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Determining chronotype in a large cohort of aging employees

Thesis of the advanced studies

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Chronotype refers to one's daily behaviour regarding their sleep-wake cycle. It can be divided into three categories: morning, intermediate or evening type. Chronotype has an effect on health and behaviour, as especially evening type has been associated with sleep complaints and mood disorders. Chronotype can be assessed with different methods, such as physiological measurements, device-based monitoring and subjective measurements, such as questionnaires.

The purpose of this study was to compare different methods of determining chronotype among Finnish aging employees and to choose the best method for the Finnish Aging and Retirement (FIREA) study conducted at the University of Turku. FIREA study is an ongoing longitudinal cohort study established in 2013, which aims to examine health behavioural and clinical risk marker changes during the transition to retirement.

This thesis is a literature review and its materials have been collected from the Turku University Library's databases using search terms such as "chronotype", "questionnaire" and "measure". It is based on peer-reviewed articles. By comparing results from different studies and utilizing other reviews, a comprehensive review of different methods of determining chronotype is assembled and the best suited method is chosen for the FIREA study.

As the basis of the study is a large cohort of aging Finnish public sector employees, methods that require laboratory environment or tools have to be excluded. Methods that suit large epidemiologic cohort studies are questionnaires and actigraphs. When comparing them, the best choice for the FIREA study is the shortened Morningness-Eveningness Questionnaire, as it is translated and validated in Finnish and is easy to carry out. It is also possible to further validate the questionnaire with actigraph measurements.

Key words: chronotype, morningess-eveningness, cohort study, measurement

CONTENTS

1. Introduction

The human circadian clock regulates the circadian rhythm, which together with the need for sleep regulates humans' sleep-wake rhythm. The circadian clock is a sum of three cycles: solar cycles, endogenous biological cycles and social cycles. The solar cycle results from Earth's rotation with its surface periodically exposed to and shielded from light. Biological cycles are a consequence of an endogenous circadian clock located centrally in the suprachiasmatic nucleus, which is regulated by the alteration between light and darkness and genetic factors. The third cycle, social time is created by the technical clock, as it is a result of the introduction of the mechanical clock. The human circadian clock is approximately 24 hours and its most important regulator is the alternation between sunlight and darkness accompanied with other signals. The combination of these three factors results in the human circadian clock, which is also slightly altered genetically by the so-called clock genes. (Roenneberg et al. 2007.)

Chronotype refers to one's actual daily behaviour regarding their sleep-wake cycle. It depends mainly on genetic and environmental factors and age (Roenneberg et al. 2007). Chronotype can also be described as individual's morningess or eveningness, which places more emphasis on preferences rather than behaviour (Bauducco et al. 2019). In this study, the focus is on chronotype as one's preference, as it is widely used in literature and other studies. Humans have been typically divided into three chronotypes: morning, evening and intermediate type. Other categorisations have also been suggested, often depending on the questionnaire, such as the more precise definition of chronotype into five types: definitely morning, moderately morning, intermediate or neither, moderately evening or definitely evening type. (Caci et al. 2008.) A study by Partonen and Merikanto (2020) divided the Finnish general population into four categories of chronotype and observed that 22% of the population were categorized as definite morning types, 29% as morning-oriented, 32% as evening-oriented and 17% as definite evening-types.

Several measures have been developed for the assessment of chronotype. These include subjective measurements, such as different questionnaires, and objective measurements, such as activity or biological measurements. Different methods have their own purposes of use and applications.

2. Aims of the study

The purpose of this study is two-fold. First, to conduct literature review on the association of chronotype and health and different methods for determining chronotype. Second, to compare different methods for assessing chronotype and then recommend the best method suited for assessing chronotype in a large epidemiological cohort study, the Finnish Retirement and Aging (FIREA) study. Factors that have to be taken into account are the size of the study (big epidemiologic cohort study), availability of the methods in participants' language (Finnish), age of the participants (65 and above), accessibility of the tools and materials and study protocol of the FIREA study.

3. Chronotype and health

Assessing chronotype is important, as it has an impact on many different aspects of human behaviour and health. For example, chronotype is associated with sleep duration, cognitive performance and mood among other things (Santisteban et al. 2018). The sleep cycles of those with an evening type are usually 2-3 hours later than morning types, which is due to differences in their endogenous circadian rhythms (Lack et al. 2009). This division into "early birds", "night owls" and something in between can help in the diagnosis and treatment of various sleep-wake disorders, such as sleep deprivation (Partonen and Urrila 2014).

