or deciles or other cutpoints [11]. In addition to information on sleep timing, the MCTQ can also be used to derive information on sleep duration. In 2013, the $MCTQ_{shift}$ extended the MCTQ to shift workers [12]. It uses the same questions as the MCTQ but focuses on different days within the duty roster. It derives the chronotype by the midsleep time of free days after evening shifts. Hence, the methodology of the MCTQ and the $MCTQ_{shift}$ to assess internal time is comparable.