There are some differences between the different chronotypes regarding how they are associated with health. Negative health outcomes, such as anxiety disorders and depression, have been more commonly linked to the evening types than in other chronotypes (Merikanto et al. 2015, Partonen 2015). Various diseases and symptoms are strongly connected to having an evening type, such as hypertension, type 2 diabetes, asthma, allergy symptoms, and nicotine addiction. Evening type has also been associated more often with an unhealthy diet and emotional eating is more common in evening types than in morning types. Unhealthy lifestyle choices might be behind many of the illnesses and disorders associated with evening type. This makes determining chronotype important, as promoting healthy lifestyle choices might be especially important among evening types. (Merikanto et al. 2015.) Morning types suffering from bipolar disorders are more prone to substance use disorders, contrary to evening types that are more likely to have a higher rate of alcohol use and to be smokers. (Partonen 2015.)

Determining chronotype has gained attention also because shift work has become more common and the literature related to the health hazards of shift work is growing rapidly. Earlier chronotypes sleep worse and less during night shifts compared to later chronotypes, while later chronotypes experience more sleep and circadian disruption than morning types when working morning shifts. Therefore, shift schedules adjusted to chronotype have been suggested to be used more often in work environments. This could have positive impacts on health outcomes and reduced circadian disruption. (Vetter et al. 2015.)

4. Determining chronotype

There are many ways to determine one's chronotype. Each method has its own applications as well as strengths and limitations. Based on how chronotype is assessed, the different methods for determining chronotype can be categorized into physiological, device-based monitoring and subjective.

4.1 Physiological measurements

The human body has an endogenous biological cycle, which takes part in determining one's circadian clock and rhythm. It consists of for example hormone secretion and temperature fluctuation, which can be objectively measured. That leads to the possibility of determining chronotype with physiological measurements, such as the dim light melatonin onset, body temperature or cortisol secretion.

4.1.1 The dim light melatonin onset

The dim light melatonin onset (DLMO) is regarded as the golden standard in assessing circadian phase in humans. Studies have shown that the onset of melatonin secretion in dim light (<50 lx) conditions is the most accurate marker for assessing the circadian pacemaker. (Lewy et al. 1999.) Melatonin can be measured from saliva or plasma samples, or metabolite 6-sulphatoxymelatonin in urine (Pandi-Perumal et al. 2007). Measuring the onset of melatonin production, which occurs around 2-3 hours before the onset of nocturnal sleep, is very time-consuming and inconvenient for patients. Even though DLMO is said to be minimally masked by exogenous factors in general, it has been shown that for example posture, exercise, sleep deprivation, the use of caffeine and certain drugs can mask the endogenous production. (Hofstra and de Weerd 2008.) In addition, as the term "dim light melatonin onset" implies, samples must be taken in a dim light setting, because bright light can suppress melatonin production (Lewy et al. 1980).

4.1.2 Body temperature

Chronotype can also be assessed based on body temperature measured orally, rectally or distally (e.g. from wrists). Core body temperature reaches maximum in the early evening and minimum in the early morning and the fluctuation is caused by the combined action of heat loss and heat production. The nocturnal decline is due to greater heat loss and vasodilatation at distal skin regions. (Hofstra and de Weerd 2008.) Body temperature is fairly easy to measure, but the masking factors, such as physical activity, body position, light exposure and environmental temperature have to be kept in mind and their effects minimized as much as possible. Measuring body temperature requires reliable tools and much more work than wearing an actigraph or filling out one questionnaire.

4.1.3 Cortisol

Cortisol is a corticosteroid hormone produced by the zona fasciculata of the adrenal cortex. The endogenous pacemaker, which regulates also melatonin production, generates a circadian rhythm in cortisol production. Its production is also regulated by the hypothalamic-pituitary-adrenal axel, which activates during stress and when blood glucose concentration is low. In addition, light and age have an effect on cortisol secretion, and sleep onset and sleep deprivation inhibit secretion, whereas sleep loss, light sleep and awakenings elevate concentration. (Bailey and Heitkemper 2001.)

The secretion rhythm of cortisol is very clear, with production decreasing during the day, then sharply increasing in the second half of the night, reaching maximum concentration early in the morning. Cortisol can be measured from saliva or serum, where the usual cutoff points are the onset of evening rise and the start or end of the quiescent period in the evening and first half of the night. (Hofstra and de Weerd 2008.) The acrophase (maximum concentration) of the circadian rhythm of serum cortisol occurs earlier in morning types than evening types among healthy adults, which is the basis of determining chronotype using cortisol secretion (Bailey and Heitkemper 2001).

4.2 Device-based monitoring

To eliminate the subjectivity of determining chronotypes with questionnaires, other more objective measurements have been developed. Information of the circadian rhythm can be attained from for example body movements and position. Chronotype can be determined with device-based monitoring, such as actigraphs or ambulatory circadian monitoring.

4.2.1 Actigraphy

Actigraphs are small wearable devices which measure movements of the body based on acceleration. They are generally placed on the wrist of the nondominant hand to. Collected data is then downloaded to the computer for analysis of the relationship of activity and inactivity, which can then be used to obtain estimates of sleep. (Ancoli-Israel et al. 2003.) In practise, increased movement indicates wake periods and reduced movement sleep periods. Actigraphs must be worn for at least 5 days to obtain reliable data and are often worn for a full week. Actigraphs have been proven to offer reliable and valid data of sleep at least in a normal healthy adult population, but its reliability decreases when sleep is more fragmented, as it has a low specificity (e.g. it is poor in detecting wakefulness during night). (Hofstra and de Weerd 2008.)

Actigraphs offer data, from which multiple parameters of sleep can be analysed, such as sleep start time, awakening time, sleep duration and the midpoint of sleep. Midpoint of sleep on free days (i.e. non-working days) (MSF) can be used to determine chronotype and often a sleep-corrected version (MSF_{sc}) is used, in which the estimate is corrected for confounding effect of sleep debt (Santisteban et al. 2018, Roenneberg et al. 2019). Actigraphs are relatively easy to use, which has made them more applicable in certain sleep studies compared to polysomnography. Actigraphy makes home recordings more accessible, as it permits the evaluation of patients' normal sleeping habits in their natural sleeping environment and minimizes the effect of laboratory that might affect patients' typical habits. (Ancoli-Israel et al. 2003.) It can also be used for long-term measurements over several weeks with less inconvenience to patients compared to polysomnography (Kosmadopoulos et al. 2014).

Actigraphy is also quite reliable, as it has been validated against polysomnography (PSG), the golden standard in sleep research and it also correlates well with sleep logs and chronotype questionnaires (Hofstra and de Weerd 2008, Santisteban, Brown et al. 2018). Actigraphs have been shown to correctly identify 83.5 ± 6.0% to 88.9 ± 9.0% of epochs as sleep or wake. However, the specificity of the actigraph is a slight problem, as they have been shown to misidentify a significantly high proportion of wake epochs as sleep. It has been concluded that activity monitors have a tendency for overestimating sleep by misidentifying quiescent wakefulness as sleep, but the bias has generally been deemed minimal, particularly when actigraphs are used together with sleep diaries. (Kosmadopoulos et al. 2014.)

Using actigraphs in determining chronotype is a useful method as it correlates well with questionnaires and the dim light melatonin onset (DLMO). It requires sleep logs or other reliable tools for recognizing sleep from sedentary behaviour, as it tends to overestimate sleep.

4.2.2 Ambulatory circadian monitoring

Ambulatory circadian monitoring (ACM) is a fairly new method of assessing circadian phase in humans, developed in 2010. It measures three variables: wrist temperature, motor activity and body position rhythms (i.e. temperature, activity and position, TAP) with an actigraph and a temperature sensor on the wrist. (Ortiz-Tudela, Martinez-Nicolas et al. 2010.)

It has been previously concluded that the TAP is a novel measurement for evaluating circadian system status and sleep wake rhythms with a level of reliability better to that of actigraphy. The data from the three variables are normalized and averaged to obtain the integrated variable TAP. Value of 0 indicates the lowest activity, a lying/horizontal position and the highest wrist temperature (sleep) and a value of 1 indicates the highest activity, upright position and the lowest wrist temperature (wakefulness). In short, ACM detects sleep with the three variables, from which the midpoint of sleep can be calculated and chronotype can be determined. (Martinez-Nicolas et al. 2019.)

ACM makes it possible to evaluate patient’s sleep-wake cycle in their normal environment, removing the laboratory effect. It is also much cheaper to conduct than PSG. (Ortiz-Tudela et al. 2014.)

4.3 Subjective measurements

In large epidemiologic cohort studies, short questionnaires are often the most effortless and quickest way to determine individuals’ chronotype. Questionnaires are quick, easy, non-invasive and widely used method, which are quite accurate. However, questionnaires are also often prone to bias, such as the influence of shift work not being taken into account. (Santisteban et al. 2018.) The most commonly used questionnaires for assessing chronotype are the Morningness-Eveningness Questionnaire and the Munich Chronotype Questionnaire, accompanied with some less used questionnaires.

4.3.1 The Morningness-Eveningness Questionnaire (MEQ)

The Morningness-Eveningness Questionnaire (MEQ) was developed in 1976 by researchers James Horne and Olov Östberg (Horne and Östberg 1976). It is a self-assessment questionnaire, which has 19 questions with Likert-type responses. In the questionnaire, respondents are asked about their daily preferences and feelings, such as when the participant usually goes to sleep and when they feel the most active and energized during the day. Thus, the questionnaire assesses subjective preferences rather than actual objective sleep behaviour. (Kantermann et al. 2015.) After completing the questionnaire, each respondent gets a score between 16-86, with a higher score indicating a stronger preference for morningness. Cutoff scores for different types are 70-86 points for definitive morning type, 59-69 points for moderate morning type, 42-58 points for neither or intermediate type, 31-12 points for moderate evening type and 16-30 points for definitive evening type. (Caci et al. 2008.)

Even though the MEQ is the most widely used questionnaire for assessing chronotype, it has some limitations. The original questionnaire was validated with young adults (18 to 32 years old), which makes it inconsistent across younger and older age groups (Levandovski et al. 2013). To address this limitation, Taillard et al. (2004) validated MEQ with middle-aged French workers and determined new cutoff points for different chronotypes. The MEQ also does not differentiate working days or free days and is not particularly suitable for shift workers. The score can also be influenced by mealtimes, age, gender and sociocultural aspects. (Adan 1992, Levandovski et al. 2013.)

The Finnish version of the MEQ has been validated with six questions taken from the original questionnaire (as shown in Appendix 1). Those six questions correlated best with the sum score of the original 19 items in the regression analysis and explained 83% of the variance in the sum (Hätönen et al. 2008.) The sum score ranges from 5 to 27, with 19-27 points indicating definite or moderate morning types, 13-18 points indicating the intermediate type and 5-12 points indicating definite or moderate evening types. This scaling correlates with the original questionnaire. (Merikanto et al. 2015.)

4.3.2 The Munich Chronotype Questionnaire (MCTQ)

Developed in 2003 by Roenneberg and others, the Munich Chronotype Questionnaire (MCTQ) is used to determine individual’s chronotype based on the midpoint of sleep during free days (MSF), which is the halfway point between sleep onset and sleep end. Midpoint of sleep is the main marker for determining chronotype, as midsleep times show a normal distribution for different age groups and it has been reported also as the best phase anchor point for melatonin onset. The focus of the MCTQ is on actual behaviour rather than on preferences and ideals. It asks the participant about their usual sleeping habits and has questions such as “I have to get up at ___ o’clock” or “I need __ min to wake up”. At the end of the questionnaire, there are also questions about the participant’s own idea of their own and family members’ chronotypes. (Roenneberg et al. 2003.) The last questions have been observed to have the best correlation with the score from the MEQ ($r = -0.80$) (Roenneberg et al. 2007). In the original 2003 publication, midsleep times showed a normal distribution for different age groups both on workdays and free days.

The MCTQ has some limitations. One of the limitations of the MCTQ is that it does not apply to all populations, which means that some groups have to be excluded, such as people who use alarm clocks on free days. Another limitation of the MCTQ are the calculations required to correct for acquired sleep debt, as the result for one’s chronotype cannot be obtained by simply adding individual scores based on one’s answers to the questionnaire, such as in the MEQ. (Levandovski et al. 2013.) In addition, it has to be kept in mind that the MCTQ assesses specifically sleep-wake patterns and is more about the actual chronotype than morningness or eveningness.

The MCTQ has also been translated into Finnish (Partonen and Urrila 2014). However, to the best of my knowledge, it has not been validated or widely used in studies in Finland.

4.3.3 Other questionnaires

There are also other questionnaires in addition to the MEQ and the MCTQ that have been created to assess chronotype. However, they are not as widely used nor have they been translated into Finnish.

The Reduced Morningness-Eveningness Questionnaire (rMEQ) is a questionnaire developed in 1990 by Ana Adan and Helena Almirall. It is composed of five questions derived from the original MEQ by Horne and Östberg, namely items 1, 7, 10, 18 and 19. The scores between rMEQ and MEQ correlate significantly ($r = -0.898$, $p < 0.001$). (Adan and Almirall 1991.) The rMEQ is a quick and reliable measure for determining chronotype (Levandovski et al. 2013), but it has not been translated into Finnish.

The Diurnal Type Scale (DTS) was developed in 1980 by Torsvall and Åkesrstedt. It is composed of seven questions that ask about, for example, preferences and thoughts on waking up at a certain time. It can be used with shift workers and its consistency is good. (Lars Torsvall, Torbjörn Åkerstedt 1980.)

The Composite Scale of Morningness (CSM) has composed the most valid items from the MEQ and the Diurnal Type Scale. It has 13 questions, 9 of which are derived from the MEQ, and the score is between 13-55. (Smith et al. 1989.) Correlation between the CSM and the MEQ is significant ($r = 0.904$) as is the correlation between the CSM and the rMEQ ($r = 0.869$) (Caci et al. 2008). It is yet to be validated against physiological markers, such as melatonin or body temperature (Levandovski et al. 2013).

Other questionnaires developed to assess chronotype include the Circadian Type Inventory (CTI) (Folkard et al. 1979), an Ultra-Short Version of the Munich Chronotype Questionnaire (the μMCTQ) (Ghotbi et al. 2020) and the Circadian Energy Scale CIRENS (Ottoni et al. 2011). However, to the best of my knowledge, these questionnaires have not been widely used.

4.4 Comparing different methods of assessing chronotype

Methods of assessing chronotype differ from each other in multiple ways. Differences in reliability, convenience and required resources are the main factors that have to be taken into account when choosing a suitable method.

4.4.1 Physiological measurements

DLMO is regarded as the golden standard in determining chronotype and other reliable physiological methods are body temperature and cortisol secretion. Using DLMO in assessing chronotype can be inconvenient and other measures have been developed and compared to the DLMO.

4.4.2 Device-based monitoring

Statistically significant correlations have been observed between activity measured by actigraphy and the DLMO for the timing of the midpoint of the 5 hours with the lowest activity ($r = 0.674$, $p = 0.012$) and for the activity offset ($r = 0.607$, $p = 0.028$) (Bonmati-Carrion et al. 2014).

When compared to the DLMO, ambulatory circadian monitoring shows a stable phase relationship, as the sleep phase markers, such as L5 (five consecutive hours with the lowest values of recorded variable) and M5 (five consecutive hours with the highest values of recorded variable), obtained from subjective sleep ($r = 0.811$ with M5), wrist temperature ($r = 0.756$ with L5) and the composite variable TAP ($r = 0.720$ with M5) were highly and significantly correlated with the DLMO (Bonmati-Carrion et al. 2014).

Ambulatory circadian monitoring seems to be a new reliable method in determining individual's chronotype, but it would require the wrist temperature monitoring and new equipment. It is a valuable method in studying other sleep complaints, as it correlates so well with polysomnography, but in this case, it is not suitable.

4.4.3 Subjective measurements

Kantermann and others (2015) studied the correlation with the MEQ and the dim light melatonin onset (DLMO) and concluded that the DLMO correlated significantly with the MEQ score ($r = -0.70$, $p < 0.001$), making it a reliable tool for assessing chronotype. In the same study, they also noticed that MEQ was the second strongest predictor of the DLMO (beta = -0.41, $p = 0.004$) after the midpoint of sleep from the MCTQ (beta = 0.51, $p = 0.001$). Although the MEQ significantly predicts the DLMO, around a 4-hour range in the DLMO could be seen at a single MEQ score, meaning that the MEQ should not be used to time light or exogenous melatonin treatment, as it could result in the mistiming of these treatments relative to the DLMO.

The MEQ has also been proven to correlate with the intrinsic circadian period of the core body temperature rhythm ($r = -0.60$, $p < 0.02$) and cortisol excretion (Baehr et al. 2000, Bailey and Heitkemper 2001, Duffy et al. 2001). Zavada and others (2005) have previously concluded that the MEQ also correlates with the MCTQ, as the strongest correlation ($r = 0.7$) was found between MEQ and the midpoint of sleep on free days (MSF) from the MCTQ. This finding might indicate that the MSF may be the best marker for sleep-based assessment of chronotype.

The MCTQ has been validated against the MEQ, with strong correlations shown between the midpoint of sleep on free days and the score from the MEQ ($r = -0.74$, $p < 0.001$). When the MSF was corrected for sleep-debt accumulated during the workweek, the correlation was moderately strong ($r = -0.66$, $p < 0.001$) and when corrected for age and sex, it was even lower ($r = -0.59$, $p < 0.001$). The age and sex corrected midpoint of sleep is a standardised measurement of chronotype and does not necessarily reflect a subject's chronotype at their present situation. (Roenneberg et al. 2007.) In another study from 2005, the MSF correlated strongly with the MEQ ($r = -0.73$, $p < 0.001$) and the correlation with midsleep on workdays was also good ($r = -0.61$, $p < 0.001$) (Zavada et al. 2005).

The MCTQ has also been compared to actigraphy and a strong correlation has been observed between the midpoint of sleep on free days derived from the MCTQ and actigraphy ($r = 0.71$, $p < 0.001$). A strong correlation was observed also between the corrected midpoint of sleep from both the MCTQ and actigraphy ($r = 0.73$, $p < 0.001$) and in both comparisons, the means were not significantly different. (Santisteban, Brown et al. 2018.) The MCTQ derived midpoint of sleep has also been shown to correlate with other measurement, such as the DLMO ($r = 0.68$, $p < 0.001$) (Kantermann et al. 2015).

5. Measuring chronotype in large cohort studies

5.1 Description of the Finnish Retirement and Aging (FIREA) study

The Finnish aging and Retirement (FIREA) study (https//:sites.utu.fi/firea/en) is an ongoing longitudinal cohort study conducted at the University of Turku. The study started in 2013 and it aims to examine health behavioural and clinical risk marker changes during the transition to retirement. The study will also examine the long-term consequences of work and retirement on health in older age. The study population consists of public sector employees approaching retirement age. Participants were first sent questionnaires, and the ones whose statutory retirement date was set between 2014 and 2019 were also asked to participate in actigraphy measurements. In the FIREA study, actigraphs have been sent to the participants by mail with instructions, which stated that participants should wear the accelerometer continuously on their non-dominant wrist for 24 hours a day for 7 consecutive days and nights. The participants were instructed to remove the accelerometer during sauna to prevent overheating of the device. They were also instructed to complete a daily log while wearing the device. (Leskinen et al. 2018, Pulakka et al. 2019, Myllyntausta et al. 2020.)

5.2 Comparing potential measures of chronotype in a cohort study

The FIREA study is a large epidemiologic cohort study with actigraphy measurements that are performed simultaneously and repeatedly for hundreds of participants and questionnaires that have many thousand respondents. In Table 1 the applicability and reliability of different methods for determining chronotype are compared.

Table 1. Comparison of different methods and their applicability for a large, epidemiological cohort study

	Translated into Finnish	Easy to carry out	Quick	Requires tools	Quick and easy to interpret	Reliability
The Morningness-Eveningness Questionnaire	x	x	x		x	validated against DLMO, correlation strong and significant
The Munich Chronotype Questionnaire	x	x	x			validated against DLMO, correlation strong and significant
The Reduced Morningness-Eveningness Questionnaire		x	x		x	validated against the MEQ, correlation strong and significant
The Diurnal Type Scale		x	x			
The Composite Scale of Morningness		x	x			validated against the MEQ, correlation strong and significant
The Circadian Type Inventory		x	x			
The Ultra-Short Munich Chronotype Questionnaire		x	x			
The Circadian Energy Scale		x	x			
Actigraphy	not applicable	x		x		validated against DLMO, correlation strong and significant
Ambulatory Circadian Monitoring	not applicable	x		x		validated against DLMO, correlation strong and significant
The Dim Light Melatonin Onset	not applicable			x		
Body temperature	not applicable			x		validated against DLMO, correlation strong and significant
Cortisol	not applicable			x		

This means that many measures that require e.g. laboratory environment, expensive equipment or constant input and checking from the participants, such as the dim light melatonin onset, measurement of core body temperature and measuring cortisol from serum or saliva have to be excluded as unsuitable options. These methods are very reliable, but there are other reliable tools that are more suitable for large cohort studies.

In the FIREA study, the actigraphs have already been applied successfully and may, thus, be used for the assessment of chronotype as well. The already existing data can also be utilized and re-analysed. That leads to actigraphy and ambulatory circadian monitoring being attractive tools, but the ACM requires wrist temperature monitoring which is not possible with the current devices used in the FIREA study. Actigraphy has been proved a reliable measure in determining chronotype as it correlates well with e.g. the dim light melatonin onset and the MCTQ and it is also very convenient for the participants. However, the actigraph measurement have not been conducted to all of the FIREA participants, which narrows down the study population. It has to be remembered also that actigraphs are very sensitive in detecting sleep, but their specificity (i.e. their ability to separate wakefulness from sleep) is quite poor. This means that they can slightly overestimate sleep by defining immobile wakefulness as sleep. If actigraphs are used for determining chronotype, they should be used with sleep logs or other tools that easily recognize sleep from sedentary behaviour, such as laying on the couch watching TV.

In large epidemiologic cohort studies, different questionnaires are usually the easiest method for both the researchers and the participants. Even though self-reports are prone to bias, they are the most effortless tools in studies with large number of participants (Girschik et al. 2012). In the FIREA study, participants have repeatedly answered to questionnaires and the answer percentage is reasonably good. Questionnaires to be considered in this study are the Morningness-Eveningness Questionnaire and the Munich Chronotype Questionnaire, as they have both been translated into Finnish (Partonen and Urrila 2014). Other questionnaires, even though proven to be reliable and valid, are not as suitable because they haven’t been translated into Finnish.

Although the MEQ and the MCTQ are similar in their layouts and techniques, they differ in the main focus of defining chronotype. The MEQ focuses on preferences and ideals, when the MCTQ focuses primarily on actual behaviour and habits. Therefore, the choice depends on the aspects which are aimed to assess, morningness and eveningness as preferences, or the actual behaviour. As the main aim is to assess chronotype in an epidemiologic study rather than conditions such as sleep deprivation, the MEQ seems to be the better alternative. Levandovski and others (2013) have suggested that for studying desynchronization the MCTQ is probably the best instrument, whereas for assessing characteristics that change under specific situations, the MEQ might be better.

Bauducco and others (2019) concluded that the MCTQ is better for evaluating the actual behaviour and for deciding the proper timing of for example light treatment.

Using the MEQ is also supported by the fact that from the two Finnish versions, it is the only one that has been validated (Hätönen et al. 2008). It is also a shorter version than the original 19-question questionnaire, which makes it easier and a bit more effortless to answer and facilitates the data collect and analysis. It has also been used in other Finnish studies (Merikanto et al. 2012). The questionnaire is clear, the questions are easy to understand and answer to and the scoring and analysing the data is very simple.

It is also possible to use actigraphs for assessing chronotype among the smaller study sample, accompanied by the questionnaire. That could furthermore be used to further validate the Finnish version of the MEQ with actigraphs, since actigraphy has been proven to be a reliable measure for chronotype. As actigraphy data has already been collected in the FIREA study, the existing data could also be utilized in determining chronotype, but it would not be as reliable. The participants could also answer the questionnaire, wear the actigraph for seven consecutive days and at the same time complete sleep logs every day. That way error would be minimized and the results would be more reliable.

6. Discussion

Determining chronotype is important, as it has an effect on multiple different factors, such as health, lifestyle choices and work. Evening types are more likely to have health problems, and conversely, morning types seem to be healthier and happier. (Partonen 2015.) In addition, knowing patient's chronotype is very important and useful in the diagnostics and treatment of different sleep complaints and mood disorders, such as depression or anxiety.

Chronotype can be determined in many ways and they each have their advantages and limitations. Available resources, time and different types of participants are usually the factors limiting the use of some methods. More easy and effortless ways of measurement should be developed in the future, such as shorter questionnaires. In large studies with a big study population, like the FIREA study, the method has to be easy, reliable and cost-effective. If filling out a questionnaire takes too long, it is much more likely to return as an unfinished one. If the actigraph is uncomfortable to wear it is much more likely to not be worn properly. In addition, analysing data from actigraphy measurements is a challenge for researchers, as it requires time and skills. Methods that require e.g. taking saliva or urine samples or sleeping in a laboratory with electrodes attached are not very practical, because they can easily disturb participants' usual sleeping habits and can be very unnatural and uncomfortable. In addition, taking samples at home is quite easy to forget and then easy to fail in. Required resources are expensive and logistics might be challenging, which means that executing physiological measurements for thousands of participants is practically impossible.

Problems with the studies referenced in this thesis were for example small study samples, different environments and methods and possibly outdated study tools. The reliability of the studies was all around good, but some were difficult to compare with each other even if they were about the same measure. Not all studies were in agreement with each other, such as the two studies comparing the DLMO with the midpoint of sleep during free days from the MCTQ, Kantermann et al. 2015 and Ruiz et al. 2020. This is interesting, as the study settings of these two studies seemed to be very similar to each other. The study conducted by Kantermann and others found that the correlation between the measures is strong ($r = 0.68$, $p < 0.001$), but the other study found no statistically significant correlation between the two measures ($r = 0.25$, $p = 0.13$). In the 2015 study, the study population was 60 people and the saliva samples were collected at half-hourly intervals starting 6 or 7 hours before the average weekly bedtime and continuing until 2 or 3 hours after average weekly bedtime. The DLMO was calculated as the clock time when the melatonin concentration exceeded the mean of 3 low consecutive daytime/early evening values plus twice the standard deviation of these points. In the 2020 study, samples were collected from 76 participants and collecting started 4.5 hours before the mean bedtime of the population. During the phase assessment participants remained awake from 18 to 23 hours in dim light and spent the sampling period watching a dimmed TV and interacting with other participants or staff. DLMO was defined as the point in time when the melatonin concentration exceeded the threshold of 3 pg/ml. The main difference between the two studies was that in the 2020 study all participants were healthy, whereas in the 2015 study there was 24 participants with a delayed sleep phase disorder. In addition, the times for collecting samples were different and the overall time of taking samples was also different. These varying methods might explain the differences in the results.

When comparing different methods of assessing chronotype, the most used tool in literature and other studies seemed to be the Horne & Östberg's Morningness-Eveningness Questionnaire, followed by the more recent Munich Chronotype Questionnaire. They both have their disadvantages, even though they try to minimize the impact of other possible affecting factors, such as shift work or age. Even using an alarm clock on a free day can disturb the results, so it would be interesting to see a questionnaire that does not have so many limitations and challenges as the existing questionnaires have. Using questionnaires in assessing chronotypes is easy, reliable, effortless and cost-effective. Many questionnaires have been developed, but there is not yet a perfect one suited for every study. There needs to be more research on alternative questionnaires, such as validation studies against the dim light melatonin onset or other physiological markers of the circadian rhythm. The Finnish version of the Munich Chronotype Questionnaire should be validated properly, as it seems to be a better alternative for utilizing in the treatment of sleep complaints and mood disorders.

It was notable that chronotype does not necessarily have a clear definition, as the term was used very incoherently across different studies. On the other hand, in some studies it was clarified that chronotype means the actual behaviour and morningness or eveningness is more about preferences. In this study, I used the term chronotype relatively freely, because it is a much shorter word than morningness-eveningness. In the future researchers should be clearer and clarify straight at the beginning the actual meaning of the word they are using. It would clarify the actual study objective they are trying to present and would make it easier for others to reference correctly.

In conclusion, the best methods for determining individual’s chronotype in Finnish large-scale epidemiological studies are the Morningness-Eveningness Questionnaire when assessing preferences, the Munich Chronotype Questionnaire when assessing actual sleep behaviour and actigraphy as an additive tool for validation. In the future, more research on utilizing the information of one’s chronotype is needed, as chronotype seems to affect many aspects in life and overall health. In addition, further validation of the Finnish versions of the questionnaires is required. Using chronotype assessment in healthcare should be more common, at least in the diagnosis and treatment of for example sleep complaints and mood disorders.

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APPENDIX

Appendix 1. The Finnish Version of the The Morningness-Eveningness Questionnaire (MEQ) (slightly modified from Merikanto et al. 2015)

Lyhyt aamuisuus-iltaisuuskysely.

Kyselyn summapistemäärän perusteella jaetaan iltavirkkuihin ne, jotka saavat 5–12 pistettä, päivävirkkuihin ne, jotka saavat 13–18 pistettä, ja aamuvirkkuihin ne, jotka saavat 19–27 pistettä.

1. Kun oletetaan sopivat ympäristön olosuhteet, kuinka helppoa teille on aamuisin vuoteesta nouseminen?	Ei lainkaan helppoa	1 p.
	Ei kovin helppoa	2 p.
	Melko helppoa	3 p.
	Hyvin helppoa	4 p.

2. Kuinka väsyneeksi tunnette itsenne aamuisin ensimmäisen puolen tunnin aikana?	Hyvin väsyneeksi	1 p.
	Melko väsyneeksi	2 p.
	Melko levänneeksi	3 p.
	Hyvin levänneeksi	4 p.

3. Oletetaan, että olette päättänyt ruveta harrastamaan jotakin urheilulajia. Ystävänne suosittelee teille harjoitusohjelmaksi kaksi kertaa viikossa tunti kerrallaan. Paras aika hänelle on aamuisin kello 7.00-8.00. Pitäen mielessänne vain oman ”parhaalta tuntuu” -rytminne, kuinka luulisitte suoriutuvanne?	Tuntuisi hyvin vaikealta	1 p.
	Tuntuisi melko vaikealta	2 p.
	Olisin kohtuullisessa vireessä	3 p.
	Olisin hyvässä vireessä	4 p.

4. Oletetaan, että teidän täytyy osallistua kahden tunnin kovaan fyysiseen työhön. Voitte täysin vapaasti suunnitella aikataulunne. Ottaen huomioon vain oman ”parhaalta tuntuu”-rytminne, minkä seuraavista vaihtoehdoista valitsisitte?	Klo 8.00-10.00	4 p.
	Klo 11.00- 13.00	3 p.
	Klo 15.00-17.00	2 p.
	Klo 19.00-21.00	1 p.

5. Oletetaan, että voitte valita työaikanne. Otaksukaa, että työpäivä on viiden tunnin mittainen, työ on mielenkiintoista ja palkkaa maksetaan tulosten mukaan. Mitkä viisi PERÄKKÄISTÄ tuntia valitsisitte?	13-18, 14–19, 15–20, 16–21, 17–22, 18–23, 19–24, 20–1, 21–2, 22–3, 23–4	1 p.
	10-15, 11-16, 12-17	2 p.
	5–10, 6–11, 7–12, 8–13, 9–14	3 p.
	4-9	4 p.
	24-5, 1-6, 2-7, 3-8, 4-9	5 p.

6. On olemassa niin sanottuja ”aamuihmisiä” (aamunvirkku, illantorkku) ja ”iltaihmisiä” (illanvirkku, aamuntorkku). Kumpaan ryhmään Te kuulutte?	Ehdottomasti ”iltaihmisiin”	1 p.
	Enemmän ”ilta-” kuin ”aamuihmisiin”	2 p.
	Enemmän ”aamu-” kuin ”iltaihmisiin”	3 p.
	Ehdottomasti ”aamuihmisiin”	4 p.

Tulos: