

Time to Eat

The diet of night shift workers from different dietary perspectives and its association with health and safety

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Thesis

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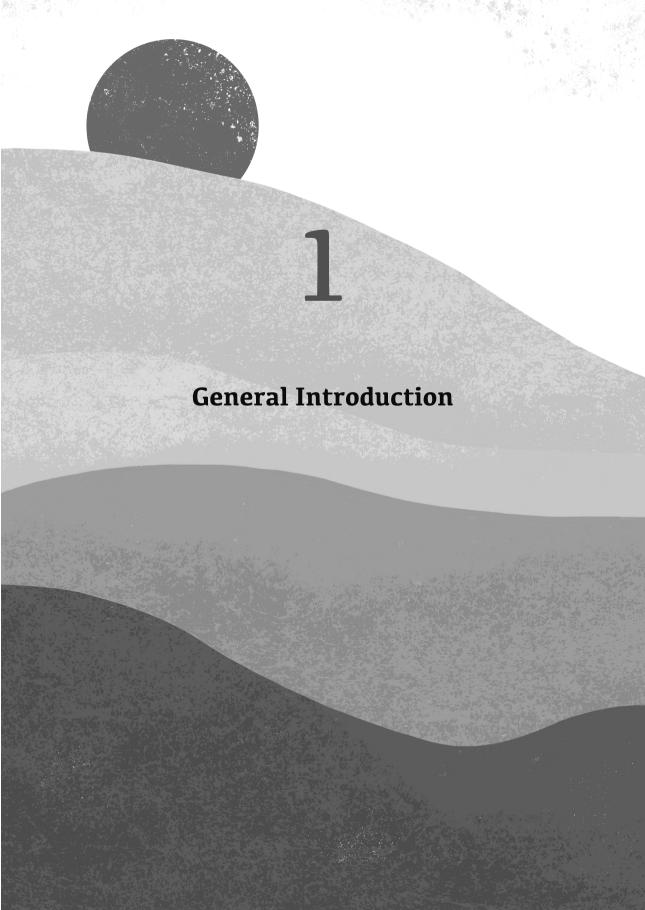
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Background

Like many other organisms, humans have developed intrinsic biological rhythms that follow a cycle of approximately 24 hours, also called circadian rhythms [1-3]. Circadian rhythms play an important role in regulating metabolic processes in the body and enable humans to anticipate daily changes in the environment and adjust their behaviour and physiology to the corresponding time of day [1]. These 24-hour rhythms are internally regulated but are adjusted by external cues, so-called Zeitgebers (German for time giver) [1, 4]. The most influential external cue is daylight exposure, caused by the rotation of the earth, which results in a 24-hour light-dark cycle [1]. Other external cues that regulate this cycle are temperature, food intake, social life and work schedules [5, 6]. External cues are processed by the suprachiasmatic nucleus (SCN) located in the hypothalamus, which is directly connected to the retina of the eye and thereby sensitive to light exposure [1, 3, 4]. The SCN serves as a central clock and ensures alignment between the external cues and the intrinsic biological rhythms [4]. Intrinsic biological rhythms are regulated by peripheral clocks, which are present in nearly every tissue and organ [1, 3, 4]. Together, these biological clocks regulate many physiological processes in a 24-hour cycle, such as body temperature, heart rate, the release of hormones, sleep, and appetite, and thus strongly influence human digestion and metabolism [4, 7]. The impact of circadian timing on human health is an emerging topic, especially due to the negative effect of circadian disruption on health [8-10].

Several factors can disrupt the circadian rhythm, especially in modern society where the light-dark cycle is no longer solely determined by the rotation of the earth [10, 11]. With the arrival of electricity and the internet, people are increasingly exposed to artificial light, smartphones and other devices with a screen [12]. Moreover, people are less exposed to daylight, because most of the work is done indoors [12]. Consequently, the sleep-wake cycle is desynchronized with the circadian rhythm [3, 11, 12]. Other factors contributing to a disrupted circadian rhythm are jetlag and (night) shift work [3, 10, 11, 13, 14]. For various professions, such as drivers, factory workers, police officers and healthcare workers, it is necessary to work outside the conventional working hours, including during the night. For example, health care workers' working hours can be scheduled both during the day and night to ensure continuous health care. In the Netherlands, about 26 per cent of the health care workers work night shifts [15]. Unlike

jet lag, where the body can slowly adjust to the new light-dark cycle, this is not the case during night shift work where the light-dark cycle is not in line with the sleep-wake cycle and consequently disturbs many physiological processes in the human body [3].

Therefore, it is unsurprising that many epidemiological studies have shown that night shift work is associated with negative health and safety consequences [16-18]. In the long term, night shift workers are at higher risk of becoming overweight or obese, and of having type 2 diabetes, cardiovascular diseases, gastrointestinal diseases, several types of cancer, sleep disorders and psychological disorders (depression) than day shift workers [14, 19-28]. In the short term, night shift workers experience more gastrointestinal complaints, poor daytime sleep, and psychological and mental health problems (stress) than day shift workers [29-32]. Moreover, night shift work is associated with higher safety risks. For example, night shift workers have a 30 per cent increased risk of making (medical) errors or having accidents than day shift workers [16-18]. This is mainly caused by shift work-related fatigue [17] and is related to the circadian regulations of sleep and alertness (cognitive performance). Alertness levels are highest during the daytime and lowest between 02:00 h and 06:00 h in the early morning [33, 34]. All in all, night shift work has many negative consequences on health and safety. In this thesis, we will focus only on the short-term health effects of gastrointestinal complaints, hunger feelings and alertness as part of physical and mental well-being [35] and linked to safety.

Several strategies have been proposed to mitigate the negative consequences of shift work on health and safety. The use of lamps that simulate daylight during the night shift is one of these strategies that are effective to increase alertness during the night shift [36]. Other strategies are applying forward rotating shift work schedules or napping during the night shift [20, 29, 37, 38]. Furthermore, melatonin and caffeine when used correctly- have been proposed to be beneficial for sleep during the day and alertness during the night shift [37]. Another way to reduce fatigue and improve alertness during the night is by applying nutrition strategies [21, 39], which could also mitigate the negative consequences of shift work on gastrointestinal complaints and other health aspects [40].

For a long time, it is globally recognized that nutrition is fundamental and a modifiable risk factor for human health across the life span [41]. Nowadays, there is increased recognition of the relationship between diet, biological rhythms and metabolism and their association with health and disease [40, 42, 43]. This interaction is also referred to as chrono-nutrition [6, 40, 42]. The field of chrono-nutrition focuses on the influence of meal timing, meal composition, meal size, meal frequency and regularity on the biological clock and vice versa [40, 42]. Nutrition may act as an environmental factor on the circadian rhythm [42, 44]. Hence, it may work in both directions: either aligning or misaligning the circadian rhythm [44, 45]. When the sleep-wake cycle is aligned with the light-dark cycle, food is consumed during the day and the human body is in a fasted state during the night. In this way, and when food is consumed at regular time points, food intake could act as a synchronizer of the biological clock [6, 45]. An increasing number of studies show that chrono-nutrition may play an important role in the health and safety of the general population but especially subpopulations such as night shift workers [40, 42].

Night shift workers redistribute their food intake from day to night [46-48], resulting in a misalignment of the circadian rhythm. Moreover, night shift workers tend to have a higher, irregular, meal frequency and a poorer diet quality than day shift workers [28, 49], which is likely not beneficial for maintaining a normal circadian rhythm. Yet, the total energy intake over 24 hours does not seem to vary between day, evening and night shifts in shift workers [21, 50]. However, the findings of studies on dietary habits among shift workers, as well as their link with health and safety, are sometimes contradictory, due to limitations in study design and dietary assessment methods [21. 47, 50-52]. For example, different food frequency questionnaires have been used and therefore results are hard to compare [52]. Moreover, meal classifications were not consistent, not well documented or were reflecting the time of day meals were consumed, for example, breakfast, lunch or dinner [21]. In addition, some studies did not take details on the meal composition into account [51]. Therefore, dietary assessment methods should be improved by validating them for the aim of the study and target population and should be well-documented. In addition, diet consists of multiple aspects (e.g. meal timing, meal composition, meal frequency), all of which can potentially be associated with health and safety.

Meal timing

Meal timing is increasingly recognized as an important factor in the field of chronobiology and nutrition in contemporary literature [44, 53, 54]. However, compared to rodent studies there is little known about how exactly meal timing regulates the circadian rhythm in humans [40]. As mentioned before, it is suggested that regular timing of food intake ensures an alignment with the biological clock. The energy, glucose and lipid metabolism has also been adapted to this circadian rhythm [5, 6]. For example, the human body seems to have greater diet-induced thermogenesis in the morning than in the evening, indicating that, in the morning, the body could burn more calories and provides more energy [40, 55]. Moreover, glucose tolerance is lower in the evening and night compared to the morning, which may be due to decreased insulin sensitivity and beta-cell function in the evening [6, 42, 56-59]. With respect to the lipid metabolism, triglycerides in the blood are higher during the day than night, while for free fatty acids it is just the opposite [6, 60-63]. In this way, the body seems to prepare for when it has to process food and provide the most energy [64].

Eating during the night shift, therefore, causes a misalignment with the circadian rhythm and consequently disrupts energy, glucose and lipid metabolism [56]. When foods are consumed later during the day, including during the evening and night, instead of earlier in the day, there is a higher risk of being overweight despite similar energy intake [5, 40, 65]. A possible explanation could be that similar energy intake in the evening, compared to the morning, result in a lower energy expenditure due to decreased diet-induced thermogenesis [40]. In addition, due to the disruption in glucose metabolism, postprandial glucose levels are higher [56, 59, 64]. These findings support the theories that foods are processed differently throughout the day and meal timing plays an important role in maintaining energy balance [40, 64-66]. It may also explain why night shift workers are at higher risk of being overweight than day shift workers. Moreover, as circadian misalignment has been shown to decrease insulin sensitivity and pancreas function, it may also explain a higher risk of type 2 diabetes in night shift workers [55, 67].

In theory, restricting food intake during the night shift prevents misalignment with energy, glucose and lipid metabolism [34, 68]. However, not eating during the night shift, while being active, could be challenging in practice, as it can lead to increased

hunger and food cravings during the night [34]. However, it is unclear what and when during the night shift you can eat best. Only a few nutrition intervention studies on the effect of eating (or not eating) during the night shift on health and safety outcomes have been conducted in night shift workers [69] and a few during simulated night shifts [68, 70, 71]. However, these are too few to draw any conclusions and establish evidence-based guidelines about what and when to eat during the night shift to ensure minimal misalignment with the biological clock and prevent hunger. Therefore, more research about meal timing is needed to be able to draw up dietary guidelines for night shift workers.

Meal composition

As the circadian clock plays an important role in the energy and nutrient metabolism, each macronutrient may have different impact on the metabolism. Therefore, besides meal timing, the composition of the meal may be an important factor for both maintaining a normal circadian rhythm and circadian disruption and consequently for health and safety [64].

Macronutrient intake also seems to be associated with cognitive performance (including alertness) [51]. Most studies on this relationship were performed during the daytime and only a few during the night [39, 72, 73]. These studies suggest that consumption of meals during the night shift with specific (macro)nutrient compositions may reduce fatigue and improve alertness [39, 74]. However, the effects of different macronutrient composition of meals are not always very distinct and sometimes even contradictory [21, 51, 72, 74]. A factor that could contribute to these contradictory results is the time interval between the consumption of a meal and the measurement of alertness. Cognitive performance (including alertness) may be different immediately after a meal than one or two hours after a meal [75]. Moreover, since a meal typically does not consist of a single macronutrient, research should particularly focus on the differential effects of the specific types of macronutrients in a mixed meal, taking into account the time interval between the meal and the alertness task [51]. Therefore, this thesis will further explore whether different time intervals result in different associations between macronutrient intake and alertness.

In addition to macronutrient composition, glycemic index (GI) and glycemic load (GL) of meals and their association with health and cognitive performance (including

alertness) are of interest. The impact of low GI and GL diets on health seems to be minimal in healthy people, but beneficial in people with impaired glucose tolerance 1761. The link between GI and GL of diets on cognitive performance is unclear and seems to depend on the type of carbohydrates, meal timing and the cognitive domain (i.e. memory, alertness) being tested [77, 78]. Also, the exact mechanisms of these associations are vet unclear. Small variations of blood glucose levels have been suggested as an explanation, because a lower postprandial glycemic response could be beneficial to cognitive performance, including alertness [77, 79]. The glycemic response depends on the rate at which carbohydrates are absorbed in the blood which can be classified by the GI or GL of carbohydrate-containing foods. This way. carbohydrate-containing foods with a high GI are absorbed guicker than low GI carbohydrate-containing foods. While the GI only takes into account the quality of the carbohydrate, the GL also includes the quantity of the carbohydrates. Thus, a lower postprandial glycemic response may be obtained by consuming carbohydrates with a lower GI or GL. Especially the effects of a meal with a low GL on alertness have not well been investigated yet [78]. In the long term, using meals with a low GL during the night shift could also be of interest for reducing the risk of developing type 2 diabetes.

Meal size and frequency

The size of a meal, in terms of energy intake, seems to be associated with alertness levels [34, 39, 70, 71, 80]. Eating a large meal (~30% of estimated daily energy requirement (EER)) during the night shift resulted in lower alertness during the circadian nadir [34, 70, 71], while a smaller meal (~10% EER) resulted in the best alertness compared to a large meal or no meal at all [34, 70, 71, 81]. Eating a small meal also reduced hunger feelings compared to not eating [82] and led to better post-prandial responses than a large meal [69, 81]. However, it is unknown whether eating several (healthy) small meals could further reduce hunger feelings while maintaining alertness levels. No intervention study investigating the effect of meal frequency on health and safety outcomes during the night shift has been conducted so far.

In such a study, gastrointestinal complaints should also be included as an outcome measure, because eating several small meals or snacks during the night might have consequences for the digestive system, as the digestive system also follows a natural day and night rhythm. At night, the digestive system is in a resting state and metabolic processes such as stomach and intestinal peristalsis, production of gastric juices and

insulin secretion are diminished compared to daytime [83]. By eating one or multiple meals at night (instead of not eating) this relative resting state is disrupted and could result in gastrointestinal complaints. It has been shown that night shift workers indeed experience more gastrointestinal complaints than day shift workers [24, 34, 84], which is likely the result of a shift in food intake from day to night and the tendency to snack more frequently instead of eating a full meal [46, 47]. In this thesis, the effect of meal frequency will be further studied.

Diet quality

Besides direct associations between nutrition, e.g. meal composition and meal frequency, and health outcomes, it is important to assess overall diet quality, which can be used to study the potential impact of overall diet on health and disease [85-87]. One of the approaches to assess overall diet quality is by calculating an index score [86, 88, 89]. One commonly-used Dutch index to assess diet quality is the Dutch Healthy Diet 2015-index (DHD2015-index) [90-92]. This index has been developed to assess adherence to the Dutch food-based dietary guidelines of 2015 [90, 93, 94]. The DHD2015-index can be calculated using data from multiple 24-hour dietary recalls or a food frequency questionnaire (FFQ) [95]. However, these methods are rather burdensome for participants and researchers, which is undesirable if diet quality is the sole diet parameter of interest [96, 97]. In that case, a short FFQ, specifically developed to assess the DHD2015-index score, may be useful.

Previous studies were inconclusive on how shift work affects diet quality and results seem to be dependent on many factors, including the type of night shift work, and regularity of work schedules [47, 52]. In general, night shift workers seem to choose unhealthier foods during the night shift and consume more saturated fatty acids and soft drinks than day shift workers, which negatively affects diet quality. Moreover, most studies did not find differences in daily energy intake between day and night shift workers [47, 52]. Therefore assessing diet quality, by calculating DHD2015-index scores, in night shift workers may add to a better overall picture of the dietary habits of night shift workers.

Taste (patterns)

One of the most important drivers of food choice and food consumption is liking, which depends on the sensory characteristics of a food, such as its taste or flavour [98, 99]. Taste has various functions; it may give warning signals or indicate nutrients [100]. In general, a bitter taste is associated with poisonous food, sour taste with unripe foods, sweet taste with the presence of carbohydrates, salt with the presence of sodium content and umami taste with the presence of proteins in the food [100, 101]. Through these signals infants already have a high preference for sweet taste and a dislike for bitter taste at birth [102, 103]. However, these innate taste preferences and aversions can develop over time, due to repeated exposure and learning processes [104]. For instance, as we get older we can also appreciate a certain bitterness in products such as coffee and beer. However, what we like is not always in line with what is healthy and a trade-off must be made between what is healthy and what is tasty [105].

When people are sleep-deprived, as is the case with night shift workers, they have fewer cognitive reserves to make informed decisions about health for example [106]. Consequently, decisions, including selecting foods, may be made more automatically and predominantly based on habits. Food choices in a sleep-deprived state may then revert back to strong innate taste preferences, such as those for sweet and salty/savoury foods, taste qualities that are initially associated with nutrient and energy content of the food [98, 99, 103, 107]. This could explain why night shift workers crave tasty but unhealthy snacks, which are most likely sweet or savoury, and rich in energy or fat [21, 102, 106, 108-112] resulting in poorer food choices [113].

As taste may be an important driver of choice and therefore of food intake [114], dietary patterns should not only be studied from a nutritional but also from a taste perspective [101, 115, 116]. One way to study dietary taste patterns is to combine food intake data with taste characteristics of the consumed foods [115, 117]. Better insight into dietary taste patterns of night shift workers in relation to diet quality may improve the understanding of their food choices.

Altogether, several nutrition strategies may be considered for night shift workers to improve health and safety [21, 28]. Yet, it is unknown what strategies work best. Previous reviews assessing dietary habits of shift workers and associations with their health and safety show conflicting findings attributing these, among other things, to the

used study designs, limited dietary assessment methods, or unclear meal definitions (e.g. meals vs snacks and eating occasions) [21, 47, 52].

Accurate dietary assessment is crucial to guarantee the quality of studies on the relationship between nutrition, health and alertness. Commonly used self-reported dietary assessment methods are food frequency questionnaires (FFQ), and 24-hour dietary recalls (24hR). FFQs are used to assess the consumption frequency of specific food groups over a specific time period (habitual intake). 24hR assesses actual food intake over the past 24 hours and provides detailed information on what, how much and when foods and beverages were consumed. Based on this information, various aspects of nutrition can be investigated such as meal composition, meal frequency, meal timing, meal size and diet quality. Moreover, food intake data can be linked to other food characteristics, such as taste and glycaemic index. It is eminent that the dietary assessment method is tailored to the population of interest to be able to investigate the diet from different dietary perspectives and its association with health and safety outcomes [118].

The complex relation between nutrition, metabolism, health, and cognitive performance (including alertness) is not fully understood [28]. A better understanding is needed, especially in night shift workers [21, 74]. The different aspects of nutrition should be taken into account, which are interlinked and what contributes to its complexity. To date, few nutrition intervention studies have been conducted in night shift workers, or in simulated night shifts, focusing on minimalization of the misalignment of circadian rhythms during night shift work [69].

Investigating the short-term effects of potential nutrition strategies on the perceived well-being and safety of night shift workers support the feasibility of nutrition strategies in the long-term. For this, insight in the current dietary habits of night shift workers is needed to be able to align nutrition interventions accordingly.

Aim and outline of this thesis

Altogether, there are many knowledge gaps and therefore this thesis aims to further investigate which nutrition strategies can be applied to night shift workers resulting in the most optimal alertness levels and the least hunger feelings and gastrointestinal complaints, or in other words, that provide the best safety and perceived well-being. To this aim, the following research questions were defined:

- How is *meal composition* associated with alertness levels during the night shift?
 (Chapters 4 and 6)
- 2. Is the impact of a meal on alertness time-dependent? (Chapter 4)
- 3. How is *meal frequency* associated with alertness, hunger feelings and gastrointestinal complaints in night shift workers? (**Chapters 5 and 6**)
- 4. What is the *diet quality* of night shift working nurses and how can it be validly assessed? (**Chapters 2, 3 and 6**)
- 5. Do dietary *taste patterns* of night shift working nurses differ from those of a general population? (**Chapter 3**)
- 6. How are *taste* patterns related to *diet quality* in night shift working nurses? (Chapter 3)

Chapter 2 describes the development of the Eetscore FFQ, a short food frequency questionnaire specifically developed to assess quality of the overall diet by evaluating adherence to the Dutch dietary guidelines by means of the DHD2015-index. We examined associations between the DHD2015-index scores, derived from the Eetscore FFQ, and participants' characteristics. Moreover, we evaluated the relative validity and reproducibility of the Eetscore FFQ by comparing the DHD15-index derived from the Eetscore FFQ with the DHD15-index derived from a full-length FFQ in a healthy adult population (n=751).

In **Chapter 3** we assessed dietary taste patterns in female night shift working nurses (n=120) and compared these during and outside the night shift. In addition, we compared the dietary taste patterns of the nurses with those of a female reference population (n=307), and studied associations between dietary taste patterns and diet quality.

In **Chapter 4** we investigated the association between macronutrient composition with objective and subjective alertness, during different time periods during the night shift in an observational study. We used the data from this observational study in **Chapter 5** to investigate

the association between eating frequency with alertness and gastrointestinal complaints in female nurses during the night shift.

In **Chapter 6** we investigated the effect of meal frequency and glycaemic load of meals during the night shift on alertness levels, hunger levels and gastrointestinal complaints in female health care workers. We studied the effect of 0, 1 or 3 small meals during the night shift, either with a low or high glycaemic load, on alertness levels, hunger levels and gastrointestinal complaints.

Finally, in **Chapter 7** we discuss the main findings and put them in perspective. In addition, we provide the implications of our findings and provide recommendations for further research.

The results of this thesis will provide more clarity on the relationship between nutrition and the health and safety of night shift workers and can be used to develop evidenced-based dietary guidelines for night shift workers as a vital part of occupational health and safety management programs in shift work.

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2

Development and evaluation of a diet quality screener to assess adherence to the Dutch food-based dietary guidelines

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Abstract

The Eetscore FFQ was developed to score the Dutch Healthy Diet index 2015 (DHD2015-index) representing the Dutch food-based dietary guidelines of 2015. This paper describes the development of the Eetscore FFQ, a short screener assessing diet quality, examines associations between diet quality and participants' characteristics, and evaluates the relative validity and reproducibility of the Eetscore FFQ in a cross-sectional study with Dutch adults. The study sample consisted of 751 participants, aged 19-91 v, recruited from the EetMeetWeet research panel. The mean DHD2015-index score based on the Eetscore FFQ of the total sample was 111 (SD 17.5) out of a maximum score of 160 points and was significantly higher in women than in men, positively associated with age and education level, and inversely associated with BMI. The Kendall's tau-b coefficient of the DHD2015- index between the Eetscore FFQ and the full-length FFQ (on average 1.7-month interval, n=565) was 0.51 (95% CI 0.47, 0.55), indicating an acceptable ranking ability. The intraclass correlation coefficient (ICC) between DHD2015-index scores derived from two repeated Eetscore FFQs (on average 3.8-month interval. n=343) was 0.91 (95% CI: 0.89, 0.93) suggesting a very good reproducibility. In conclusion, the Eetscore FFQ was considered acceptable in ranking participants according to their diet quality compared with the full-length FFQ and showed good to excellent reproducibility.

Introduction

Adherence to dietary guidelines is often evaluated by quantifying overall diet quality, which on its turn can be used to study the potential impact of overall diet on health and disease [1-3]. Diet quality is also frequently used to adjust for overall diet in epidemiological studies exploring associations between specific dietary factors, such as alcohol consumption, and health outcomes [4-6]. One of the approaches to assess overall diet quality is by calculating an index score [2, 7]. One of a commonly-used Dutch index used to assess diet quality is the Dutch Healthy Diet 2015-index (DHD2015-index) [8-10].

The DHD2015-index has been developed to assess adherence to the Dutch food-based dietary guidelines of 2015 [8, 11, 12]. The DHD2015-index can be calculated using data from multiple 24-hour dietary recalls (24hR) or a food frequency questionnaire (FFQ) designed to estimate daily energy intake, macronutrients [13], and relevant food groups. Calculating the DHD2015-index is particularly relevant to quantify diet quality for use in epidemiological analyses as either an exposure factor or covariate. However, administering multiple recalls or a general FFQ is rather time-consuming and burdensome for participants, researchers and interviewers, and in case diet quality is the sole parameter of interest, aforementioned dietary assessment methods may be unnecessarily time consuming [14, 15].

Therefore, we developed the Eetscore FFQ to assess intake for estimating the DHD2015-index score for monitoring and ranking individuals based on their diet quality. The Eetscore FFQ could be used for research purposes but also for use in clinical settings to assess adherence to the Dutch food-based dietary guidelines and to monitor dietary changes [16-18]. In the present paper we describe the development of the Eetscore FFQ and examine associations between the DHD2015-index scores, derived from the Eetscore FFQ, and participants' characteristics. Moreover, we evaluated the relative validity and reproducibility of the Eetscore FFQ.

Methods

Participants

Participants were recruited from the EetMeetWeet research panel, a longitudinal observational study on diet and health in Dutch adults. This research panel consisted of inhabitants living in or near five cities located in the central part of the Netherlands (i.e., Wageningen, Renkum, Ede, Arnhem and Veenendaal) [19]. The present observational study was conducted between February 2017 and July 2017. All participants of the EetMeetWeet research panel (n 4936) were invited and 1055 participants were willing to participate in this study. Participants with data of at least one Eetscore FFQ (n 760) were included in the study (**Suppl. Figure 2.1**). We excluded seven participants who were pregnant, and two participants with a BMI above 45 kg/m2. The final study sample included 751 participants to examine associations between DHD2015-index scores and participants' characteristics, 565 participants to evaluate the relative validity of the Eetscore FFQ, and 343 participants to evaluate the reproducibility of the Eetscore FFQ.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki. As human participants were not subjected to procedures or were required to follow rules of behaviour and the study did not concern medical scientific research, the study was not subjected to the Medical Research Involving Human Subjects Act (WMO) and did not need approval of the Medical Ethical Committee of Wageningen University. All participants registered themselves and gave written informed consent.

Study design

Participants were asked to complete various questionnaires on their dietary intake as well as some general demographic and lifestyle characteristics. Dietary intake data were collected from the Eetscore FFQ and a full-length FFQ (**Suppl. Figure 2.1**). FFQs were administered online in a random order separated by at least one month, where 47% of the participants first completed the Eetscore FFQ and subsequently the full-length FFQ. In order to evaluate the reproducibility of the Eetscore FFQ, all participants were asked to complete the Eetscore FFQ for a second time.

DHD2015-index

The DHD2015-index consists of 15 food components representing the Dutch dietary guidelines; vegetables, fruit, whole grain products, legumes, nuts, dairy, fish, tea, fats and oils, coffee, red meat, processed meat, sweetened beverages and fruit juices, alcohol, and salt. The scoring for the DHD2015-index has been described in detail elsewhere [9] and is summarised in **Table 2.1** including cut-off and threshold values. For each component a maximum of 10 points can be allotted which means complete adherence to the Dutch dietary guidelines. Assessment of all scores together result in a total score ranging between 0 and 150 points. The DHD2015-index score gives an indication of diet quality and is positively associated with nutrient density [9] and negatively associated with all-cause mortality [20].

Development Eetscore FFQ

The Eetscore FFQ was specifically developed to assess the Dutch Healthy Diet 2015 index [9] using data of the Dutch National Food Consumption Survey (DNFCS) 2007-2010 [21] as a reference. Foods were selected that were part of a component in the Dutch dietary guidelines [22-25]. Thereafter, foods were aggregated into food items based on their food group, portion size and eating time. For example, 'fruit' was considered as one food item whereas 'cheese' was divided into 'cheese on bread' and 'cheese with dinner'. Furthermore, sodium intake was separated into two parts: sodium intake from foods and discretionary salt. Two items on discretionary salt were included to estimate the frequency of salt or Na-rich products (i.e. soy sauce and soup flavouring) added during cooking and at the table.

In addition to the 15 components of the DHD2015-index, the Eetscore FFQ was also developed to score one additional component on unhealthy foods. This so-called unhealthy choices component was based on a guideline of the Netherlands Nutrition Centre (NNC) [8, 12] aiming to get insight in dietary intake beyond the Dutch dietary guidelines. Foods that are high in energy, saturated fat and sugar have been categorized as unhealthy by the NNC. Therefore, food items that contributed most to total energy, saturated fat and mono- and disaccharide intake of the adult population in the DNFCS 2007-2010 [21] were selected to be included in the unhealthy choices component, unless they were already included in one of the other DHD2015-index components. For example, although orange juice was categorised as an unhealthy choice, it was not included in the unhealthy choices component as it was already

included in the component sugar-containing beverages. Food items included in the unhealthy foods component were sweet spreads, cakes, cookies, chips or pretzels, chocolate, savoury snacks, sauces, and use of sugar in coffee or tea. Together these unhealthy food items contributed for at least 80% to total energy, saturated fat and mono- and disaccharide intake [26].

The aggregation of foods resulted in a list of fifty-five food items, which together accounted for 85% of energy intake from the adult population of the DNFCS 2007-2010 (**Suppl. Table 2.1**). These fifty-five food items were interrogated in forty questions covering the intakes of all components over the previous month. The six answer categories for frequency questions ranged from 'never' to 'every day' for regularly consumed foods and from 'not this month' to '4 times a month' for episodically consumed foods. Portion sizes were assessed in standard portions and commonly used household measures [27]. Average daily intakes of food items were calculated by multiplying frequency of consumption by portion size in grams. The sodium content of a food item was calculated by multiplying the weighted frequency of use by the sodium content of each food in that food item [21, 28]. The Eetscore FFQ was administered via the open-source survey tool LimeSurveyTM (LimeSurvey Project Team / Carsten Schmitz, Germany, 2012).

Scoring DHD2015-index from Eetscore FFQ

The food components vegetables, fruit, wholegrain products, legumes, nuts, dairy, fish, tea, fats and oils, coffee, red meat, processed meat and sweetened beverages and fruit juices were scored according to the scoring of the original DHD2015-index (**Table 2.1**). The scoring for the components alcohol and sodium deviates from the scoring of the original DHD2015-index. The Eetscore FFQ distinguishes between alcohol consumption during week and weekend days to account for binge drinking [29]. For both subcomponents a maximum score of 5 points can be allotted. The intake of discretionary salt contributed at maximum 2 points out of 10 based on the assumption that about 20% of total sodium intake from the Dutch population is from added salt [21, 30-32]. Sodium intake from foods contributed to the remaining 8 points. The unhealthy choices component was scored as a moderation component based on the guideline to limit consumption of unhealthy foods. A score of 0 was assigned when seven or more unhealthy foods per week were consumed. The maximum score of 10 points was assigned when less than three unhealthy foods per week were consumed (**Table 2.1**).

Table 2.1. Cut-off and threshold values for the calculation of the DHD15-index component scores and the additional component "Unhealthy choices".

	July 2				
	Component	Component type	Dutch dietary guidelines 2015	Minimum score (= 0 points)	Maximum score (= 10 points)
-	Vegetables	A	Eat at least 200g of vegetables daily	0 g/day	≥ 200 g/day
7	Fruit	∢	Eat at least 200g of fruit daily	0 g/day	≥ 200 g/day
က	Wholegrain	⋖	Eat at least 90g of wholegrain products daily	0 g/day	≥ 90 g/day
	products	ď	Replace refined cereal products by wholegrain products	No consumption of wholegrain products <u>or</u> ratio of whole grains to refined grains ≤0.7	No consumption of refined products <u>or</u> ratio of whole grains to refined grains ≥11
4	Legumes	∢	Eat legumes daily	0 g/day	≥ 10 g/day
2	Nuts	∢	Eat at least 15g of unsalted nuts daily	0 g/day	≥ 15 g/day
9	Dairy*	0	Eat a few portions of dairy products daily, including milk or yogurt	0 g/day <u>or</u> ≥ 750 g/day	300-450 g/day
_	Fish†	⋖	Eat one serving of fish weekly, preferably oily fish	0 g/day	≥ 15 g/day
_∞	Теа	4	Drink three cups of black or green tea daily	0 g/day	≥ 450 mL/day
o	Fats and oils	œ	Replace butter, hard margarines and cooking fats by soft margarines, liquid cooking fats and vegetable oils	No consumption of soft margarines, liquid cooking fats and vegetable oils <u>or</u> ratio of liquid cooking fats to solid cooking fats ≤0.6	No consumption of butter, hard margarines and cooking fats <u>or</u> ratio of liquid cooking fats to solid cooking fats ≥13
10	Coffee	Ø	Replace unfiltered coffee by filtered coffee	Any consumption of unfiltered coffee	Consumption of only filtered coffee OR No coffee consumption
7	Red meat	Σ	Limit consumption of red meat	≥ 100 g/day	≤ 45 g/day
12	Processed meat	Σ	Limit consumption of processed meat	≥ 50 g/day	0 g/day
13	Sweetened beverages and fruit juices	Σ	Limit consumption of sweetened beverages and fruit juices	≥ 250 g/day	0 g/day
4	Alcohol	Σ	If alcohol is consumed at all, intake should be limited to one Dutch unit (10g ethanol) daily	Women: ≥ 20 g ethanol/day Men: ≥ 30 g ethanol/day	Women: ≤ 10 g ethanol/day Men: ≤ 10 g ethanol/day
15	Salt	Σ	Limit consumption of table salt to 6g daily	≥ 3.8 g Na/day	≤ 1.9 g Na/day
16	Unhealthy choices	Σ	Limit consumption of unhealthy day and week choices	> 7 week choices/week	≤ 3 week choices/week

A, adequacy component (consume an adequate amount); R, ratio component (replace less healthy products by more healthy alternatives); O, optimum component (optimal consumption range); Q, qualitative component (choose healthier option); M, moderation component (limit consumption).

*maximum of 40 g cheese could be included.

†maximum of 4 g lean fish could be included.

Full-length FFQ and its scoring with the DHD2015-index

A 166-item semi-quantitative FFQ was used to assess habitual dietary intake. Food items for this version were selected based on the DNFCS 2007-2010. This FFQ was evaluated for energy intake, macronutrients, dietary fibre and selected vitamins [13, 33]. The reference period was the previous month. This full-length FFQ has previously been evaluated against two 24-hour dietary recalls to assess the DHD2015-index (tau-b: 0.56; 95% CI 0.52, 0.61) [9]. Answer categories for frequency questions ranged from 'not this month' to '7 d/week', and portion sizes were estimated using standard portions and commonly used household measures [27]. Average daily intake (in grams) of food items were calculated by multiplying frequency of consumption by portion size. Average daily sodium intake was calculated by multiplying frequency of consumption by portion size and energy and nutrient content per gram using the 2010 Dutch Food Composition Table [34]. The full-length FFQ was administrated via the Dutch FFQTOOL [35].

Because of a technical problem with administering the full-length FFQ (results of questions on fish intake and use of cooking fats were not saved correctly), we were not able to calculate all component scores of the DHD2015-index. Moreover, the full-length FFQ does not distinguish between types of coffee (filtered vs. unfiltered). Therefore, the component scores for fish, fats and oils and coffee are not presented.

Covariates

Age, body weight, height, educational level (low: primary school, vocational or lower general secondary education; moderate: higher secondary education or intermediate vocational training; high: higher vocational education or university), smoking status (current, former, never), and drug use were self-reported when completing the Eetscore FFQ. Body weight and height were used to calculate the Body Mass Index (BMI).

Statistical analysis

Baseline characteristics are presented as mean and standard deviation scores of the DHD2015-index and its components, calculated from the Eetscore FFQ and the full-length FFQ, separately for men and women. Differences in participant characteristics between men and women were quantified by means of Mann-Whitney U tests and chi-square tests. ANOVA and ANCOVA, adjusting for age and BMI, were performed to

compare the total DHD2015-index score derived from the Eetscore FFQ between men and women, while Mann-Whitney U tests and chi-square tests were performed to compare the subcomponents of the DHD2015-index. Linear trends in participants' characteristics across sex-specific quartiles of the DHD2015-index scores were examined using general linear models.

A Bland-Altman plot was used to examine the agreement between the Eetscore FFQ and the full-length FFQ [36]. Kendall's tau-b correlation coefficients were calculated between scores derived from the Eetscore FFQ and the full-length FFQ to examine ranking of participants according to diet quality. For the component dairy, a Kendall's tau-b correlation coefficient was calculated between grams of dairy intake as well. Spearman's correlation coefficients were calculated, to allow comparison with previous studies. Correlation coefficients of p >0.4 were considered to indicate an acceptable association and p=0.5-0.7 were considered to indicate a reasonably good association [37, 38], Confidence intervals were calculated using Fisher's z-transformation. The proportion of participants assigned to the same or adjacent DHD2015-index score quartiles were calculated to evaluate agreement between the two methods. Kappa (κ) coefficients were calculated between the quartile scores to further evaluate the level of agreement between the two methods. κ coefficients between 0.21-0.40 indicate a fair level of agreement, κ=0.41-0.60 a moderate and κ=0.61-0.80 a substantial level of agreement [39]. Correlation coefficients were calculated with and without under and over reporters in energy intake as identified by the Goldberg cut-off method [40]. However, we decided to include all participants in our analysis, because excluding under and over reporters (n=55) did not affect the ranking of participants in their diet quality (Suppl. Table 2.2).

Reproducibility of the Eetscore FFQ was examined by Intraclass correlation coefficients (ICC), where an ICC >0.4 was considered fair to good and an ICC \geq 0.75 excellent [37, 38]. Moreover, the minimal detectable change (MDC) at the 95% confidence levels for the total DHD2015-index score was calculated. The MDC95 provides the minimal change in DHD2015-index score that indicates a true change, with 95% certainty, which is not due to variation in performance or measurement error [41, 42]. The MDC was calculated with the following formula: MDC95 = 1.96 × pooled SD × $\sqrt{2}$ (1-ICC).

All data were analysed using SAS statistical software version 9.4 (SAS Institute Inc.) and SPSS statistics 25 (IBM), and a P value of <0.05 was considered to be statistically significant.

Results

Participant characteristics

Sixty-eight percent of the study sample were women and mean age of the study sample was 56.9 (SD 15.8) years (**Table 2.2**). Mean BMI was 24.2 (SD 3.8 kg/m2) and 65% of the study sample had a high educational level. Thirty-five percent of the study sample was classified as being overweight or obese. Men were older (mean 63.4 (SD 12.4) years) than women (mean 53.9 (SD 16.2) years) and had a significantly higher BMI (mean 25.4 (SD 3.6) kg/m2) than women (mean 23.7 (SD 3.8) kg/m2). Men also used more lipid modifying, anti-diabetic and anti-hypertensive medication than women (P<0.001).

The mean DHD2015-index score for the total study sample, based on the Eetscore FFQ, was 111 (SD 17.5) out of a possible maximum total score of 160 points (**Table 2.2**). Mean DHD2015-index scores were significantly lower for men than for women (103 (SD 18.0) points versus 114 (SD 16.0) points) and this difference increased after adjustment for age and BMI (104 (SE 1.08) points versus 115 (SE 0.72) points). Women scored significantly higher on the components vegetables, fruit, ratio whole to refined grains, tea, red meat, processed meat, sugar-containing beverages, alcohol, salt, and unhealthy choices. Men scored significantly higher on the component dairy. Age was positively associated with the DHD2015-index score as derived from the Eetscore FFQ (P<0.001, using sex-specific quartiles). Mean BMI was lower in the higher DHD-15 index quartiles (P<0.001), while educational level was higher (P=0.008) (**Table 2.3**). Smoking, and medication use were not significantly associated with the DHD2015-index.

Table 2.2. General characteristics, mean scores and standard deviations of the total score of the Dutch Healthy Diet 2015 index (DHD15-index) and its components based on the Fetscore FFQ in 541 women and 237 men.

	Won	nen	Me	en	
	(n 5	14)	(n 2	37)	_
	Mean	SD	Mean	SD	P value*
Age, years ± SD	53.9	16.2	63.4	12.4	<0.001
Body mass index, kg/m ² ± SD	23.7	3.84	25.4	3.60	<0.001
Body weight, kg ± SD	67.7	11.3	83.2	13.5	<0.001
Educational level †					0.076
-Low, n (%)	70	(14)	33	(14)	
-Middle, n (%)	113	(22)	47	(20)	
-High, n (%)	331	(64)	154	(65)	
Smoking status					<0.001
-Current, n (%)	26	(5)	20	(8)	
-Former, n (%)	177	(34)	134	(57)	
-Never, n (%)	311	(61)	83	(35)	
Medication use					
-Lipid modifying, n (%)	32	(6)	58	(25)	<0.001
-Anti-diabetic, n (%)	15	(3)	22	(9)	<0.001
-Anti-hypertensive, n (%)	74	(14)	62	(26)	<0.001
DHD15-index, score ± SD ‡	114.4	16.0	102.8	18.0	<0.001
1. Vegetables, score ± SD	7.2	2.8	5.7	2.9	<0.001
2. Fruit, score ± SD	7.9	2.8	6.7	3.3	<0.001
3. Wholegrain, score ± SD	7.7	2.3	7.4	2.5	0.152
4. Legumes, score ± SD	8.0	3.4	8.3	3.2	0.090
5. Nuts, score ± SD	5.6	3.7	5.3	3.9	0.151
6. Dairy, score ± SD	5.9	3.3	6.6	3.3	0.009
7. Fish, score ± SD	6.8	3.4	6.5	3.5	0.292
8. Tea, score ± SD	6.5	4.1	4.4	4.1	<0.001
9. Fat and oils, score ± SD	6.0	4.6	6.5	4.5	0.326
10. Coffee, score ± SD	7.9	2.7	7.8	2.8	0.862
11. Red meat, score ± SD	9.6	1.4	9.1	2.3	<0.001
12. Processed meat, score ± SD	6.3	3.3	4.1	3.6	<0.001
13. Sugar-containing beverages, score ± SD	8.2	2.6	7.1	3.3	<0.001
14. Alcohol, score ± SD	8.2	3.2	7.3	3.2	<0.001
15. Sodium, score ± SD	8.5	1.6	7.1	2.8	<0.001
16. Unhealthy choices, score ± SD	3.9	4.1	2.9	4.0	0.004

^{*} Mann-Whitney U test and Chi-square test were used to compare general characteristic values and the component scores between women and men and an ANOVA was used to compare the total DHD15-index score.

[†] Low education = primary school, vocational and lower general secondary education; moderate = higher secondary education and intermediate vocational training; high = higher vocational education and university.

[‡] The total score ranges between 0 and 160 points.

[§] Maximum score for subcomponents is 5 points.

Table 2.3. Participant characteristics across sex-specific quartiles of the DHD2015-index based on the Eetscore FFQ1 in 751 participants.

		Quartil	es DHD2()15-index	derived fi	Quartiles DHD2015-index derived from Eetscore FFQ	ore FFQ		
	Q1 (1	Q1 (n 190)	Q2 (n 197)	197)	Q3 (r	Q3 (n 182)	Q4 (n 182)	182)	P for trend
DHD2015-index score (mean, SD)*	89	11.1	107	6.9	117	9	131	7	
Age, y (mean, SD)	53.7	16.2	56.2	15.5	57.6	16.4	60.4	14.2	<0.001
Body weight, kg (mean, SD)	75.9	16.1	72.7	13.9	71.8	13.9	8.69	11.5	<0.001
BMI, kg/m2 (mean, SD)	25.1	4.2	24.4	3.8	24.1	3.9	23.3	3.2	<0.001
Smoking (n,%)									0.23
Never	63	48.9	104	52.8	101	55.5	96	52.7	
Former	28	41.1	81	41.1	73	40.1	79	43.4	
Current	19	10	12	6.1	80	4.4	7	3.8	
Education (n,%)									0.008
Low	32	18.4	33	16.8	24	13.2	7	9	
Intermediate	4	21.6	38	19.3	47	25.8	34	18.7	
High	114	09	124	62.9	11	61	136	74.7	
Medication use (n,%)									
Lipid modifying drugs	56	13.7	25	12.7	21	11.5	18	6.6	0.70
Diabetic drugs	13	8.9	9	က	7	3.8	7	9	0.27
Anti-hypertensive drugs	35	18.4	32	16.2	28	15.4	41	22.5	0.29

* The total score ranges between 0 and 160 points.

Table 2.4. Total score and 13 component scores of the Eetscore FFQ and the full-length FFQ in 565 participants (mean values and standard deviations, Kendall's tau-b coefficients, Spearman's correlations and 95% confidence intervals).

		Eetscore FFQ	FFQ	Full-length FFQ	h FFQ				
		Mean	SD	Mean	SD	Tau-b	95% CI	Я	95% CI
-	Vegetables	6.9	2.9	7.1	3.0	0.41	0.36, 0.46	0.55	0.48, 0.61
5.	Fruit	7.6	3.1	7.8	3.2	0.63	0.58, 0.68	0.72	0.67, 0.77
69	Wholegrain products	7.7	2.3	7.0	3.1	0.22	0.15, 0.28	0.29	0.20, 0.37
4.	Legumes	8.0	3.4	8.2	3.4	0.43	0.35, 0.50	0.47	0.38, 0.55
2	Nuts	5.6	3.8	5.0	4.0	0.48	0.43, 0.54	0.59	0.52, 0.65
9	Dairy	6.1	3.3	6.3	3.3	0.32	0.26, 0.38	0.43	0.35, 0.50
7.	Fish	6.7	3.4						
œ	Теа	5.9	1.1	7.1	3.6	0.63	0.58, 0.68	0.72	0.66, 0.77
6	Fat and oils	6.2	4.6						
10.	Coffee	7.9	2.7						
Έ.	Red meat	9.4	4.8	9.2	2.0	0.30	0.22, 0.38	0.32	0.24, 0.41
12	Processed meat	2.7	3.5	0.9	3.5	0.55	0.51, 0.60	0.71	0.66, 0.76
13.	Sugar-containing beverages	7.9	2.9	6.9	3.5	0.50	0.45, 0.56	0.61	0.55, 0.68
4.	Alcohol	7.9	3.3	2.8	4.4	0.41	0.37, 0.45	0.45	0.40, 0.50
15.	Salt	8.1	2.2	7.7	2.7	0.36	0.31, 0.42	0.48	0.41, 0.55
16.	Unhealthy choices	3.6	4.1	1.0	5.6	0.39	0.33, 0.45	0.45	0.38, 0.52
	DHD2015-index 13 components*	90.5	15.5	82.2	15.1	0.51	0.47, 0.55	0.70	0.66, 0.75
	DHD2015-index all components†	111.3	17.3	82.2	15.1	0.47	0.43, 0.51	0.65	0.60, 0.70
*	*The total score ranges between 0 and 130 points. The score of components '7. Fish' '9. Fats and pils' and '10. Coffee' were not available for full-lie	130 points	The ecor	of compon	± 2, studi	, o, , vi	ate and oile' and	110 01	fee' were not available for

*The total score ranges between 0 and 130 points. The score of components '7. Fish', '9. Fats and oils' and '10. Coffee' were not available for full-length FFQ. †The total score ranges between 0 and 160 points.

Relative validity of Eetscore FFQ compared to full-length FFQ

Mean time difference between filling in the Eetscore FFQ and the full-length FFQ was 1.7 (SD 1.15) month. The mean DHD2015-index score based on 13 components and calculated from the Eetscore FFQ was 90.5 (SD 15.5) out of a possible total score of 130 points (**Table 2.4**), which was significantly higher than the total score calculated from the full-length FFQ (82.2 (SD 15.1)). Absolute agreement and limits of agreement were studied using a Bland-Altman plot (**Figure 2.1**). The DHD2015-index score calculated from the Eetscore FFQ was 8.3 (SD 11.6) points higher than the score of the full length FFQ. The limits of agreement were -15.0 and 31.5 points. The Kendall's tau-b coefficient between the two scores was 0.51 (95% CI 0.47, 0.55) (**Table 2.4**), indicating a reasonably good ranking ability.

When comparing the mean DHD2015-index component scores between the Eetscore FFQ and the full-length FFQ, the largest absolute difference was observed for the component alcohol (mean difference 5.1 (SD 4.4) points) and the smallest absolute difference was observed for the component dairy (mean difference 0.1 (SD 3.5) points). The lowest tau-b coefficient was seen for the component whole grain (0.22; 95% CI 0.15, 0.28). Tau-b correlations ranged between 0.2 and 0.4 for the components dairy, red meat, salt and unhealthy choices. For the components vegetables, legumes, nuts, processed meat, sugar-containing beverages and alcohol, tau-b correlations ranged between 0.4 and 0.6. Tau-b correlations of 0.6 or higher were seen for the components fruit and tea. The Kendall's tau-b coefficient between the grams of dairy intake was 0.57 (95% CI 0.53, 0.61). Based on the DHD2015-index score quartiles, 47% of the participant were placed in the same quartiles, 43% in the adjacent quartiles and 1% in the extreme quartiles. The Kappa coefficient was 0.29 (95% CI 0.24, 0.35), indicating a fair level of agreement between the two methods.

Reproducibility of the Eetscore FFQ

On average, participants completed the second Eetscore FFQ 3.8 (SD 0.82) months after the first Eetscore FFQ. Mean total DHD2015-index scores were 112.6 (SD 17.0) for the first Eetscore FFQ and 111.9 (SD 17.2) for the second Eetscore FFQ (**Table 2.5**), with a mean difference of 0.8 (SD 10.0) points (p=0.16). The intraclass correlation coefficient (ICC) between both Eetscore FFQs was 0.91 (95% CI 0.89, 0.93). The largest difference in component scores was observed for tea (mean difference 0.4 (SD

2.4) points); the smallest difference was observed for coffee (mean difference 0.0 (SD 1.6) points). The lowest ICCs were observed for the components red meat (0.71; 95% CI 0.64, 0.77) and legumes (0.72; 95% CI 0.65, 0.77), indicating a good reproducibility. The components fruit, tea and alcohol had an ICC of 0.9 or higher, indicating excellent reproducibility. All other components had an ICC between 0.8 and 0.9. The minimal detectable change (MDC) for the total DHD2015-index score was 14.5 points.

Table 2.5. Total score and 16 component scores of both Eetscore FFQs in 343 participants (mean values and standard deviations, intraclass correlation coefficient (ICC) and 95% confidence intervals between both Eetscore FFQs).

	_	Eetscore	FFQ-1	Eetscore	FFQ-2		
		Mean	SD	Mean	SD	ICC	95% CI
1.	Vegetables	6.9	3.0	6.7	2.9	0.82	0.77, 0.85
2.	Fruit	7.8	3.0	7.7	3.0	0.91	0.89, 0.93
3.	Wholegrain products	7.7	2.4	7.4	2.6	0.84	0.80, 0.87
4.	Legumes	8.1	3.4	7.9	3.5	0.72	0.65, 0.77
5.	Nuts	5.6	3.7	5.5	3.8	0.82	0.78, 0.85
6.	Dairy	6.3	3.3	6.4	3.2	0.84	0.80, 0.87
7.	Fish	6.8	3.4	6.7	3.4	0.88	0.85, 0.90
8.	Tea	6.2	4.1	5.9	4.1	0.90	0.88, 0.92
9.	Fat and oils	6.1	4.6	6.1	4.6	0.80	0.75, 0.84
10.	Coffee	8.3	2.4	8.3	2.5	0.87	0.84, 0.90
11.	Red meat	9.5	1.7	9.6	1.4	0.71	0.64, 0.77
12.	Processed meat	5.8	3.5	5.7	3.6	0.87	0.84, 0.89
13.	Sugar-containing beverages	7.8	3.0	7.9	2.8	0.87	0.84, 0.90
14.	Alcohol	8.0	3.2	7.9	3.3	0.93	0.91, 0.94
15.	Sodium	8.1	2.1	8.4	2.0	0.80	0.76, 0.84
16.	Unhealthy choices	3.6	4.0	3.8	4.0	0.86	0.83, 0.89
	DHD2015 index *	112.5	17.2	111.9	17.4	0.91	0.89, 0.93

^{*} The total score ranges between 0 and 160 points.

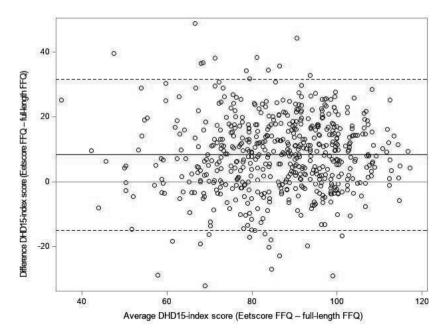


Figure 2.1. Bland-Altman plot of total score based on 13 components of the Dutch Healthy Diet 2015 index (DHD2015-index) based on the Eetscore FFQ and the full-length FFQ in 565 participants.

Discussion

The Eetscore FFQ is a screener designed to assess diet quality based on adherence to the Dutch dietary guidelines by calculating DHD2015-index scores. We showed that DHD2015-index scores differed significantly between men and women. The DHD2015-index score was inversely associated with BMI, while it was positively associated with age and education. The Eetscore FFQ showed a moderate Kendall's tau-b correlation with the full-length FFQ indicating that the Eetscore FFQ can be used for ranking of participants according to their diet quality. Furthermore, the intraclass correlation coefficient (ICC) between both Eetscore FFQs was 0.91 showing good reproducibility.

Associations with individual characteristics

DHD2015-index scores derived from the Eetscore FFQ differed significantly between men and women. This difference became even larger after adjusting for age and BMI. Women scored significantly higher on the total DHD2015-index score, which was explained by higher intakes of fruit, vegetables and tea and lower intakes of red and processed meat, sugar-containing beverages and alcohol. Worldwide, studies have

shown that women have a better diet quality than men [43]. In general, women are probably more health-oriented and have better knowledge of nutrition than men [43-45].

On average, older people had higher diet quality scores than younger people, which is also comparable with results of other studies [43, 46]. Furthermore, the DHD2015-index derived from the Eetscore FFQ was inversely associated with BMI. The DHD2015-index scores derived from a full-length FFQ or two 24-h dietary recalls previously showed similar associations with sex, age, BMI and education level in other general Dutch populations (EPIC-NL, DNFCS 2007-2010, NQ-Plus) [9, 10, 15, 20, 47, 48]. However, the DHD2015-index was previously also inversely associated with smoking, which was not seen in the present study [9, 20, 47]. This could be explained by the high percentage of highly educated participants and the low percentage of current smokers in the present study.

Relative validity

Using Bland-Altman analysis, absolute agreement showed an overestimation of the DHD2015-index score derived from the Eetscore FFQ compared with the DHD2015-index score derived from the full-length FFQ, based on 13 components (mean difference 8.3 (SD 11.6) points). Furthermore, the Bland-Altman plot showed relatively wide 95% limits of agreement.

The DHD2015-index score calculated from the Eetscore FFQ showed a reasonably good Kendall's tau-b correlation (0.51; 95% CI 0.47, 0.55) with the DHD2015-index score calculated from the full-length FFQ. This Kendall's tau-b correlation was slightly higher than the correlation between the full-length FFQ and the DHD-FFQ (0.40; CI 0.37, 0.43) [15]. The DHD-FFQ was developed to assess the DHD-index, the precursor of the DHD2015-index [10, 15]. The observed correlation in the present study was comparable with that of Whitton et al. [49] who observed a Spearman's correlation coefficient of 0.51 comparing the 'Diet Screener' and a 163-item FFQ in Singapore residents. A study of Rifas-Shiman et al. [50] found a Spearman's correlation coefficient of 0.61 comparing 'PrimeScreen' with a 131-item FFQ in an American population. Two studies by Schröder et al., both performed in a Spanish population, observed comparable Pearson correlation coefficients for the 'short Diet Quality Screener' (r = 0.61), the 'Mediterranean Diet Adherence Screener' (r = 0.52) and the 'brief Mediterranean Diet Screener' (r = 0.40) [18, 51]. Furthermore, a correlation of

0.38 was observed for the 'Diet Quality Score', developed in the UK, derived from the short-form FFQ (SFFQ) compared with a 217-item FFQ [16]. Correlation coefficients ranging between 0.5 and 0.7 are common in validation studies of dietary assessment methods [37, 38]. The Kappa coefficient showed a fair level of agreement (0.29; 95% CI 0.24, 0.35) between the DHD2015-index calculated from the Eetscore FFQ and with the DHD2015-index score calculated from the full-length FFQ. This Kappa coefficient was lower than coefficients found for comparable screeners were kappa ranges between 0.38 to 0.58 [16, 49, 52]. Taking all above mentioned correlation coefficients together, the correlation coefficient for DHD2015-index scores between the two methods was considered acceptable, even though the full DHD2015-index score could not be assessed for the full-length FFQ.

For the components whole grains, dairy, red meat and unhealthy choices, the correlations between the DHD2015-index score based on the Eetscore FFQ and the full-length FFQ were lower than the expected value of 0.4. The low correlation for the component whole grains could be explained by the difference in food items for this component between the Eetscore FFQ and the full-length FFQ. For example, the Eetscore FFQ distinguishes between whole grain and white rice and pasta whereas the full-length FFQ was not able to make this distinction. Second, the dairy component was scored as an optimum component. For example, a score of 5 points is allotted when someone consumes one portion (150g) of dairy, but also when someone consumes four portions (600a) of dairy. The correlation between dairy intake in grams was therefore higher than the correlation between component scores. Not surprisingly. also red meat showed a very low correlation between the two instruments. This could be explained by the grouping of the food items of the full-length FFQ. Some food items of the full-length FFQ consisted of both red meat and processed meat, while the Eetscore FFQ made a clear distinction between these two food items. The assumptions we made regarding the percentages of foods in the full-length FFQ that can be classified as red meat or processed meat may therefore deviate from the amounts actually consumed and therefore result in a different score. The low correlation for the component unhealthy choices could be explained by the smaller number of foods included in the Eetscore FFQ compared to the full-length FFQ (8 versus 15 items respectively); for example, the consumption of candies, pancakes and pizza was not covered in the Eetscore FFQ whereas these items were available from the full-length FFQ.

Although the correlation was acceptable, the largest mean difference in scores between the Eetscore FFQ and the full-length FFQ was seen for the component alcohol, which could be explained by the difference in questions. The Eetscore FFQ takes into account binge drinking, whereas it was not possible to assess binge drinking with the full-length FFQ. Additionally, the full-length FFQ used in the present study was not able to distinguish between types of coffee (filtered or unfiltered); therefore, the component scores for coffee could not be evaluated in the present study.

The Eetscore FFQ and the full-length FFQ showed a low correlation between sodium intake (0.36; 95% CI 0.31, 0.42). This could partly be explained by the availability of information on salt added during cooking and at the dinner table in the Eetscore FFQ, whereas this information was lacking in the full-length FFQ. In general, FFQs are not suitable to assess sodium intake, which usually underestimates true sodium intake. The results on the salt component should therefore be interpreted with caution. Ideally, sodium intake is estimated based on 24-h urinary Na, which is considered the gold standard [53].

Taking all the above suggested explanations for differences between the two FFQs together, the Eetscore FFQ may be better to distinguish between food items regarding the components whole grains, red meat, alcohol and coffee than the full-length FFQ and therefore may be better able to assess diet quality. This raises the question whether the full-length FFQ used in this study was the most appropriate FFQ to evaluate the Eetscore FFQ. In future studies, a method able to distinguish between types of coffee, to assess binge drinking and to distinguish between food items of whole grains and red meat, should be used to evaluate these components.

Reproducibility

The reproducibility of the Eetscore FFQ was assessed over an interval period of approximately four months. The observed intraclass correlation coefficient (ICC) of 0.91 for the total DHD2015-index score and ICC ranging from 0.71 to 0.93 for the component scores indicate good to excellent reproducibility of habitual diet quality. The Eetscore FFQ also showed good reproducibility in comparison with other studies. For instance, an ICC of 0.69 was observed after a four month interval for the 'Diet Screener' assessing the Alternative Healthy Eating Index-2010 (AHEI-2010) in an Asian population [49]. Furthermore, an ICC of 0.69 was observed for the reproducibility after a one month interval period of the 'Mediterranean Diet Adherence Screener' assessing

adherence to the Mediterranean diet [54]. Correlation coefficients between 0.5 and 0.7 are common in reproducibility studies of food frequency questionnaires [37, 38]. Thus, our findings indicate that the Eetscore FFQ is a reliable instrument for assessing adherence to the Dutch dietary guidelines over time.

Strengths

Both the Eetscore FFQ and the full-length FFQ were administered online, which is assumed to be less burdensome for the interviewee and expected to be less biased by social desirable answering [14]. The order in which participants received the questionnaires was at random. Therefore, it is unlikely that the order could have influenced the results. Furthermore, additional adjustments for the order of questionnaires did not alter our correlation coefficients notably (**Suppl. Table 3**).

Limitations

The Eetscore FFQ was designed to capture the quality of the dietary pattern of the general Dutch population. In the present study, we evaluated the Eetscore FFQ in a population that might not be representative for the general Dutch population because of the large proportion of highly educated participants and the interest in participating in a study on nutrition and health. Furthermore, fewer people were overweight (BMI ≥25 kg/m2; 27%) or obese (BMI ≥30 kg/m2; 8%) in our study population compared to the general Dutch population (35% and 15% respectively) indicating that our study population is a health-conscious population. We expect that the use of the Eetscore FFQ in a more representative general population will result in lower DHD2015-index scores, but in similar correlations between diet quality and health outcomes [55, 56]. The Eetscore FFQ was initially developed for the adult population (18-69y), based on data of the DNFCS 2007-2010 [21]. However, also participants over 70 years of age were recruited from the EetMeetWeet study (n 147). Excluding them did not affect the ranking of participants in their diet quality; therefore, we decided to include data of all participants in our analysis (Suppl. Table 2.4).

A full-length FFQ is no "golden standard" reference method, therefore we can only determine relative validity. Furthermore, the Eetscore FFQ and the full-length FFQ were designed similarly and may have correlated errors. This may cause an overestimation of relative validity [37, 57]. Therefore, it is suggested to also assess relative validity between the Eetscore FFQ and multiple 24-h dietary recalls or multiple

food records in the future. It is also suggested to evaluate the Eetscore FFQ against biological markers for dietary intake in future studies since these are considered more objective than self-reported dietary assessment methods [14, 58].

Because of a technical problem with administering the full-length FFQ, i.e. questions on fish intake and use of cooking fats were not saved, we were not able to calculate all components of the DHD2015-index. It was therefore also not possible to calculate associations between the DHD2015-index scores derived from the Eetscore FFQ and energy, and macro- and micronutrient intakes derived from the full-length FFQ. Others found significant positive correlations between diet quality scores and energy, and macro- and micronutrient intakes [15, 18, 51, 54, 59]. However, the DHD2015-index was previously evaluated against the same full-length FFQ, as used in this study, and 24-h dietary recalls. This previous study showed significant associations for energy and several macro- and micronutrient intakes across quintiles of the DHD2015-index scores [9]. We therefore expect the associations between the Eetscore FFQ and energy and macro- and micronutrient intakes to be in the same direction.

The Eetscore FFQ was specifically designed to assess the DHD2015-index and is therefore not designed to estimate daily energy and macro and micronutrients.

Conclusion

In conclusion, the Eetscore FFQ is a screener of diet quality assessing adherence to the Dutch dietary guidelines by calculating DHD2015-index scores. The results showed that DHD2015-index scores differs between men and women. The score is also positively associated with age and educational level, and inversely associated with BMI. The Eetscore FFQ was considered an acceptable screener to rank participants according to their diet quality, but relatively poor for assessing diet quality on the individual level. Further validation for this purpose is necessary. Moreover, the Eetscore FFQ showed good to excellent reproducibility and is therefore able to monitor diet quality of individuals.

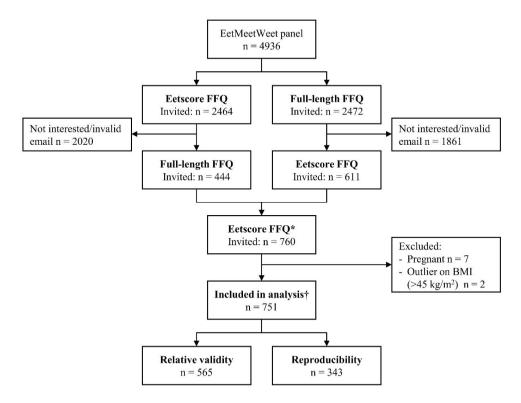
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Supplementary materials



Supplemental Figure 2.1. Flow diagram of participants of the Eetscore evaluation study. *Participants were only invited when first Eetscore FFQ was completed †Total study sample is used to examine participants characteristics.

Supplemental Table 2.1. Item list Eetscore FFQ.

Item Number	Question	Item Name	Component
1	1	Whole grain breakfast cereals	Wholegrain products
2	1	Refined breakfast cereals	Wholegrain products
3	1	All kinds of breakfast cereals	Wholegrain products
4	2	Croissants and currant bread	Wholegrain products
5	3	Wholegrain rusks, crispbread or crackers	Wholegrain products
6	3	Naturel rusks, crispbread or crackers	Wholegrain products
7	3	All kinds of rusks, crispbread or crackers	Wholegrain products
8	4	Wholegrain, brown and multigrain brood	Wholegrain products
9	4	White bread	Wholegrain products
10	4	All kinds of bread	Wholegrain products
11	5	(Low fat) margarine	Fats and oils
12	5	(Semi-skimmed) butter	Fats and oils
13	5	All kinds of margarines and butter	Fats and oils
14	6	Cheese (topping)	Dairy
15	7	Cold cuts	Processed meat
16	8	Sweet toppings	Unhealthy choices
17	9	Milk, buttermilk and other dairy drinks without sugar	Dairy
18	10	Sweetened drink yogurt or dairy drinks	Dairy and Sweetened beverages and fruit juices
19	11	(Fruit) yogurt, (fruit) quark, custard, pudding or ice cream	Dairy
20	12	Soup	Salt
21	13	Legumes	Legumes
22	14	Boiled or stir-fried vegetables	Vegetables
23	15	Crudités	Vegetables
24	16	Wholemeal pasta	Wholegrain products
25	16	White pasta	Wholegrain products
26	16	All kinds of pasta	Wholegrain products
27	17	Brown rice	Wholegrain products
28	17	White rice	Wholegrain products
29	17	All kinds of rice	Wholegrain products
30	18	Red meat	Red meat
31	18	Processed meat	Processed meat
32	18	White meat	-
33	19	Savoury snacks	Unhealthy choices
34	20	Lean fish	Fish
35	21	Fatty fish	Fish
36	22	Butter	Fats and oils
37	22	Margarine product solid	Fats and oils
38	22	Margarine product liquid	Fats and oils
39	22	Oils	Fats and oils
40	23	Sauces	Unhealthy choices
41	24	Cheese (cubes or with a hot meal)	Dairy

Item Number	Question	Item Name	Component
42	25	Nuts and peanuts	Nuts
43	26	Chips or pretzels	Unhealthy choices
44	27	Large cookies, cake and pie	Unhealthy choices
45	28	Small cookies, biscuit and gingerbread	Unhealthy choices
46	29	Chocolates	Unhealthy choices
47	30	Fresh fruit	Fruit
48	31	(Fruit) juices or fruit based breakfast drinks	Sweetened beverages and fruit juices
49	32	Soft drinks, lemonade, sport drinks or energy drinks	Sweetened beverages and fruit juices
50	33	Green or black tea	Tea
51	34	Sugar in tea	Unhealthy choices
51	36	Sugar in coffee	Unhealthy choices
52	35	Coffee	Coffee
53	37	Alcoholic drinks during the weekend	Alcohol
53	38	Alcoholic drinks during the week	Alcohol
54	39	Salt during cooking	Salt
55	40	Salt at the table	Salt

Supplemental Table 2.2. Total score and 13 component scores of the Eetscore FFQ and the full-length FFQ in 510 participants (without misreporters, n=55) of the EetMeetWeet study (mean values and standard deviations, Kendall's tau-b coefficients, Spearman's correlations and 95% confidence intervals).

		Eetscore FFQ 1	FFQ 1	Full-length FFQ	ngth റ				
		:	ı (:	ű	Tau-	3	ſ	3
		Mean	SD	Mean	SD	q	95% CI	ď	95% CI
	Vegetables	7.0	2.9	7.3	2.9	0.39	0.34, 0.45	0.52	0.44, 0.60
2	Fruit	9.7	3.1	7.9	3.2	0.64	0.60, 0.68	0.73	0.68, 0.78
က်	Wholegrain products	7.8	2.3	7.4	2.9	0.20	0.14, 0.27	0.26	0.18, 0.35
4.	Legumes	8.2	3.3	8.4	3.2	0.39	0.32, 0.47	0.43	0.35, 0.51
5.	Nuts	2.7	3.7	5.2	4.0	0.46	0.40, 0.52	0.56	0.50, 0.63
9	Dairy	6.3	3.2	6.4	3.3	0.29	0.23, 0.35	0.39	0.31, 0.47
œ	Теа	5.8	4.2	7.1	3.7	0.62	0.56, 0.67	0.70	0.64, 0.76
Ξ.	Red meat	9.4	6.1	9.2	2.0	0.29	0.20, 0.37	0.31	0.21, 0.41
12.	Processed meat	5.6	3.6	5.8	3.5	0.56	0.51, 0.61	0.72	0.67, 0.77
13.	Sugar-containing beverages	7.8	2.9	6.7	3.5	0.51	0.45, 0.56	0.62	0.55, 0.69
4.	Alcohol	6.7	3.3	2.8	4.4	0.42	0.37, 0.46	0.46	0.40, 0.51
15.	Salt	8.0	2.2	7.5	2.7	0.35	0.29, 0.41	0.47	0.39, 0.54
16.	Unhealthy choices	3.2	3.9	0.7	2.1	0.34	0.27, 0.41	0.39	0.31, 0.47
	DHD15 index *	90.4	15.3	82.3	15.1	0.49	0.45, 0.54	0.69	0.64, 0.73
* T	* The total score ranges between 0 and 130 points	nd 130 no	into:						

^{*} The total score ranges between 0 and 130 points.

Supplemental Table 2.3. Mean scores and standard deviations of the total score of the Dutch Healthy Diet 2015 index (DHD15-index) and its components based on the Eetscore FFQ in 565 participants by order of filling out FFQs; the Eetscore FFQ before full-length FFQ (order 1) or full-length FFQ before Eetscore FFQ (order 2).

				Orde	er 1	Orde	er 2	
		Tot	tal	(n 2	65)	(n 3	00)	_
		Mean	SD	Mean	SD	Mean	SD	P value*
1.	Vegetables	6.9	2.9	7.1	2.9	6.7	2.9	0.08
2.	Fruit	7.6	3.1	7.6	3.0	7.5	3.2	0.80
3.	Wholegrain products	7.7	2.3	7.8	2.2	7.6	2.4	0.62
4.	Legumes	8.0	3.4	8.1	3.4	8.0	3.4	0.35
5.	Nuts	5.6	3.8	5.3	3.9	5.9	3.7	0.05
6.	Dairy	6.1	3.3	5.9	3.3	6.3	3.2	0.18
7.	Fish	6.7	3.4	6.5	3.4	6.9	3.5	0.11
8.	Tea	5.9	4.1	5.7	4.2	6.1	4.1	0.23
9.	Fats and oils	6.2	4.6	6.0	4.7	6.4	4.6	0.44
10.	Coffee	7.9	2.7	8.0	2.6	7.9	2.8	-
11.	Red meat	9.4	1.8	9.5	1.8	9.4	1.8	0.36
12.	Processed meat	5.7	3.5	5.9	3.5	5.4	3.6	0.09
13.	Sugar-containing beverages	7.9	2.9	7.9	2.9	7.9	2.8	0.75
14.	Alcohol	7.9	3.3	7.8	3.5	8.0	3.1	0.74
15.	Sodium	8.1	2.2	8.2	2.1	8.0	2.2	0.55
16.	Unhealthy choices	3.6	4.1	3.5	4.0	3.6	4.2	0.99
	DHD15-index †	111.3	17.3	111.0	17.6	111.7	17.1	0.80

^{*} Mann-Whitney U test and Chi-square test were used to compare the component scores between order 1 and order 2 and an ANOVA was used to compare the total DHD15-index score.

[†] The total score ranges between 0 and 160 points.

Supplemental Table 2.4. Total score and 13 component scores of the Eetscore FFQ and the full-length FFQ in 418 participants (without participants ≥70 years old, n=147) of the EetMeetWeet study (mean values and standard deviations, Kendall's tau-b coefficients, Spearman's correlations and 95% confidence intervals).

		Eetscore FFQ 1	FFQ 1	Full-length FFQ	ngth Q				
		Mean	SD	Mean	SD	Tau-b	95% CI	~	95% CI
-	Vegetables	7.1	2.9	7.2	3.0	0.41	0.34, 0.47	0.54	0.46, 0.62
2	Fruit	7.4	3.1	7.7	3.3	0.65	0.59, 0.70	0.75	0.68, 0.80
69	Wholegrain products	7.6	2.3	7.1	3.1	0.24	0.17, 0.31	0.32	0.22, 0.41
4.	Legumes	7.9	3.5	8.1	3.5	0.41	0.32, 0.49	0.46	0.35, 0.54
5.	Nuts	5.7	3.7	5.1	4.0	0.47	0.41, 0.54	0.58	0.51, 0.66
9.	Dairy	0.9	3.3	6.1	3.3	0.34	0.28, 0.40	0.46	0.38, 0.54
œ.	Теа	0.9	4.1	7.2	3.6	0.62	0.56, 0.68	0.70	0.64, 0.77
Έ.	Red meat	9.5	1.6	9.3	1 .8	0.29	0.18, 0.39	0.31	0.20, 0.42
12.	Processed meat	5.8	3.5	6.1	3.4	0.55	0.49, 0.60	0.71	0.64, 0.76
13.	Sugar-containing beverages	7.9	2.9	6.9	3.5	0.48	0.42, 0.55	09.0	0.52, 0.67
4.	Alcohol	6.7	3.2	3.0	4.5	0.44	0.39, 0.49	0.48	0.43, 0.54
15.	Salt	8.1	2.2	7.7	2.7	0.34	0.27, 0.40	0.45	0.36, 0.53
16.	Unhealthy choices	3.4	4.1	1.0	5.6	0.38	0.29, 0.45	0.44	0.33, 0.52
	DHD15 index*	90.5	16.0	82.6	15.6	0.53	0.49, 0.57	0.73	0.68, 0.77
* +	* The total coerc research total	04 120 par	440						

^{*} The total score ranges between 0 and 130 points.







3

Dietary taste patterns and diet quality of female nurses around the night shift

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Submitted for publication



Abstract

Night shift workers are at risk of making poor food choices: e.g. sleep deprivation may lead to higher food intake with innate preferred tastes, such as sweet, savoury and fatty foods. Therefore, better insight in dietary taste patterns of night shift workers may improve the understanding of their food choices. This observational study assessed dietary taste patterns of 120 female night shift working nurses and compared them to 307 women of a reference population. Dietary intake, assessed with 24-hour dietary recalls, was combined with a taste intensity database, including taste profiles of 557 foods. The contribution to the daily intake of 6 taste clusters was assessed; fat. neutral. sweet/fat, sweet/sour, salt/umami/fat and bitter. During night shifts, nurses consumed a significantly higher energy percentage (en%) of 'neutral' (5.9 en%), 'sweet/sour' (8.1 en%) and 'sweet/fat' (6.5 en%) tasting foods and a lower en% of 'fat' (-17.1 en%) and 'bitter' (-2.1 en%) tasting foods than outside the night shift. They consumed a larger en% from foods with a 'sweet/sour' (1.9 en%) taste and a lower en% from foods with a 'bitter' (-2.1 en%) taste than the reference population, irrespective of age, BMI and smoking status. A higher en% and gram% of 'fat' tasting foods and a higher gram% 'fat/salt/umami' tasting foods were associated with lower diet quality. In conclusion, our results only partly support our hypothesis that nurses would select foods with more innate taste preferences. In addition, fat and savoury tasting foods were negatively associated with their diet quality.

Introduction

Working outside conventional working hours has become inevitable in the current 24-hour economy. For a part of the working population this means that they regularly have to work the night shift, i.e. working more than one hour between 1:00 and 6:00 AM. In the Netherlands, around 15 percent of the working population works a night shift on a regular basis [1]. In some professions this percentage is even higher. For example, 26 percent of health care workers regularly work the night shift [1].

Working the night shift is associated with higher risks of gastrointestinal and cardiovascular diseases, several types of cancer, metabolic disorders, diabetes and overweight [2-9]. These increased risks are mainly the result of a mismatch between working a night shift and natural rhythms of activity during the day and inactivity (sleep) during the night, i.e. the circadian rhythm. This circadian rhythm is mainly affected by light and darkness and is controlled by the suprachiasmatic nucleus (SCN) located in the hypothalamus. The SCN regulates many physiological processes in a 24-hour cycle such as body temperature, sleep, and appetite. By working the night shift, these circadian rhythms are disrupted and could result in sleep loss [10]. Another consequence of working the night shift is that food intake is redistributed from day to night [11-13], which could disrupt the circadian rhythm even further. Moreover, night shift workers have a tendency to have a higher meal frequency and a poorer diet quality than day shift workers [9, 14], which is likely not conducive to maintaining a normal circadian rhythm. All in all, people working night shifts are at risk of having poor food choices due to changes in their circadian rhythm, which could consequently contribute to the higher health risks.

Sleep-deprived people have a higher preference for sweet and savoury tastes and favour energy-rich and high-fat foods [2, 15-18], which could explain their choice for snacks instead of regular meals [19-22]. When people are sleep-deprived, they have fewer cognitive reserves to make informed decisions [19]. Consequently, decisions may be made more automatically and predominantly based on habits. This may also be the case when making food choices. Food choices in a sleep-deprived state may then revert back to strong innate taste preferences, such as those for sweet and

salty/savoury foods [20, 23], taste qualities that are initially associated with nutrient and energy content of the food [23-26].

Altogether, an altered circadian rhythm together with a high risk on sleep deprivation, caused by working the night shift, could shift dietary patterns towards an unhealthy diet [9]. As sensory characteristics (flavour) of foods are important drivers in these food choices [24, 26, 27] it is recommended to study dietary patterns not only from a nutritional perspective but also from a sensory perspective [28-30]. One way of doing this is to combine food intake data with taste characteristics of the consumed foods.

Therefore, the main aim of this study was to assess dietary taste patterns in female night shift working nurses and compare these during and outside the night shift. In addition, we compared the dietary taste patterns of the female night shift working nurses with those of a female reference population. Lastly, we studied associations between dietary taste patterns and the adherence to Dutch dietary guidelines in night shift working nurses. A better insight into the dietary taste patterns of night shift workers may contribute to a greater understanding of their food choices and to dietary guidelines for night shift workers.

Methods

Study populations

Night shift working nurses – Etmaal study

The observational, so-called Etmaal, study was conducted between April 2015 and July 2018 in nurses working the night shift in three hospitals located in the surrounding of Wageningen, the Netherlands [31]. In total, 164 nurses, aged 20 to 61 year, participated in this study. Nurses were included in the study when they were working the night shift for at least 6 months, were not using drugs that could cause or reduce sleep problems, were not using daylight lamps on the workplace during the night shift, were eating according to a Dutch eating pattern (2 cold meals and 1 hot meal), were not pregnant or breastfeeding and were not donating blood one week before and during the data collection period. In addition, in the current analysis we only used data of 120 female nurses that completed at least two 24-hour dietary recalls. Ten males were excluded from the data analysis, as they formed a minority of the study population

and could affect the study results. Male nurses, for example, had a higher energy intake, a higher variation in intake and different taste patterns than female nurses [29]. All participants provided oral and written informed consent before the start of the study. The study was approved by the medical ethical committee of Wageningen University (ABRnr: NL54414.081.15) and was conducted according to the declarations of Helsinki 2013.

Reference population - Dutch National Food Consumption Survey

A selected group from the most recent Dutch National Food Consumption Survey (DNFCS) 2012-2016 was used as a reference population. The DNFCS consists of a representative sample of the Dutch population regarding age, gender, region, educational level and level of urbanisation [32]. We selected 24-hour dietary recall data from females, aged 20 to 61 years, with an intermediate or higher educational level to be able to have similar demographic characteristics as the night shift working nurses. We did not include data from participants when one of the 24-hour dietary recalls included a special day because of fasting, illness, night work and traveling. Moreover individuals who were pregnant, breast feeding or seriously underweight were not included. In total, we included data from 307 females in the data analysis as a reference population.

Dietary intake assessment

Night shift working nurses – Etmaal study

In the Etmaal study, food consumption data was self-administered by the nurses via Compl-eat, a web-based program. Compl-eat is based on a validated technique to increase the accuracy of dietary recalls [33], and includes foods that are consumed in a Dutch food pattern [34]. Nurses were asked to complete a 24-hour dietary recall three times over the first day of three non-consecutive night shifts series. They reported all the foods and drinks they consumed from the evening meal prior to the night shift until the evening meal after the night shift, including the time of day. All foods and drinks reported before and after the night shift in the 24-hour dietary recall were considered as food consumption 'outside the night shift'.

Reference population - Dutch National Food Consumption Survey

In the DNFCS food consumption data was assessed via two non-consecutive 24-hour dietary recalls conducted by trained interviewers [32]. The interview took place via the telephone and the interviewers used the computer-based program GloboDiet for standardisation of the 24-hour dietary recalls [35]. The recalls were conducted throughout the year to cover for any seasonal effects and to represent all days of the week, including weekend days. There were at least 4 weeks between the two recalls.

Dietary taste patterns

To assess dietary taste patterns of both the nurses and the reference population, the dietary intake data of each individual was combined with taste intensity values. Each reported food was linked to taste intensity values of the specific food derived from a taste database. The construction of the taste database is described elsewhere and the database itself is available online [36]. Briefly, trained panellists evaluated 557 selected foods on the intensity of sweet, salt, sour, bitter, umami and fat sensation according to a modified SpectrumTM method [37]. The tested foods were selected from the Dutch National Food Consumption Survey 2007-2010 (DNFCS 2007-2010) based on consumption frequency, largest contribution to energy and macronutrients intake, and contribution to consumption variety [34, 37].

From the 557 tested foods, 468 foods were reported in the more recent DNFCS 2012-2016 from which we selected the reference population. For the 1,172 foods that were not tested, but reported in this survey, a taste intensity value was estimated. This was done by using the average taste values of corresponding food groups (**Suppl. Figure 3.1**) [32]. The same procedure was performed for the additional 141 foods, that were consumed only by the night shift working nurses. Foods that were not consumed as a single food did not receive an estimated food group average taste intensity value, because no foods were tested in these food groups, or were not frequently consumed by the Dutch population or the night shift working nurses (less than 5 times), were neglected in this analysis, e.g. foods from the food groups 'herbs and spices', and 'preparations' including medical nutrition and sport drinks. Furthermore, we recoded sugar in coffee and tea, milk in coffee, and lemonade syrup in water as these are reported as single foods in the 24-hour dietary recalls, but were most often consumed in combination with the aforementioned foods and also tested by the taste panel in this combination. So finally we had taste intensity values for 1,781 food codes. In total,

foods responsible for 99% of energy intake in both study populations were classified into one of the taste clusters. Based on this, 6 taste clusters were identified using hierarchical cluster analyses, yielding a 'neutral', 'fat', 'bitter', 'sweet and sour', 'fat, salt and umami', and 'sweet and fat' taste cluster [29, 37-39] (**Suppl. Table 3.1**). We assessed dietary taste patterns based on the average food intake of the 24-hour dietary recalls. For each individual we calculated the percentage of total energy intake and percentage of total consumed amount (in gram) for each taste cluster.

Dutch Healthy Diet 2015 index

To determine diet quality for both populations, we calculated the Dutch Healthy Diet 2015 index (DHD2015-index) score based on the food and nutrient intake of the average of the two or three 24-hour dietary recalls. The DHD2015-index assesses to what extent someone's diet complies with the Dutch dietary guidelines from 2015 [40]. It consists of fifteen components: vegetables, fruit, wholegrain products, legumes, nuts, dairy, fish, tea, fats and oils, coffee, red meat, processed meat, sweetened beverages and fruit juices, alcohol and salt. For each component a maximum of 10 points can be allotted, which means complete adherence to the Dutch dietary guideline for that specific component [41]. Since the 24-hour dietary recalls did not distinguish between types of coffee products, this component score was not calculated. This resulted in a total score ranging between 0 (no adherence) and 140 (complete adherence with the 2015 Dutch dietary guidelines).

Covariates

At the start of the data collection period of the Etmaal study, nurses filled out a demographic questionnaire and their height and body weight were measured by de researchers at the working place. Height was measured without shoes using a stadiometer to the nearest 0.5 cm. Body weight was measured without shoes using an analogue weighing scale to the nearest 0.5 kg or digital weighing scale to the nearest 0.1 kg depending on the scale that was available in the hospital where they worked. For the reference population, height and body weight were self-reported by the participants during the first interview. For both populations, height and body weight were used to calculate body mass index (BMI) in kg/m2.

Statistical analysis

Data was analysed using IBM SPSS Statistics 25. P-values below 0.05 were considered statistically significant. ANOVA and chi-squared analysis were used to compare demographic characteristics between night shift working nurses and the reference population.

Repeated measures ANOVA was used to determine differences in the percentages of energy intake and amount consumed (gram) between the taste clusters in night shift working nurses during the night shift and outside the night shift. The energy percentages of the six taste clusters were included as a dependent variable. MANCOVA was used to determine differences in the percentages of energy intake and consumed amount (gram) between the taste clusters of the night shift working nurses and the reference population. All models were adjusted for age (years), BMI (kg/m²), and smoking status (yes/no). Adjustment for education level did not result in a better model or different results and was therefore not included in the model. Intraclass correlation coefficients (ICC) were calculated to determine day-to-day variation of energy intake, and taste clusters between the 24-hour dietary recalls of both study populations (Suppl. Table 3.2). Intraclass correlation coefficients (ICC) above 0.4 were considered to show fair to good reliability and an ICC above 0.75 show excellent reliability and thus less day to day variation [42].

A General Linear Model (ANCOVA) was used to determine differences in the total DHD2015-index score, adjusted for age, BMI, and smoking status, between the night shift working nurses and the reference population. Generalized Linear Models were used to determine differences in the component scores of the DHD2015-index between the night shift working nurses and the reference population. All models were adjusted for age, BMI, and smoking status. Spearman correlation coefficients were used to investigate the association between the percentage of energy intake and consumed amount (gram) of each taste clusters with the adherence to the Dutch dietary guidelines (DHD2015-index). The 95% confidence interval was calculated using Fisher's Z-transformation.

Sensitivity analyses: Misreporting of energy intake

We performed sensitivity analysis to examine the effects of misreporting of reported energy intake (EI) on dietary taste patterns. We identified potential low and high energy reporters by evaluating the ratio EI: Basal Metabolic Rate (BMR) at the individual level

[43, 44]. BMR was estimated by the Henry equation from body weight, taking into account age and gender [45]. For the night shift working population we calculated a lower cut-off limit for the ratio of 0.97 and an upper cut-off limit of 2.46. For the reference population we calculated a lower cut-off limit of 0.93 and an upper cut-off limit of 2.57.

Results

Demographic characteristics

On average the night shift working nurses were slightly older than the reference population (41.4 vs 38.2 y), their BMI was slightly lower (25.0 vs 25.9 kg/m2), and a smaller proportion defined themselves as currently smoking (5.8% vs 21.5%) (**Table 3.1**).

Table 3.1. Demographic characteristics of night shift working nurses and the Dutch reference population.

	Night shift working nurses	Reference population	
	n=120	n=307	p-value*
Age, years mean ± SD	41.4 ±11.9	38.2 ± 12.0	0.014
Body weight, kg mean ± SD	72.0 ± 12.6	74.4 ± 15.2	0.098
BMI, kg/m² mean ± SD	25.0 ±4.0	25.9 ± 5.2	0.066
< 18.5 (underweight), n (%)	1 (0.8)	9 (2.9)	0.197
18.5 – 24.9 (normal weight, n (%)	64 (53.3)	143 (46.6)	0.208
25 – 29.9 (overweight), n (%)	46 (38.3)	93 (30.3)	0.112
> 30.0 (obese), n (%)	9 (7.5)	62 (20.2)	0.002
Educational level†			0.656
Intermediate, n (%)	61 (50.8)	154 (50.2)	
High, n (%)	55 (45.8)	153 (49.8)	
Smoking status†			<0.001
Current smoker, n (%)	7 (5.8)	66 (21.5)	
Non-smoker, n (%)	111 (92.5)	241 (78.5)	

^{*} ANOVA for continuous variables and Chi-square for class variables. † 4 participants had missing data on educational level or smoking status.

Dietary taste patterns during and outside the night shift

Different taste patterns were observed when dividing the intake assessed by the 24-hour recalls between the foods consumed during and outside the night shift. When expressed in energy percentage, night shift working nurses consumed most energy

from neutral tasting foods during (35.7 \pm 15.1 en%) and outside (29.9 \pm 11.8 en%) the night shift (**Figure 3.1A**). Bitter tasting foods contributed least to energy intake, both during (1.3 \pm 2.5 en%) and outside (2.0 \pm 3.5 en%) the night shift. During the night shift 'neutral', 'sweet and sour' and 'sweet and fat' tasting foods significantly contributed more to energy intake and 'fat' and 'bitter' tasting foods contributed less to energy intake than outside the night shift.

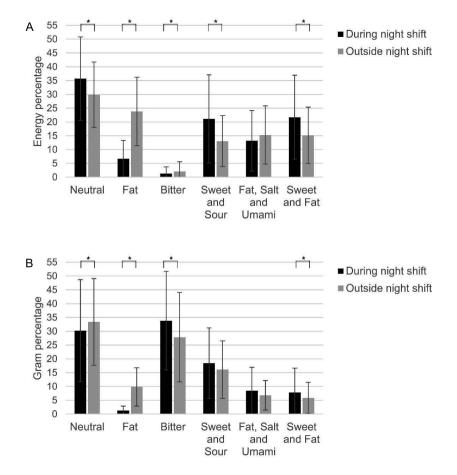


Figure 3.1A and 3.1B. Mean ±SD percentage of total daily energy intake (1A) and total consumed amount in grams (1B)) contributed by each taste cluster during and outside a night shift (n=120), *Significant P<0.05.

In the neutral taste cluster, during the night shift most energy was derived from bread (24.9 % of daily energy intake) and outside the night shift from bread (8.1 en%) and pasta and rice (6.7 en%). For the 'sweet and sour' taste cluster, fruit and yoghurt were

the main contributors to energy, of which most energy from these foods were consumed during the night shift. Considering food choices from the 'sweet and fat' taste cluster, the night shift nurses consumed mainly large cookies and pastries during and small cookies outside the night shift. Regarding the 'fat' taste cluster during the night shift, the food group margarine and cooking fats was the main energy contributor, while outside the night shift potatoes, including fried potatoes, and margarine and cooking fats contributed most to energy.

When examining the percentage of the consumed amount (in grams) per taste clusters (**Figure 3.1B**), the largest contribution was provided by the 'bitter' tasting foods coffee and tea, especially during the night shift ($33.8 \pm 17.9 \, \text{gram}\%$). Also neutral tasting foods contributed a relative large amount during and outside the night shift, but the proportion was lower during than outside the night shift.

Comparison of dietary taste patterns between night shift workers and reference population

Night shift working nurses consumed on average ±SD (166 ± 55.5 kcal) less energy per 24 hours than the reference population (p=0.002) (Suppl. Table 3.2). The night shift working nurses consumed proportionally more energy from protein, carbohydrates and dietary fibre and less from fat and alcohol around (during and outside) their night shift than the reference population. Similar to the night shift workers, the reference population consumed the highest energy percentage from neutral tasting foods (32.3) ± 9.5 en% and 32.3 ± 9.8 en%, respectively) and the lowest energy percentage from bitter tasting foods (1.8 ± 2.9 en% and 3.9 ± 5.3 en%) (Figure 3.2A). The energy contribution of foods with a 'bitter' taste was significantly lower in the nurses than the reference population (p= 0.030). In the night shift working population this energy mainly came from coffee (with milk), while in the reference population this energy mainly came from wine. Night shift workers also tended to consume a higher energy percentage of foods with a 'sweet and sour' taste (mainly from fruit and yoghurt) than the reference population (mainly from fruit and soft drinks; p= 0.05). Compared to the reference population, the night shift nurses consumed similar amounts of energy from the other taste clusters.

When examining the percentage of the consumed amount (in grams) per taste cluster (**Figure 3.2B**); both night shift workers and the reference population consumed

proportionally the largest amount of 'neutral' (32.2 ± 15.1 and 38.0 ± 15.0 gram%) and 'bitter' (30.4 ± 14.9 and 30.7 ± 15.8 gram%) tasting foods. Night shift working nurses proportionally consumed a significantly lower amount of 'neutral' tasting foods and a significantly higher amount of 'fat' and 'fat, salt and umami' tasting food than the reference population. The percentage of the consumed amount contributed by the "sweet and fat" cluster was similar.

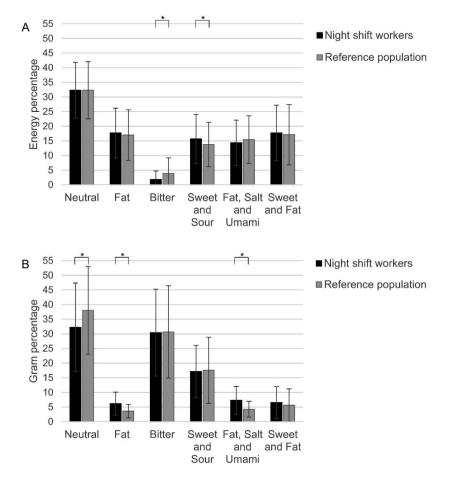


Figure 3.2A and 3.2B. Mean \pm SD percentage of total daily energy intake and total consumed amount (grams) contributed by each taste cluster in night shift working nurses (n=120) and in the reference population (n=307). *Significant P<0.05, adjusted for age, BMI and smoking.

Misreporting of energy intake

From the night shift working population, 26.7% of the participants was identified as potential low energy reporter, while in the reference population this was 17.9%. When excluding these low energy reporters the difference between percentage of total daily energy intake of 'sweet and sour' tasting foods between the night shift workers and the reference population disappeared (**Suppl. Table 3.3**). In addition, the difference in the percentage of consumed amount (in grams) of 'neutral' tasting foods between the night shift workers and the reference population was attenuated (p=0.077) (**Suppl. Table 3.3**).

Adherence to Dutch dietary guidelines

The overall DHD2015-index score of the two populations was similar (p=0.720); night shift workers scored on average 77 \pm 15 points and the reference population scored on average 74 \pm 16 points (**Table 3.3**). However, there were differences in the scores of the individual components. The night shift working nurses scored significantly higher on the components 'fruit', 'whole grain products', 'nuts', 'sugar sweetened beverages' and 'alcohol' and significantly lower on the components 'tea' and 'fat and oils' compared to the reference population.

Night shift workers scored highest on the components 'alcohol' $(9.9 \pm 0.9 \text{ points})$ and 'red meat' $(9.0 \pm 2.5 \text{ points})$, meaning that they almost completely adhere to the Dutch dietary guidelines for these components. The lowest adherence scores were found for 'fish' $(1.3 \pm 2.9 \text{ points})$ and 'legumes' $(1.4 \pm 3.4 \text{ points})$.

Associations between dietary taste patterns and adherence to Dutch dietary guidelines

The proportional intake of energy from 'fat' tasting foods was negatively associated with the DHD2015-index score (r= -0.31, p<0.001) (**Table 3.4**) in night shift working nurses. This means that a higher energy intake from 'fat' tasting foods was associated with a lower adherence - and thus a lower diet quality - to the Dutch dietary guidelines. The proportional amount of foods from the 'fat' (r= -0.36, p<0.001) and 'fat, salt and umami' (r= -0.28, p=0.002) clusters were also negatively associated with the DHD2015-index score. The proportional amount of foods from the 'bitter' tasting foods (r=0.24, p=0.008) was, on the other hand, positively associated with DHD2015-index score (**Table 3.4**).

Table 3.3. Mean scores and standard deviations of the total score of the Dutch Healthy Diet 2015 index (DHD2015-index) and its component scores, reflecting the adherence to Dutch dietary guidelines of 120 night shift working nurses and compared with the reference population.

	Night work n=1	ers	Refere popula n=3	ation	
DHD2015-component score	Mean	SD	Mean	SD	<i>p</i> -value‡
Vegetables	6.9	2.7	6.3	3.2	0.186
Fruit	7.3	3.4	5.2	3.9	<0.001
Whole grain products	5.3	2.7	4.5	2.9	0.044
Legumes	1.4	3.4	0.9	2.8	0.163
Nuts	2.0	3.6	1.1	2.9	0.033
Dairy	6.3	3.2	6.0	3.4	0.802
Fish	1.3	2.9	1.6	3.2	0.387
Tea	4.7	4.0	6.5	4.1	<0.001
Fats and oils	3.3	4.1	6.6	4.4	<0.001
Red meat	9.0	2.5	9.2	2.1	0.386
Processed meat	4.6	3.9	4.7	4.0	0.767
Sugar sweetened beverages	7.4	3.4	5.3	4.3	<0.001
Alcohol	9.9	0.9	8.5	3.3	<0.001
Sodium	7.5	2.9	7.9	2.6	0.106
Overall DHD2015-index score*	77.0	14.9	74.2	15.8	0.720

^{*}The score ranges between 0 and 140 points. ‡ Generalized Linear Models were performed to compare DHD2015-index component scores between night shift workers and the reference population, General Linear Model was used to compere the total DHD2015-index score. All models were adjusted for age, BMI and smoking.

Table 3.4. Spearman correlation coefficients between the DHD2015-index score and the percentage consumed energy and amount from 6 taste clusters among night shift working nurses (n=120).

		% Energy		9	6 Amount (gran	າ)
Taste cluster	r	95% CI	p-value	r	95% CI	p-value
Neutral	0.15	(-0.02, 0.31)	0.097	0.08	(-0.12, 0.26)	0.412
Fat	-0.31	(-0.47, -0.13)	<0.001	-0.36	(-0.51, -0.19)	<0.001
Bitter	0.07	(-0.13, 0.26)	0.477	0.24	(0.04, 0.42)	0.008
Sweet and Sour	0.16	(-0.03, 0.35)	0.073	-0.06	(-0.25, 0.14)	0.544
Fat, Salt and Umami	-0.02	(-0.19, 0.16)	0.836	-0.28	(-0.44, -0.11)	0.002
Sweet and Fat	0.04	(-0.14, 0.23)	0.640	-0.04	(-0.24, 0.15)	0.641

Discussion

This study assessed dietary taste patterns of female night shift working nurses and compared these during the night shift and outside the night shift. Moreover, these dietary taste patterns were compared with those of a female reference population. Last dietary taste patterns were associated with the diet quality of the nurses.

In light of our hypothesis, some of our results were inconsistent. As hypothesized we observed a higher contribution of energy from the 'sweet and fat' and 'sweet and sour' taste cluster during the night shift than outside the night shift, however there were no differences for the 'fat, salt and umami' taste cluster. This higher energy intake from the 'sweet and sour' taste cluster during the night shift was also reflected by a higher total daily energy intake from the 'sweet and sour' taste cluster in night shift working nurses than the reference population. However, we did not observe differences in energy intake from the 'sweet and fat' and 'fat, salt and umami' taste cluster between the night shift working nurses and the reference population. Also, we did not find a worse diet quality in the nurses as compared to the reference population. However, nurses with a higher energy and gram intake from 'fat' tasting foods and a higher gram intake of 'fat, salt and umami' tasting foods had a lower diet quality. On the other hand, a higher gram intake of 'bitter' tasting foods was associated with a better diet quality in night shift working nurses.

We expected that especially the energy intake from 'sweet and fat' tasting foods would be higher in night shift working nurses than in the reference population. This would be due to lower cognitive reserves and therefore a higher innate preference for sweet foods [19, 20, 23], and because sleep restriction might lead to a preference for fat foods [16]. In the current study, we indeed found that night shift working nurses consumed more energy from the 'sweet and fat' taste cluster during the night shift than outside the night shift. However, this higher energy intake during the night shift did not result in a higher total daily energy intake from the 'sweet and fat' taste cluster than the reference population. Nonetheless, we found that nurses had a higher intake of the 'sweet and sour' taste cluster, not only during the night shift but also compared to the reference population. To explain these inconsistent results it is important to realize that food choices are not only made on the basis of appetite or hedonic (taste) values, but are also based on the nutritional value of the food and health goals which requires

cognitive control [24]. Another important factor is the availability of foods. Some companies offer meals during the night shift on the worksite. However, the meal provision in the participating hospitals was limited and therefore foods were probably taken from home. Consequently, the nurses were making their food choices at home when they were less tired and able to make well informed, healthier food choices than during the night shift. Indeed during the night shift mainly healthy foods were eaten such as bread, fruit and yoghurt. Thus, our results may become clearer if in future research other determinants of food choice and intake are taken into account.

The explanation that selected foods of the nurses foods were taken from home may also explain why we observed no differences between the intake of 'fat, salt and umami' tasting foods during and outside the night shift and as compared to the reference population. Another explanation may be that our study was performed in a female study population. Earlier research showed that females had a lower preference for savoury tasting foods (than men), making it unlikely that they would increase their intake of these foods during the night shift [29].

It may seem surprising that the gram percentage of 'bitter' tasting foods was higher during the night shift than outside the night shift, while the energy percentage was, as expected, lower during the night shift than outside the night shift. Typically, bitter is not a preferable taste and therefore you would expect that 'bitter' tasting foods do not contribute a lot to total energy intake and consumed amount during a night shift [24]. However, outside the night shift, the second largest source after coffee (with milk), of energy from this 'bitter' taste cluster comes from alcohol intake which has a considerably higher energy content than coffee and tea (as typically most consumed bitter drinks), while during the night shift no alcohol was consumed. This is also reflected in a higher energy percentage by alcohol in the refence population. On the other hand, the higher gram percentage from 'bitter' tasting foods during the night shift than outside the night shift may be explained by the fact that bitter tasting foods such as coffee and tea contain caffeine, which is known for its stimulating effects on the brain [46, 47], and therefore a tempting food for nurses working the night shift.

Within the neutral taste cluster there was also a discrepancy between energy and gram percentage of neutral tasting foods. Most energy and gram percentage from the neutral

taste cluster outside the night shift came from bread, pasta/rice, milk and vegetables typically eating during the evening dinner, while a considerable energy percentage during the night shift was contributed by bread. While vegetables contribute most to gram percentage but not to energy percentage, for bread it is the other way around.

Diet quality of the night shift nurses was with a DHD2015-index score of 76.2 ±14.5comparable to that of the reference population (74.2 ±15.8). Nurses ate more fruit and vegetables and drank less sweetened beverages and alcohol than the reference population. This was in line with the results of the dietary taste patterns in this current study. Fruit was, together with vogurt, the main source of energy intake from the 'sweet and sour' taste cluster, and alcohol was one of the energy sources in the reference population that contributed to a higher energy intake from the 'bitter' taste cluster compared to the night shift working nurses. Yet a higher energy intake from this 'sweet and sour' taste cluster was not associated with a better diet quality. Probably because this taste cluster also includes soft drinks and some sweet and sour sauces which are not part of a healthy diet and thus do not contribute to a better diet quality [41]. A higher gram percentage from the 'bitter' taste cluster was however associated with a better diet quality. This is in contrast with previous studies which showed a negative association between bitter tasting foods and a healthy and sustainable diet [48, 49]. In the previous studies, energy intake from bitter tasting foods mainly came from alcohol which is negatively associated with several health outcomes [41]. However, as mentioned before, the energy and gram percentage of bitter tasting foods of the night shift working nurses did not come from alcohol which explains why there was not an inverse correlation.

We also showed that energy and gram percentage of the 'fat' cluster and gram percentage of the 'fat, salt and umami' taste cluster were negatively associated with diet quality. This is partly in line with other studies that found that a higher energy intake of 'fat, salt and umami' tasting foods and a higher gram intake of 'fat' tasting foods was associated with a lower diet quality [48, 49]. A healthy diet has been associated with less 'fat, salt and umami' tasting foods and more neutral taste foods than an unhealthy diet [48], where as a 'tasteful' diet is related to a lower diet quality. This is further reflected in an American population where the importance of taste was negatively correlated with diet quality [50].

This is the first study that investigated differences in dietary taste patterns of nurses between inside and outside the nightshift, and compared dietary taste patterns and diet quality with a reference population. Using a taste database in addition to a diet composition database gives an extra opportunity to not only investigate the diet of night shift working nurses from a nutrient and diet quality perspective, but also from a sensory perspective. Assessing dietary taste patterns gives a better understanding of potential drivers of food choice and intake in night shift working nurses. Given that intake data is the result of foods selected (and subsequently consumed) by the nurses, any relationship of taste (intensity) with intake must be the result of its impact on food preference and choice. This information can be used in formulation of nutrition strategies for night shift workers to improve their nutritional status and consequently promoting health and well-being [51, 52]. A nutritional strategy could be recommending foods during the night shift that are perceived as 'sweet and fat', but are healthier than large cookies and pastries, for example a portion of low fat voghurt with fruit. Since these foods were already consumed by some of the nurses, this could be a viable strategy for all.

A previous study by van Langeveld already showed that a taste database in combination with two 24-hour dietary recalls can be used to assess dietary taste patterns [29]. In this study we also used multiple dietary 24-hour dietary recalls per individual. While the total energy intake over the multiple 24-hour dietary recalls did not show much day to day variation, the energy percentage from the different taste clusters over the multiple 24-hour dietary recalls did. The Intraclass Correlations Coefficients (ICC) ranged from 0.10 for 'fat' taste cluster and 0.70 for 'sweet and sour' taste cluster in the night shift working population and from 0.14 for 'fat' and 0.54 for the 'bitter' taste cluster in the reference population. This means that especially energy intake from the 'fat' taste cluster varied greatly from day to day in both study populations, while the energy intake from the 'sweet and sour' taste cluster in the night shift working population was less prone to day to day variation. As we used average dietary taste patterns per person and we only compared dietary taste patterns at the group level this day to day variations was nullified [53].

We allocated the foods to the taste clusters by using hierarchical cluster analyses based on the (average) taste intensity values of each food. Although the allocation of the taste clusters to foods was done in an objective and repeatable manner, the actual

taste intensity values of an untested food may deviate from the average taste intensity values it was assigned to and therefore did not end up in the correct taste cluster. However, the deviations in the assigned taste intensity values compared to the actual taste intensity values may be expected to be random, and therefore probably did not affect the current results, because we looked at dietary taste patterns at the group level and not at an individual level. Random errors may be expected to cancel out if the population is large enough.

Another methodological constraint is that nightshift working nurses were underreporting their daily energy intake. This is a well-known issue when assessing dietary intake [42, 44], but could be more prevalent in the current population due to night shift related fatigue. However, excluding potential under reporters from the analysis did not result in different dietary taste patterns.

In general, a positive energy balance will result in overweight. However, a higher BMI in night shift workers may not necessarily result from a higher energy intake. Previous studies have shown similar energy intakes among day and night shift workers [2]. It has been shown that meal timing also could have metabolic consequences for the development of overweight and for weight loss [54]. Eating the same amount of energy earlier in the day resulted in a lower body weight than eating the same amount of energy later during the day, which is the case for night shift workers [54, 55]. In addition, the human body processes foods differently during the night than during the day. Glucose and fat metabolism are following a circadian rhythm and are disrupted by food intake during the night shift resulting in higher glucose spikes during the night than during the day [56-58]. Snacks most likely contain more sugar and fat resulting in even higher spikes. This could result in a higher disruption of the circadian rhythm and consequently higher health risks. With this observational study we aimed to assess dietary taste patterns in night shift workers and whether a higher preference and choice of sweet and savoury tasting foods could explain the snack tendency and eventually the higher risk of having overweight.

Ideally, we would have compared dietary taste patterns around a night shift as well as around a day shift in the same population. Unfortunately, this data was not available and the current reference population is assumed to be a good alternative, although

one could speculate that night shift working nurses eat healthier during a day shift than during a night shift and than the current reference population.

The dietary intake data from night shift working nurses was only assessed during the first night shift. It is hypothesized that night shift workers suffer mostly from sleep loss during this first night shift as they prolong their day and make food choices more automatically and based on habits due to fewer cognitive reserves [19]. Potential differences in dietary taste patterns between night shift workers and the reference population would therefore be expected to be most pronounced with dietary taste patterns of night shift workers around the first night shift. However, one study showed that the energy intake of night shift workers is highest during the second consecutive night shift; nevertheless fat intake was the highest during the first night shift [13]. Dietary taste patterns could therefore be different across consecutive night shifts. Thus, we must be careful in extrapolation of our results for a first night shift to consecutive night shifts.

Lastly, the night shift working nurses in this study consisted solely of women, and might be more interested in the role of nutrition than those who did not participate; they could therefore have been more health-conscious. This could explain the higher fruit and vegetable intake but also the higher energy percentage from 'sweet and sour' foods compared to the reference population. Thus, our results may not generalise to all nurses and especially not to other night shift working populations. Males, for example, differ in their dietary taste patterns and consume more foods with a 'fat, salt and umami' and 'bitter' taste and less foods with a 'sweet and sour' and 'sweet and fat' taste than women [29]. It would be interesting to assess dietary taste patterns in other night shift working populations especially in those with other shift work rotations or an unhealthier diet than in our population.

In conclusion, diet quality and dietary taste patterns seem to be related in night shift working nurses. Also, our findings suggest differences between the dietary taste patterns of night shift working nurses and populations without nightshifts and within the nurses between dietary taste patterns during and outside the nightshift. However, not all findings were consistent with our hypothesis that the nurses would select foods with more of the innate taste preferences of sweet and savoury. For example, a possible

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taste preference for sweet in night shift working nurses was not reflected by a higher intake of 'sweet and fat' tasting foods over 24 hours. This also indicates that other factors, such as availability, are involved in the food choice of night shift working nurses. Lastly, we showed that a higher intake from 'fat' and 'fat, salt and umami' tasting foods were associated with a lower diet quality. Therefore, to improve diet quality in night shift working nurses, it seems to be important to include their taste preferences in nutrition strategies. Whether this finding is also true for other night shift working populations must be explored in future research.

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Supplementary materials



Supplementary Figure 3.1. Flowchart of assigning mean taste intensity values to untested foods in night shift working nurses and the reference population. *DNFCS = Dutch National Food Consumption Survey.

Supplementary Table 3.1. Taste intensity values (mean ±SD) of the 6 taste modalities and energy and nutrient content stratified by taste clusters calculated from the foods (n=1,781) consumed in the Etmaal study and by adults in the DNFCS* 2012-2016.

			,			•	•					
	Neutra		Fat		Bitter		Sweet & Sour	our	Fat, Salt & Umami	lmami	Sweet & Fat	Fat
	n= 376		n= 275		n= 68		n= 323		n= 365		n= 374	
Taste modality	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Sweet	8.9	3.9	7.5	6.2	13.9	7.0	31.8	11.8	9.8	5.8	45.3	10.7
Sour	4.2	4.0	4.2	2.8	15.6	12.1	31.4	9.6	12.4	6.2	3.4	2.8
Bitter	3.2	2.7	1.3	4.	34.7	13.8	2.3	1.6	2.2	2.6	3.1	3.8
Umami	4.1	2.7	11.6	4.1	1.3	13.8	2.5	1.6	23.6	2.6	0.8	3.8
Salt	9.6	5.4	24.0	10.7	2.1	6.0	8.9	9.6	42.9	7.0	8.4	2.9
Fat sensation	12.5	8.5	46.1	25.6	4.5	3.1	19.7	21.0	49.6	12.7	32.8	15.2
Nutrient content / 100g												
Energy (kcal)	191	179	329	248	123	124	110	124	248	134	332	152
Protein (g)	6.9	6.1	10.6	9.7	1.3	3.3	1.7	2.5	13.1	8.6	4.9	3.6
Fat (g)	6.5	14.3	25.9	30.7	1.7	6.2	5.5	12.6	17.7	15.0	11.8	10.8
Carbohydrates (g)	24.0	24.0	13.1	21.5	9.3	13.6	12.7	15.0	8.8	14.3	20.7	25.7
Mono- and disaccharides (g)	3.7	6.1	1.7	2.7	8.9	6.6	11.3	13.4	3.1	7.1	33.2	22.5
Dietary fibre (g)	4.4	4.9	1.3	2.1	6.0	2.7	1.0	2.1	0.8	2.0	2.4	3.2
Alcohol (g)	0.0	0.0	0.0	0.0	10.1	11.8	0.0	0.0	0.0	0.1	0.0	0.1
Sodium (mg)	200	294	265	413	22	64	105	209	1006	1983	146	138

Supplementary Table 3.2. Mean total energy intake, macronutrient intake as energy intake percentages (en%) and en% per taste cluster of night shift working nurses and reference population with intraclass correlation coefficients (ICC) and 95% confidence intervals.

		Night	Night shift workers n=120	rkers		Refere	Reference population n=307	ulation
	Mean	SD	*	95% CI	Mean	SD	CC	95% CI
Nutrient content								
Energy intake, kcal	1690	471	0.67	(0.54, 0.77)	1856	532	0.62	(0.54, 0.69)
Protein, en%	16.9	3.6	0.68	(0.56, 0.77)	15.8	3.6	0.58	(0.49, 0.65)
Fat, en%	32.9	6.9	09.0	(0.45, 0.72)	35.2	7.0	0.41	(0.28, 0.51)
Saturated fatty acids, en%	12.9	3.5	0.59	(0.43, 0.71)	12.9	3.4	0.44	(0.33, 0.54)
Carbohydrates, en%	46.7	7.3	0.67	(0.55, 0.77)	44.6	7.8	0.49	(0.39, 0.58)
Taste clusters								
Neutral, en%	32.3	9.5	0.34	(0.08, 0.53)	32.3	9.8	0.45	(0.31, 0.56)
Fat, en%	17.7	8.4	0.10	(-0.25, 0.36)	17.0	8.6	0.14	(-0.07, 0.31)
Bitter, en%	1.8	2.9	0.68	(0.55, 0.77)	3.9	5.3	0.54	(0.43, 0.63)
Sweet & sour, en%	15.6	8.4	0.70	(0.58, 0.79)	13.7	9.7	0.48	(0.35, 0.58)
Fat, salt and umami, en%	14.3	7.7	0.38	(0.14, 0.56)	15.4	8.1	0.40	(0.24, 0.52)
Sweet and fat, en%	17.7	9.5	0.67	(0.54, 0.77)	17.1	10.3	0.48	(0.35, 0.59)
*based on three dietary recalls in 103 night shift working nurses	lle in 103	night e	hiff worki	אס אווע אר				

Supplementary Table 3.3. Percentage of total daily energy intake and total consumed amount (gram) contributed by each taste cluster in night shift working nurses (n=87) and in the reference population (n=252), potential low energy reporters are excluded.

	Night shif	t workers	Reference	population	
	Mean	SD	Mean	SD	p-value*
Neutral, en%	31.6	9.5	31.4	9.1	0.239
Fat, en%	18.2	7.5	17.4	8.4	0.662
Bitter, en%	1.7	2.8	4.2	5.4	<0.001
Sweet & sour, en%	14.4	7.6	13.8	7.2	0.813
Fat, salt and umami, en%	14.8	7.2	15.3	8.1	0.855
Sweet and fat, en%	18.8	8.6	17.5	9.7	0.917
Neutral, gram%	31.8	14.7	36.5	14.2	0.077
Fat, gram%	6.7	3.8	3.8	2.4	<0.001
Bitter, gram%	29.9	13.6	31.4	15.0	0.125
Sweet & sour, gram%	16.9	9.1	17.9	11.0	0.577
Fat, salt and umami, gram%	7.3	4.4	4.3	2.7	<0.001
Sweet and fat, gram%	7.2	5.2	6.0	5.4	0.188

^{*}Adjusted for age, BMI and smoking.







4

Macronutrient intake and alertness during night shifts – the time interval matters

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Abstract

Background: Working night shifts is associated with higher safety risks due to shift work-related fatigue. Nutrition, especially certain (macro)nutrient compositions, has been suggested to reduce fatigue, however, results of studies are contradictory. This could be explained by differences in the time interval investigated between the consumption of a meal and measurement of cognitive performance. Therefore, this observational study investigated the association between macronutrient intake and objective alertness at different time intervals during the night shift in nurses.

Methods: 128 nurses, aged 20-61 years, completed an alertness test (Psychomotor Vigilance Task) during the night shift and a 24-hour dietary recall after the night shift. This was repeated three times, always on the first night shift in a night shift series. The associations between macronutrient intake 0 to 1, 1 to 2, and 2 to 3 hours before the PVT with alertness during the night shift were analyzed through Linear Mixed Models. The basic model was adjusted for age and gender and the adjusted model additionally for BMI, start time of PVT and energy and caffeine intake during the relevant time interval.

Results: Protein intake was not associated with objective alertness levels, while fat and carbohydrates intake had opposite associations with objective alertness levels over similar time intervals. Fat intake up to 1 hour prior to the PVT was borderline associated with a longer median reaction time (RT) (ß=9.00 ms/10 g fat, 95% CI: -0.21, 18.20), while a higher carbohydrate intake up to 1 hour prior to the PVT was borderline associated with shorter median RTs (ß=-3.89, 95% CI: -7.85, 0.06).

A higher fat intake 2 to 3 hours prior to the PVT was associated with less lapses (log transformed ß=-0.16; 95% CI: -0.31, -0.02), while a higher carbohydrate intake 2 to 3 hours prior to the PVT was associated with more lapses (ß=0.06, 95% CI: 0.01, 0.12). **Conclusion**: Our results contribute to understanding the association between macronutrient intake, as part of a mixed meal, and alertness levels. Conflicting results from previous studies may probably be due to time differences between macronutrient intake and alertness testing.

Introduction

In healthcare, continuous care is provided 24 hours a day, 7 days a week. This means that health care workers, including nurses, have to work outside the conventional working hours, including at night [1-3]. Unfortunately, night shift work is associated with higher health and safety risks. For example, night shift workers have a 30 percent increased risk of making (medical) errors or having accidents than day shift workers [4-6]. This is mainly caused by shift work-related fatigue [5].

Several studies have investigated how shift-work related fatigue can be reduced, e.g. by using lamps that simulate daylight during the night shift [7]. Another way to reduce fatigue and thereby improve alertness during the night is by applying nutrition strategies [8, 9]. For example, consumption of meals during the night shift with specific (macro)nutrient compositions may reduce fatigue and improve cognitive performance [8, 10].

Studies investigating the effect of (macro)nutrient composition on cognitive performance (e.g., sustained attention, memory, processing speed) have mostly focused on glucose intake and were conducted during the daytime [10, 11]. Compared to sweeteners, glucose has been shown to improve memory, but might also benefit other cognitive functions [10]. However, it is not yet clear whether cognitive performance is solely affected by glucose intake or by consumption of carbohydraterich foods in general [11], or what the impact of other macronutrients (protein and fat) would be. One study showed that carbohydrate-rich meals increase sleepiness, but only in obese night shift workers [12]. Another study showed that a protein-rich breakfast, as well as a protein and carbohydrate-balanced breakfast, resulted in better overall cognitive performance directly after the meal than a carbohydrate-rich breakfast. In addition, a carbohydrate-rich breakfast resulted in better peripheral attention but worse central attention after 135 minutes than a protein and carbohydrate-balanced breakfast [13]. Yet another pilot study found that cognitive performance during the night improved after a test meal that was higher in fat and lower in carbohydrates than the baseline meal that was relatively low in fat and high in carbohydrates [8]. Hence, the effects of different macronutrient composition of meals are not always very distinct and sometimes even contradictory [9, 10, 12, 14].

A factor that could contribute to these contradictory results is the time interval between the consumption of a meal and measurement of cognitive performance. As mentioned earlier, Fischer et al (2002), reported differences in cognitive performance tested directly and 135 minutes after the meal. Besides meal related aspects, the various types of tests that have been used to measure cognitive performance may also contribute to the contradictory study outcomes [10, 14]. Most studies focusing on the effect of glucose intake found that it was positively associated with the domains of short term and delayed memory performance, while the effect of a specific macronutrient composition of a meal was suggested to be better reflected in tasks that involve sustained attention [10]. In addition to this objective measure of alertness, it is recommended to assess subjective alertness [14, 15]. Subjective alertness may be seen as a perceivable benefit that consequently leads to higher motivation to comply with dietary intervention strategies.

Although the recent advancements in the studies of diet and cognitive performance are promising, a better understanding is needed of the association between diet and sustained attention especially in night shift workers [9, 10]. Since a meal does not solely consist of a single macronutrient, research should particularly focus on the differential effects of the specific types of macronutrients in a mixed meal, taking into account the time interval between the meal and the cognitive task [14]. Therefore, we investigated the association between macronutrient intake with objective and subjective alertness, measured during different time periods in nurses during the night shift. The results of this study can be used to develop nutrition intervention strategies as a vital part of occupational health and safety management programs in shift work.

Methods

Participants

Nurses were recruited in three hospitals located in the surrounding area of Wageningen, the Netherlands. They were invited via email by the researcher and via advertisements on the internal website for employees of the hospitals. Nurses were included in the study if they were working the night shift for at least 6 months, were not using drugs that could cause or reduce sleep problems, were not using daylight lamps on the workplace during the night shift, were eating according to a Dutch eating pattern

(2 bread meals and 1 hot meal) and were not donating blood during the data collection period as this may cause fatigue [16]. In total, we included 164 nurses in the study, 24 of whom dropped out before nutritional data was collected. We additionally excluded nine smokers and three nurses with missing data for smoking, as smokers typically go outside for their cigarette break, which could have affected the results of the alertness test. The final study sample consisted of 128 nurses. All nurses gave written consent before the start of the study.

Study design and procedure

This observational study was conducted between April 2015 and July 2018. At the start of the data collection period, nurses' height and body weight were measured and they filled out a demographic questionnaire. Thereafter, based on the night shift timetables, nurses were scheduled for the measurements. They were asked to complete an alertness test once during the night shift and to complete a 24-hour dietary recall after the night shift. These measurements were repeated three times, always during the first night of three different night shift series with at least one month in between. The study was approved by the Medical Ethical Committee of Wageningen University and Research (ABR: NL54414.081.15) and was conducted according to the principles of the Declaration of Helsinki.

Objective and subjective alertness

Objective alertness was assessed by the Psycho Vigilance Test (PVT). The PVT is a validated 10-minute visual reaction time task that measures sustained attention [17]. This task was carried out on a computer between 2:00 AM and 5:00 AM. Nurses were instructed to press the space bar as quickly as possible when a white circle, the stimulus, appeared on the black screen. The visual stimulus appeared every 2 to 10 seconds for 10 minutes at a fixed point on the screen. For each completed PVT, we determined the mean reaction time (RT; ms), mean reciprocal response time (1/RT), number of lapses (RT > 500 ms), and number of false starts (responding prior to a stimulus or RT < 100 ms).

Subjective alertness was assessed by the 7-point Samn-Perelli Scale (SPS). At the start of the PVT, nurses were asked to complete the SPS. With the SPS, nursers are asked how they feel at that moment. The answer scores ranges from 1 ("fully alert, wide awake") to 7 ("completely exhausted, unable to function effectively") [18].

Dietary intake

Each 24-hour dietary recall was completed by the nurses on the day after the first night shift. Nurses were asked to record all the foods and drinks they consumed during 24 hours: from the evening meal prior to the first night shift until the evening meal after the night shift. They were also asked to write down the time of day when each food or drink was consumed. Each recall was self-administered via Compl-eat, a web-based program, based on a validated technique to increase the accuracy of dietary recalls [19], and includes foods used in a Dutch food pattern. Portion sizes of foods or recipes were reported by household measures, standard portion sizes, or weights in gram. When the reported recall was not clear (e.g. missing portion sizes), the participant was called or emailed by the researcher or research dietitian for clarification. Average daily intakes of energy, macronutrient, alcohol and caffeine of each participant were calculated by multiplying frequency of consumption of food items by portion size and energy and nutrient content using the 2013 Dutch Food Composition Table [20]. In addition, based on the reported start and end times of the night shift, it was determined what each participant consumed during the night shift, and what was consumed 0 to 1 hour, 1 to 2 hours and 2 to 3 hours before the PVT.

Anthropometrics and demographics

Height and body weight were measured without shoes by trained researchers and used to calculate body mass index (BMI) in kg/m2. Height was determined using a stadiometer to the nearest 0.5 cm. Body weight was assessed using an analogue scale to the nearest 0.5 kg or digital weighing scale to the nearest 0.1 kg depending on the hospital. The demographic questionnaire included questions about e.g. education, smoking, and working hours.

Statistical analysis

Data was analyzed using IBM SPSS Statistics 25. P-values below 0.05 were considered statistically significant. Raw data were checked for quality (outliers, omissions) and normality. If normally distributed, data are presented in mean ± SD or in n (%), otherwise in median and interquartile range. Three cases of outliers (average median RT> 600 ms) in alertness levels were detected, of which two in the same participant. To meet the assumption for linear mixed models (LMM) that the residuals were normally distributed, this participant was excluded from the data analysis.

Therefore, the final study sample includes 127 participants. Eight of these participants completed only one 24-hour dietary recall, 15 participants two recalls, 101 participants three recalls, and three participants four recalls, resulting in a total of 353 recalls.

A paired t-test was performed to investigate differences between the macronutrient intake in energy percentages during the whole day (including the night shift) and solely during the night shift. We calculated Spearman correlation coefficients between subjective alertness and median RT, 1/RT and log transformed number of lapses. To analyze the associations between macronutrient intake 0 to 1 hour, 1 to 2 hours and 2 to 3 hours before the PVT with alertness during the night shift, we used LMM with alertness as a dependent variable (objective and subjective measures separately) and each macronutrient intake in gram as the independent variables. We also controlled for dependence amongst the repeated measurements in each nurse and controlled for cluster effects within the three hospitals. In the basic model, we adjusted for age and gender and in the adjusted model we additionally adjusted for BMI, start time of PVT, and energy and caffeine intake during the relevant time interval.

Misreporting of daily energy intake

Misreporting of daily energy intake is a widely known phenomenon [21]. Potential recalls of poor validity were identified by using the principles of the Goldberg cut-off evaluating the ratio energy intake:basal metabolic rate (EI:BMR) at the individual level [21, 22]. BMR was estimated by the Henry equation from body weight, taking into account age, and gender [23]. Recalls with EI:BMR values lower than 0.87 and higher than 2.75 were classified as misreported recalls, which was the case for 22.7% of the recalls. All statistical analyses were performed with and without misreported recalls. However, because excluding misreported recalls did not alter the associations, we presented only the results of the total study sample.

Results

Participant characteristics

The majority of the nurses were female (92.1%) and were classified as having normal BMI (55.9%) (**Table 4.1**). Nurses started their night shift between 10:00 and 11:15 PM and ended their night shift between 7:00 and 8:15 AM. Eighty-one percent of the nurses (n=103) commuted sometimes or always by car. Of these nurses, 26 nurses reported

to have ever fallen asleep behind the wheel after a night shift, and 5 nurses had actually been involved in an accident after a night shift because of fatigue.

Objective and subjective alertness

The PVT, including the SPS question, was on average done at $3:08 \pm 0:34$ AM. Nurses had a median reaction time (RT) of 412.9 [IQR: 382.2-461.6] ms and 9.7 [IQR: 4.0-19.3] lapses on the PVT. They scored on average 3.2 ± 0.7 out of a score of 7 on the SPS, which is considered as 'Okay, somewhat fresh' [18]. The SPS score was positively correlated with the number of total lapses (log transformed) (r=0.162, p=0.002) and median RT (r=0.117, p=0.028) and inversely correlated with 1/RT (r=-0.129, p=0.015). The objective and subjective alertness levels did not significantly differ between the three study periods.

Dietary intake

All nurses consumed foods or drinks during the night shift, with a median of 3.3 (IQR:2.3-4) eating occasions at varying time points. Nurses consumed foods or drinks in 49.3% of the recalls 1 hour before the PVT, in 44.8% of the recalls 1 to 2 hours before the PVT and in 33.7% of the recalls 2 to 3 hours before the PVT. During the night shift, dietary intake consisted on average ±SD of 15.6 ±4.5 energy percent (en%) protein, 29.2 ±10.1 en% fat, 52.3 ±11.1 en% carbohydrates and 25.4 ±12.2 en% monoand disaccharides (**Table 4.2**). These relative intakes of macronutrients significantly differed (p<0.001) from those consumed during the whole day, especially for carbohydrates and mono- and disaccharides that were higher during the night shift.

Macronutrient intake and alertness

The associations of macronutrient intake for different time intervals to the PVT and objective and subjective measures of alertness are presented in **Table 4.3**. Significant associations were observed with objective but not with subjective alertness levels.

Protein

Irrespective of age and gender, absolute protein intake was inversely associated with median RT and positively associated with 1/RT, but only 1 to 2 hours before the PVT. However, this was not reflected by significantly less lapses. Moreover, these associations disappeared after additional adjustments for BMI, start time of PVT and energy and caffeine intake during the relevant time interval.

Table 4.1. Anthropometrics and demographics of all nurses (n=127) and by sex in mean ± SD, median (IQR) or n (%).

	C	Overall	W	omen		Men
	ı	n=127	n	=117	ı	n=10
Age, years (IQR)	42.3	(29.4-51.3)	43.4	(30.0-51.4)	33.3	(23.4-48.8)
Weight, kg ±SD	72.6	13.0	71.7	12.8	82.8	10.9
Height, cm ±SD	170.4	7.3	169.2	5.8	184.1	9.3
Body Mass Index, kg/m ² ±SD	25.0	4.1	25.0	4.1	24.6	24.6
- Underweight (<18 kg/m²), n (%)	1	(8.0)	1	(0.9)	0	(0.0)
- Normal (18-25 kg/m²), n (%)	71	(55.9)	65	(55.6)	6	(60.0)
- Overweight (25-30 kg/m²), n (%)	45	(35.4)	42	(35.9)	3	(30.0)
- Obese (>30 kg/m²), n (%)	10	(7.9)	9	(7.7)	1	(10.0)
Education						
- Intermediate education, n (%)	65	(51.2)	61	(52.1)	4	(40.0)
- Higher education, n (%)	60	(47.2)	54	(46.2)	6	(60.0)
Married/cohabiting						
- Yes, n (%)	104	(81.9)	97	(82.9)	7	(70.0)
Children						
- Yes, n (%)	69	(54.3)	64	(54.7)	5	(50)
Hours of employment, per week ±SD	28.9	5.7	28.5	5.7	34.4	2.1
Night shifts series/month, series (IQR)	2.0	(1.0-4.0)	2.0	(1.0-4.0)	2.5	(1.0-4.0)
Night shifts/serie, nights ±SD	2.7	1.0	2.6	1.0	3.6	1.1
Night shift experience, years ±SD	17.0	11.6	17.3	11.5	13.2	12.7
Commute by car, n (%)	103	(81.1)	97	(82.9)	6	(60.0)
Fallen asleep behind the wheel, n	26		24		2	
Involved in an accident caused by fatigue, n	5		5		0	

Fat

A higher fat intake up to 1 hour prior to the PVT was associated with a longer median RT (β =4.48 ms/10 g fat, 95% CI: 0.30, 8.67) and a lower 1/RT (β =-0.03 ms/10 g fat, 95% CI: -0.05, 0.00). This association was slightly attenuated after the additional adjustments.

No associations were found between fat intake 1 to 2 hours prior to the PVT and objective alertness levels.

A higher fat intake 2 to 3 hours prior to the PVT was associated with slightly shorter median RTs (ß=-15.31 ms/10 g fat, 95% CI: -31.16, 0.54, p=0.058). This was also reflected by less lapses; every 10 gram of fat consumed 2 to 3 hours before the PVT was associated with 0.16 less lapses (log transformed; 95% CI: 0.02, 0.31, p=0.029).

Carbohydrates

In contrast to a higher fat intake, a higher absolute carbohydrate intake up to 1 hour prior to the PVT was associated with a slightly shorter median RT (β =-3.89, 95% CI: 7.85, 0.06, p=0.054) and 1/RT (β =0.02, 95% CI: 0.00, 0.05, p=0.064) in the adjusted model. Especially a higher mono- and disaccharides consumption was associated with a shorter median RT (β =-3.83, 95% CI: -7.53, -0.13, p=0.042) and better 1/RT (β =0.02, 95% CI: 0.00, 0.05, p=0.043) in the adjusted model.

Just as for fat, no associations were found between carbohydrate intake 1 to 2 hours prior to the PVT and objective alertness levels.

Also in contrast with fat intake, a higher carbohydrate consumption 2 to 3 hours prior to the PVT was associated with longer median RTs (β =2.67, 95% CI: 0.36, 4.98, p=0.024) in the basic model and borderline associated with longer median RTs (β =6.04, 95% CI: -0.35, 12.43, p=0.064) after additional adjustments. A higher carbohydrate consumption and a higher polysaccharide consumption 2 to 3 hours before the PVT was also associated with more lapses (β =0.06, 95% CI: 0.01, 0.12, p=0.031 and β =0.09, 95% CI: 0.00, 0.18, p=0.043, respectively, in the adjusted model).

Covariates and alertness

We also examined the association between alertness levels and covariates separately (**Table 4.4**). Age was inversely associated with SPS (β =-0.01, p=0.019), meaning that an older age was associated with feeling more alert. Gender and BMI were not associated with objective or subjective alertness. The start time of the PVT was significantly associated with both objective and subjective alertness levels, indicating that nurses were less alert later during the night shift (p<0.001). Energy intake was associated with better median RT (β =-4.01, p<0.001) and 1/RT (β =0.03, p<0.001) and less lapses (β =-0.02, p=0.015) after adjustment for the other covariates, but only when energy was consumed 1 to 2 hours before the PVT and not at the other time points. Caffeine intake up to 1 hour before starting the PVT was associated with worse median RT (β =1.38, p=0.047) and 1/RT (β =-0.01, p=0.036). This means that a higher caffeine intake was associated with a slower reaction time. However, this was not reflected by more lapses or higher feeling of sleepiness (higher SPS score).

Discussion

This study is one of the first that reports on the association between macronutrient composition as part of mixed meals, meal timing, and (sustained) alertness in a real life night shift setting. There are two key findings, First, we found opposite associations for objective alertness levels for the intake of fat and carbohydrates. These associations were not only opposite between fat and carbohydrates, but also between fat and carbohydrate intake up to 1 hour, and 2 to 3 hours before the PVT. Fat consumption 1 hour prior to the PVT was associated with poorer alertness levels, while fat consumption 2 to 3 hours prior to the PVT was associated with better alertness levels, and for carbohydrates we observed opposite time dependent associations. Second, we found no associations between the intake of any of the macronutrients (protein, fat and carbohydrates) 1 to 2 hours before the PVT and objective alertness levels. This suggests a kind of tipping point with fat and carbohydrate intake 1 to 2 hours before the PVT and their association with alertness. However, an overall higher energy intake 1 to 2 hours before the PVT was associated with better alertness levels. We did not find an association between protein intake and alertness levels, nor did we observe a difference in timing. No associations were found between macronutrient intake and subjective levels of alertness.

The opposite time dependent associations for fat and carbohydrate intake and objective alertness levels could explain why some studies showed positive effects of macronutrient intake on alertness while others showed negative effects. Of the previous studies on this topic, only two (pilot) studies were conducted during the night shift [8, 24]. One study did measure cognitive performance at several time points during the night but averaged the scores, by which time differences could have been missed, [8] and the other did not provide information about the time at which cognitive performance was measured [24]. Moreover, neither of the studies presented details about consumption time and macronutrient composition. Therefore, it is hard to conclude from these earlier studies how macronutrient intake is associated with objective alertness levels and how the time interval between meal and alertness testing affected their results.

Table 4.2. Average dietary intake of nurses (n=127) derived from 24-hour recalls presented in median (IQR) intake and mean ±SD energy percentage.

									0 to	0 to 1 hour	1 to	1 to 2 hour	2 to	2 to 3 hour
		Whole day	day		ο	ring ni	During night shift	_	pefo	before PVT	peto	before PVT	peto	before PVT
	Mean	SD	En%	SD	Mean	SD	En%	SD	Median	(IQR)	Median	(IQR)	Median	(IQR)
Energy, kcal	1697	504			618	230			78	(0.0-210.6)	52	(0.0-161.4)	7	(0.0-74.3)
Energy, kJ	7118	2113			2597	964			331	(0.0-883.6)	220	(0.0-681.7)	29	(0.0-313.9)
Protein, g	70.3	21.2	16.9	3.7	23.6	9.2	15.6	4.5	2.3	(0.0-8.4)	1.2	(0.0-6.1)	0.2	(0.0-2.3)
- Plant protein, g	28.4	9.2	6.7	1.5	11.3	5.1	7.3	2.0	1.	(0.0-3.6)	0.5	(0.0-3.0)	0.1	(0.0-1.2)
- Animal protein, g	42.0	17.2	10.2	4.0	12.3	8.9	8.3	4.5	0.5	(0.0-4.1)	0.1	(0.0-2.9)	0.0	(0.0-0.7)
Fat, g	63.1	25.9	32.7	7.5	20.8	11.6	29.2	10.1	1.6	(0.0-7.1)	0.8	(0.0-5.2)	0.1	(0.0-2.4)
- Saturated fatty acids, g	24.5	10.9	12.7	3.7	8.7	9.6	12.3	5.4	9.0	(0.0-2.8)	0.3	(0.0-1.7)	0.0	(0.0-0.8)
- MUFA, g	20.8	9.6	0.4	0.2	6.3	4.2	0.4	0.3	0.4	(0.0-1.8)	0.2	(0.0-1.2)	0.0	(0.0-0.7)
- PUFA, g	11.8	5.6	10.8	3.1	3.7	5.6	8.8	4.3	0.2	(0.0-1.1)	0.1	(0.0-0.8)	0.0	(0.0-0.3)
- Trans fatty acids, g	0.8	0.5	6.1	2.0	0.3	0.3	5.2	2.7	0.0	(0.0-0.1)	0.0	(0.0-0.0)	0.0	(0.0-0.0)
Carbohydrates, g	197.9	64.1	47.0	7.8	80.0	33.3	52.3	1.1	10.9	(0.0-24.5)	7.7	(0.0-18.5)	0.4	(0.0-10.3)
- Mono- and disaccharides, g	86.8	38.6	20.6	6.9	37.9	22.6	25.4	12.2	3.9	(0.0-0.9)	1.9	(0.0-8.5)	0.2	(0.0.0-4)
- Polysaccharides, g	111.0	37.3	26.4	5.4	42.0	21.4	26.9	9.6	3.8	(0.0-13.5)	1.7	(0.0-10.0)	0.0	(0.0-4.8)
Dietary fibers, g	21.2	6.9	2.6	0.7	8.4	3.4	2.8	1.0	1.0	(0.0-2.4)	0.5	(0.0-2.3)	0.0	(0.0-0.8)
Alcohol, g	0.7	2.5	0.3	1.2	0.0	0.0	0.0	0.0	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)
Water, g	2332	756			1007	409			164	(50-263)	126	(0.0-246.3)	54	(0.0-156.6)
Caffeine, mg	108.4	118.2			55.9	63.3			0.0	(0.0-13.8)	0.0	(0.0-2.1)	0.0	(0.0-0.0)
							,	,,						

IQR: interquartile range, MUFA: Mono unsaturated fatty acids, PUFA: Poly unsaturated fatty acids.

Table 4.3. Association between (specific) macronutrient intakes 0 to 1, 1 to 2 and 2 to 3 hours prior to PVT and objective and subjective alertness in nurses (n=127) during the night shift.

		Š	Median Reaction Time	action T	me			Rec	Reciprocal Reaction Time	eaction	Time	
		Basic model*		•	Adjusted model†	÷		Basic model		•	Adjusted model†	±
	≥	95% CI	P value	€	95% CI	P value	≅	95% CI	P value	~	95% CI	P value
Protein / 10g												
< 1 hour before PVT	3.74	(-0.53, 8.01)	0.085	2.17	(-8.89, 13.23)	0.700	-0.03	(-0.05, 0.00)	0.056	-0.01	(-0.08, 0.05)	9.676
1-2 hours before PVT	-6.14	(-10.52, -1.76)	0.006	-6.42	(-18.03, 5.19)	0.277	0.04	(0.02, 0.07)	0.002	0.00	(-0.07, 0.07)	0.987
2-3 hours before PVT	5.14	(-2.66, 12.93)	0.195	-1.71	(-17.26, 13.84)	0.829	-0.02	(-0.07, 0.02)	0.351	0.00	(-0.10, 0.09)	0.982
Fat / 10g												
< 1 hour before PVT	4.48	(0.30, 8.67)	0.036	9.00	(-0.21, 18.20)	0.055	-0.03	(-0.05, 0.00)	0.026	-0.05	(-0.11, 0.00)	0.074
1-2 hours before PVT	-5.25	(-9.54, -0.97)	0.016	-2.43	(-12.9, 8.04)	0.648	0.04	(0.02, 0.07)	0.001	0.03	(-0.03, 0.09)	0.348
2-3 hours before PVT	1.76	(-4.92, 8.43)	0.605	-15.31	(-31.16, 0.54)	0.058	0.00	(-0.04, 0.04)	0.922	0.08	(-0.02, 0.18)	0.098
Carbohydrates / 10g												
< 1 hour before PVT	0.74	(-0.84, 2.32)	0.358	-3.89	(-7.85, 0.06)	0.054	-0.01	(-0.02, 0.00)	0.266	0.02	(0.00, 0.05)	0.064
1-2 hours before PVT	-1.87	(-3.60, -0.15)	0.034	1.88	(-2.79, 6.54)	0.429	0.02	(0.01, 0.03)	0.004	-0.01	(-0.04, 0.02)	0.412
2-3 hours before PVT	2.67	(0.36, 4.98)	0.024	6.04	(-0.35, 12.43)	0.064	-0.01	(-0.03, 0.00)	0.095	-0.03	(-0.07, 0.01)	0.129
- Mono- and disaccharides/10g												
< 1 hour before PVT	-0.74	(-3.73, 2.25)	0.627	-3.83	(-7.53, -0.13)	0.042	0.00	(-0.01, 0.02)	0.724	0.02	(0.00, 0.05)	0.043
1-2 hours before PVT	-1.52	(-5.17, 2.12)	0.411	1.80	(-2.44, 6.04)	0.405	0.02	(0.00, 0.04)	0.099	-0.01	(-0.03, 0.02)	0.652
2-3 hours before PVT	4.32	(0.39, 8.25)	0.031	4.08	(-1.88, 10.04)	0.179	-0.02	(-0.04, 0.00)	0.117	-0.02	(-0.05, 0.02)	0.318
- Polysaccharides / 10g												
< 1 hour before PVT	2.15	(-0.21, 4.51)	0.074	0.83	(-4.12, 5.78)	0.742	-0.01	(-0.03, 0.00)	0.048	-0.01	(-0.04, 0.02)	0.681
1-2 hours before PVT	-3.06	(-5.47, -0.66)	0.013	-0.36	(-5.89, 5.17)	0.898	0.02	(0.01, 0.04)	0.002	-0.01	(-0.04, 0.03)	0.669
2-3 hours before PVT	4.08	(-0.24, 8.39)	0.064	3.19	(-6.67, 13.04)	0.525	-0.02	(-0.04, 0.01)	0.169	-0.02	(-0.08, 0.04)	0.504
Dietary fibres / 10g												
< 1 hour before PVT	9.29	(-3.87, 22.45)	0.165	-10.97	(-36.83, 14.9)	0.405	-0.07	(-0.15, 0.01)	0.077	0.03	(-0.12, 0.19)	0.662
1-2 hours before PVT	-11.04	(-24.78, 2.69)	0.114	14.72	(-11.59, 41.04)	0.271	0.09	(0.01, 0.18)	0.028	-0.11	(-0.26, 0.05)	0.174
2-3 hours before PVT	14.56	(-8.65, 37.76)	0.218	-13.53	(-53.85, 26.79)	0.509	-0.07	(-0.21, 0.08)	0.367	90.0	(-0.19, 0.30)	0.658

* Basic models are adjusted for age and gender. † Models are additional adjusted for BMI, start time PVT, and energy and caffeine intake of the relevant time interval.

Table 4.3 Continued.

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		Ž		apses ((80)			•	Jan III - Lei	פווו סכם	b	
		Basic model	*	`	Adjusted model†	ŧ		Basic model*		⋖	Adjusted model†	±
	2	95% CI	P value	€	95% CI	P value	2	95% CI	P value	€	95% CI	P value
Protein / 10g												
< 1 hour before PVT	0.02	(-0.02, 0.06)	0.257	-0.02	(-0.12, 0.09)	0.753	-0.01	(-0.11, 0.10)	0.878	-0.04	(-0.31, 0.23)	0.778
1-2 hours before PVT	-0.02	(-0.06, 0.02)	0.303	0.01	(-0.10, 0.12)	0.816	0.01	(-0.10, 0.13)	0.807	-0.08	(-0.39, 0.23)	0.600
2-3 hours before PVT	0.01	(-0.06, 0.08)	0.753	-0.03	(-0.17, 0.11)	0.697	-0.01	(-0.21, 0.18)	0.900	-0.26	(-0.66, 0.14)	0.201
Fat / 10g												
< 1 hour before PVT	0.03	(-0.01, 0.07)	0.151	0.05	(-0.04, 0.13)	0.271	-0.01	(-0.12, 0.09)	0.794	-0.02	(-0.26, 0.23)	0.887
1-2 hours before PVT	-0.02	(-0.06, 0.01)	0.212	-0.03	(-0.12, 0.07)	0.561	90.0	(-0.05, 0.17)	0.293	0.20	(-0.08, 0.47)	0.166
2-3 hours before PVT	-0.02	(-0.08, 0.04)	0.607	-0.16	(-0.31, -0.02)	0.029	0.03	(-0.13, 0.18)	0.746	-0.03	(-0.44, 0.38)	0.884
Carbohydrates / 10g												
< 1 hour before PVT	0.01	(-0.01, 0.02)	0.317	-0.02	(-0.05, 0.02)	0.358	0.00	(-0.04, 0.04)	0.905	0.01	(-0.09, 0.12)	0.847
1-2 hours before PVT	-0.01	(-0.02, 0.01)	0.300	0.01	(-0.03, 0.05)	0.659	0.00	(-0.04, 0.05)	0.967	-0.07	(-0.19, 0.06)	0.292
2-3 hours before PVT	0.02	(0.00, 0.04)	0.119	90.0	(0.01, 0.12)	0.031	0.03	(-0.03, 0.08)	0.350	90.0	(-0.11, 0.23)	0.491
- Mono- and disaccharides/10g												
< 1 hour before PVT	0.00	(-0.03, 0.03)	0.930	-0.02	(-0.06, 0.01)	0.197	0.01	(-0.06, 0.09)	0.769	0.02	(-0.08, 0.12)	0.688
1-2 hours before PVT	-0.01	(-0.05, 0.02)	0.497	0.00	(-0.04, 0.04)	0.939	0.00	(-0.10, 0.09)	0.917	-0.03	(-0.14, 0.08)	0.593
2-3 hours before PVT	0.02	(-0.01, 0.06)	0.214	0.02	(-0.03, 0.07)	0.457	0.05	(-0.05, 0.14)	0.333	0.05	(-0.11, 0.20)	0.552
- Polysaccharides / 10g												
< 1 hour before PVT	0.02	(0.00, 0.04)	0.118	0.01	(-0.03, 0.06)	0.565	0.00	(-0.06, 0.06)	0.963	-0.02	(-0.14, 0.11)	0.778
1-2 hours before PVT	-0.01	(-0.03, 0.01)	0.314	0.01	(-0.04, 0.06)	0.651	0.00	(-0.06, 0.07)	0.890	-0.04	(-0.19, 0.11)	0.601
2-3 hours before PVT	0.03	(-0.01, 0.07)	0.125	0.09	(0.00, 0.18)	0.043	0.04	(-0.07, 0.14)	0.495	0.02	(-0.23, 0.26)	0.901
Dietary fibres / 10g												
< 1 hour before PVT	0.08	(-0.04, 0.20)	0.183	-0.05	(-0.28, 0.18)	0.656	0.08	(-0.25, 0.41)	0.631	0.21	(-0.45, 0.88)	0.522
1-2 hours before PVT	-0.04	(-0.16, 0.09)	0.536	0.08	(-0.16, 0.32)	0.501	-0.05	(-0.41, 0.30)	0.775	-0.66	(-1.38, 0.05)	0.068
2-3 hours before PVT	0.08	(-0.13, 0.29)	0.432	0.00	(-0.37, 0.36)	0.994	0.10	(-0.48, 0.67)	0.739	-0.35	(-1.32, 0.61)	0.473
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* Basic models are adjusted for age and gender. † Models are additional adjusted for BMI, start time PVT, and energy and caffeine intake of the relevant time interval.

Table 4.4. Association between covariates and objective and subjective alertness in nurses (n=127) during the night shift. All models are controlled for dependence amongst the repeated measurements for each nurse and for cluster effects within the three hospitals.

		Median RT			Reciprocal RT	Ļ.	Num	Number of Lapses (Log)	(Loa)		SPS	
	8	95% CI	P value	2	95% CI	P value	2	R 95% CI	P value	≥	95% CI	P value
Age, years*	0.19	0.19 (-0.54, 0.92)	0.607	-0.00	-0.00 (-0.01, 0.00)	0.853	-0.00	-0.00 (-0.01, 0.00)	0.588	-0.01	-0.01 (-0.02, 0.00)	0.019
Gender, male*	-11.54	-11.54 (-42.73, 19.65)	0.465	0.08	0.08 (-0.12, 0.28)	0.410	-0.21	-0.21 (-0.47, 0.04)	0.099	0.01	0.01 (-0.46, 0.47)	0.977
BMI, kg/m2*	0.37	0.37 (-1.68, 2.43)	0.721	00.00	0.00 (-0.02, 0.01)	0.594	0.00	(-0.02, 0.02)	0.882	-0.01	-0.01 (-0.04, 0.02)	0.368
Start time PVT, min*		0.16 (0.08, 0.24)	<0.001	-0.00	-0.00 (-0.00, -0.00)	<0.001	0.00	(0.00, 0.00)	<0.001	0.00	0.00 (0.00, 0.01)	<0.001
Energy / 100 kcal†												
< 1 hour before PVT	1.25	1.25 (-0.66, 3.16)	0.199	-0.01	-0.01 (-0.02, 0.00)	0.137	0.01	0.01 (-0.01, 0.03)	0.173	0.00	0.00 (-0.05, 0.05)	0.879
1-2 hours before PVT	-4.01	(-5.98, -2.05)	<0.001	0.03	(0.02, 0.04)	<0.001	-0.02	(-0.04, 0.00)	0.015	-0.02	-0.02 (-0.07, 0.04)	0.564
2-3 hours before PVT	1.13	(-1.86, 4.11)	0.457	-0.00	(-0.02, 0.02)	0.735	0.00	(-0.02, 0.03)	0.859	0.00	0.00 (-0.07, 0.07)	0.971
Caffeine / 10 mg†												
< 1 hour before PVT	1.38	1.38 (0.02, 2.74)	0.047	-0.01	-0.01 (-0.02, 0.00)	0.036	0.00	0.00 (-0.01, 0.02)	0.526	0.01	0.01 (-0.03, 0.04)	0.631
1-2 hours before PVT		1.23 (-0.20, 2.66)	0.091	-0.01	-0.01 (-0.02, 0.00)	0.059	0.01	0.01 (0.00, 0.02)	0.206	0.03	0.03 (-0.01, 0.06)	0.143
2-3 hours before PVT	1.17	1.17 (-0.14, 2.48)	0.080	-0.01	-0.01 (-0.01, 0.00)	0.165	0.00	0.00 (-0.01, 0.01)	0.782	0.00	0.00 (-0.03, 0.03)	0.930
* Models are adjusted for age and gender. † Models are additional adjusted for BMI, start time PVT and energy or caffeine intake of the relevant time interval	ed for ag	e and gender.	· Models ar	e additions	adjusted for I	BMI, start tim	ıe PVT ar	id energy or ca	ffeine intake	of the re	levant time inte	rval.

Studies that were conducted during the day around breakfast and lunchtime do support the time dependent associations of fat and carbohydrate intake with objective alertness levels. Our finding of a time dependent association between carbohydrate intake and objective alertness is in line with the findings from a review of Dye et al. (2000) [14]. They also suggest that carbohydrate intake in general seems to deteriorate attention and reaction time but that it depends on the type of carbohydrates, time of the day and ratio of carbohydrates to protein [14]. For example, glucose intake was associated with improved short-term and delayed memory immediately after a meal but was also associated with impaired memory after 60 minutes [11, 14], Indeed, we also observed a positive association with objective alertness and the intake of mono- and disaccharides 1 hour before the PVT but not 2 to 3 hours before the PVT. Moreover. absolute intake of carbohydrates 2 to 3 hours before the PVT was associated with borderline significant slower reaction times and significantly more lapses. This association could be driven by the polysaccharide intake as a higher polysaccharide intake was also associated with more lapses. Lloyd et al (1994) showed that a highcarbohydrate low-fat meal resulted in slower reaction times 90 and 150 minutes after ingestion compared to a medium-carbohydrate medium-fat meal [25]. This also supports the idea that a higher carbohydrate consumption has a negative impact on alertness levels after about two hours, as found in our current study. On the other hand it could also be that higher fat intake resulted in better reaction times. Fischer et al (2001) showed that overall cognitive performance was best after a pure fat meal. compared to meals that consisted of solely protein or carbohydrates [26]. However. this finding was not replicated in a study of Jones et al (2012) [11], and -again-timing could be a reason for these inconclusive results. Jones et al [11] tested cognitive performance 15 minutes and 60 minutes after the test meal, whereas Fischer et al tested cognitive performance 60, 120 and 180 minutes after the test meal. Although Jones et al. observed some beneficial effects of fat intake compared to placebo on the cognitive domain processing 15 minutes after the test meal, this beneficial effect was not maintained after 60 minutes, nor was it more beneficial compared to the protein or carbohydrate intake. They suggested that they possibly missed the time frame to detect beneficial effects of fat intake [11].

Another point of attention is the difficulty and by this the domain of cognitive performance that was tested; each domain can be more or less sensitive to manipulations of the intake of one specific macronutrient or macronutrient composition

in general [10, 14]. The effect of macronutrients, and especially glucose, are highest for memory processes [10, 14]. The exact mechanisms behind it have not been elucidated, but it has been shown that a rise in glucose levels – glucose is the primary source of energy for the brain - is associated with better performance on memory and reaction time tasks [10]. Also, tasks that require a greater or longer cognitive demand are possibly more sensitive to macronutrient manipulations [10]. We here assessed the cognitive domain sustained attention, which requires a longer cognitive demand and is therefore suggested to be more affected by macronutrient manipulations compared to most other cognitive domains [10].

Taking the above into account we carefully conclude that time is an important factor when measuring associations between fat and carbohydrate intake and objective alertness levels. Carbohydrates, especially the mono and disaccharides, are associated with better objective alertness levels directly after a meal but are associated with lower levels of objective alertness after two hours, probably due to the presence of polysaccharides. The association between fat and objective alertness is less clear cut, especially directly after the meal. Two hours after intake, fat may be associated with better objective alertness levels, but this warrants further investigations.

In contrast to previous literature, we did not find an association between protein intake and alertness levels, nor did we observe a difference in timing. Even though there was an inverse association between protein intake 1 to 2 hours before the PVT and objective alertness levels after adjustment for age and gender, this association disappeared after additional adjustment for BMI, start time of PVT, and energy and caffeine intake. Some studies found a positive effect of protein intake on cognitive performance. These studies focused more on single macronutrients in a meal or at protein rich meals relatively to carbohydrate rich meals [11, 13, 26], whereas we examined absolute protein intake as part of a mixed meal. The enhancing effect of protein may be less pronounced in a mixed meal or absolute protein intake was too low to find an association with alertness. Furthermore, protein intake may still be associated with better cognitive performance in comparison to carbohydrate intake, but less pronounced as fat intake. Fischer et al (2002), for example, suggested that a balanced or protein rich-meal will result in better overall performance than a medium or high carbohydrate-rich meal. This may be due to less variation in blood glucose levels, as high variation in the glucose levels could impair cognitive performance [13].

Another explanation could be that protein intake has the least negative effects on alertness levels compared to fat and carbohydrate intake.

Similar to protein intake, we did not find associations between fat and carbohydrate intake 1 to 2 hours before the PVT and objective alertness level. On the other hand, a higher (overall) energy intake 1 to 2 hours prior to the PVT was associated with better objective alertness levels. This may suggest that, to improve alertness 1 to 2 hours after consumption, it is not so much the macronutrient composition of the meal but rather the consumption of food as such which is most relevant. A positive association between energy intake, independent of the macronutrient composition, and cognitive performance is also suggested by the review of Dye [14]. However, the association between energy intake and cognitive performance was not linear. Large meals in terms of energy intake may deteriorate alertness levels even further during the night shift, while smaller meals may not [8, 27]. In our study energy intake during the different time frames was only small and might thus explain why we found a positive association with alertness levels.

We did not find associations of macronutrient intake and subjective alertness levels. Other studies are also inconclusive about these associations. In the study of Paz and Berry (1997) participants' regular diet seemed to result in better subjective alertness levels than a high protein and high carbohydrate diet, although this was not statistically significant [24]. In the study of Nehme et al (2014) carbohydrates seemed to result in lower subjective alertness levels, but only in overweight participants [12]. Similar to objective alertness levels, subjective alertness levels could be associated with energy intake independently. Landström et al. (2001) found a direct positive effect of consuming food on subjective feelings of alertness in sleep deprived persons [28]. However, these effects disappeared after half an hour [28], a time frame that we did not assess and which could explain why we did not see these effects. Moreover, all the meals provided in the study of Landström et al. contained carbohydrates to a greater or lesser extent [28]. Altogether, it remains uncertain whether there is an association between macronutrient intake and subjective alertness levels. Moreover, our results indicated a negligible correlation between subjective and objective alertness [29]. This weak correlation is not unexpected, as subjective alertness might be overestimated especially during the night [15]. Therefore, better and more sensitive

methods are needed to assess subjective alertness, specifically over a longer time period.

In our models, caffeine intake was associated with median reaction time (RT) and reciprocal reaction time (1/RT), but not the way we expected. More caffeine was associated with a higher median RT and lower 1/RT, and thus with poorer objective alertness levels. In addition, the number of lapses and subjective feeling of alertness were not associated with caffeine intake. Explanations could be that the intake of caffeine was too low to improve alertness or that individuals that were the most tired had the most caffeine (i.e. reverse causation).

We observed that the time at which the PVT and SPS was performed was associated with both subjective and objective alertness. The PVT was performed between 2:00 AM and 5:00 AM and nurses were more tired later in the night shift. Grant et al (2017) also found a significant effect of time of day on number of lapses and median RT, where the highest number of lapses and median RTs were seen at 04:00 AM [30]. This effect of time on PVT performance was also seen in other studies with shorter versions of the PVT [31, 32]. Ganesan et al (2019) found an increase in number of lapses and RT over time during the night shift measured by a 5-min PVT [31]. Gupta et al (2016) also found an increase in number of lapses and RT at 03:00h compared to 20:30h measured by a 3-min PVT in shift workers [32]. This deterioration in alertness, independent of food intake, is not only observed during the night but also around lunch time [14, 33]. It cannot be prevented, but food intake can strengthen or mitigate it. Thus, besides the time interval between consumption and testing, it is also important at what time of day alertness levels are measured.

This study is to our knowledge the first study that investigated the association between macronutrient composition together with meal timing, and (sustained) alertness in nurses in a real life night shift setting. Despite that under-reporting was present in the current study, the nurses were very motivated to take part in this study and were well instructed to successfully complete the 24-hour recalls. Also, removal of identified poor reports of energy intake in some nurses did not alter the associations that we found. Therefore, we had reliable information not only about what they aet, but also about when and how often they ate before, during and after a night shift, and how this was

associated with alertness [34]. Another strength of this study is our relatively large sample size compared to other studies. This allowed us to investigate specific time frames and to deal with the large variation in dietary intake. Lastly, this study showed the value that research in this field can have for night shift workers. Besides the increased risks of (medical) errors or having work-related accidents during the night shifts compared to day shifts [5], this study showed that nurses also reported fatigue related road traffic accidents after their night shift, which is in line with earlier findings [35, 36]. These results supports the importance of proper nutrition strategies for night shift workers to promote safety during and after the night shift.

The observational design of this real life study comes with some limitations. One limitation related to this observational design is that we cannot draw conclusions about causal relationships between macronutrient intake and alertness levels. Moreover, we have to interpret the observed associations with caution, as the reported regression coefficients are rather small. In addition, some participants consumed foods up to 1 hour as well as 2 to 3 hours before the PVT. We did not adjust for food consumption up to 1 hour before the PVT, which means this could have influenced the associations between macronutrient intake 2 to 3 hours before the PVT and alertness. Another limitation is the uncontrolled environment in which nurses performed the PVT and where nurses could be distracted by colleagues or patients. However, they could restart the PVT when necessary, and therefore we assume this has had little impact on the results. Moreover, other confounders that we did not collect such as menstrual cycle and napping, sleep duration, and sleep quality prior to the night shift could have influenced alertness levels and could have resulted in more power when taken into account. Although we observed that half of the nurses took a nap before the night shift, we do not know when and how long they napped. It is presumed that in a more controlled setting the results could lead to distinct associations and more clinical relevant results.

Lastly, the study sample consisted almost exclusively of female nurses. Results remained the same when men were excluded, but the number of men was too small to study them separately. Therefore, it remains speculative whether these associations also holds true in a (larger) male sample. Moreover, participating nurses might have been more interested in the role of nutrition in health, well-being and safety than other

nurses or other night shift professionals, and could therefore be health oriented. In a more unhealthy study sample, there may be more variation in macronutrient intake and this could potentially result in more distinct associations with alertness. The type of work might have also affected alertness levels; work that is more monotonous and less distracting can lead to lower alertness levels and therefore be more susceptible to changes in macronutrient composition. Therefore, the results of this study cannot be generalized to other night shift working professions. It would be interesting to see how macronutrient composition is associated with alertness levels in other night shift working professions, especially in those who have an unhealthier lifestyle and relative higher BMI, such as production employees. It is suggested that a higher BMI could mediate the effect of carbohydrates on sleepiness [12].

In conclusion, our results contribute to understanding the association between macronutrient intake, as part of a mixed meal, and alertness levels. It seems plausible that conflicting results from previous studies are due to the time between macronutrient intake and alertness testing. Fat intake was associated with lower alertness levels shortly after consumption, but could be associated with better alertness levels 2 to 3 hours after intake. The opposite seems plausible for carbohydrate intake. Protein consumption did not appear to have a distinct association with alertness levels or appeared to have the least negative impact on alertness levels compared to fat and carbohydrate consumption. Based on these results we would advise a small macronutrient-balanced meal or a high-protein meal during the night shift to maintain and achieve the most optimal alertness levels. However, it is not yet known which macronutrient composition would be optimal. This should be tested in an intervention study, in which meal timing, meal frequency, and energy intake are included.

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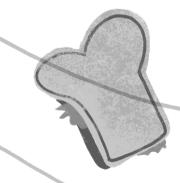
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5

The association between eating frequency with alertness and gastrointestinal complaints in nurses during the night shift

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Abstract

We investigated the association of the number of eating occasions and energy intake with alertness and gastrointestinal complaints in nurses during their night shift. During this observational study we collected data on anthropometrics and demographics. eating frequency, energy intake, alertness and gastrointestinal complaints in 118 healthy female nurses, aged 20 to 61 years. Nurses completed an alertness test (Psychomotor Vigilance Task) during the night shift and a 24-hour dietary recall and a questionnaire about gastrointestinal complaints after the night shift. This was repeated three times, always on the first night shift in a night shift serie. The number of eating occasions during the night shift was negatively associated with reaction times (β=-4.81 ms. 95% CI: -9.14 - -0.43, p=0.030), and number of lapses (β =-0.04, 95% CI: -0.07 --0.00, p=0.030). However, the number of eating occasions was not associated with subjective alertness and gastrointestinal complaints. Energy intake during the night shift was not associated with objective or subjective alertness nor with gastrointestinal complaints. These associations were independent of caffeine intake, age, body mass index and dependence among the repeated measurements. This study showed that eating frequency was positively associated with objectively measured alertness levels in female nurses during the night shift. The results need to be confirmed in an intervention study, where also timing, size and composition of the meal will be taken into account. In practice, optimizing nutritional guidelines on these aspects could lead to faster responses, less (medical) errors and a better well-being of night shift workers.

Introduction

Hospitals provide healthcare 24 hours per day and 7 days a week. In order to facilitate continuous healthcare, health care workers have to work outside the conventional working hours [1], and a part of them work in night shifts. In the Netherlands, about 26 percent of the health care workers is regularly working the night shift [2]. However, working the night shift is associated with increased health and safety risks and a reduced well-being [3-6].

For instance, night shift workers have a 30 percent higher risk of making (medical) errors or having accidents than day shift workers [7-9]. This is probably because of a mismatch with the biological clock of workers during the night shift [4]. The biological clock modulates physiological processes in the human body as a function of time, and is characterized by activity during the day, and inactivity during the night, a circadian rhythm. This is also reflected in the alertness levels, which are at lowest between 2:00 and 6:00 h in the early morning [10, 11] and could result in shift work-related fatigue [8]. Especially tasks that require a high cognitive load or sustained attention are more prone to errors due to these lowered alertness levels.[12]. Optimizing alertness levels is therefore crucial in health care, because patient safety could be compromised [13].

Moreover, cognitive performance appears to be sensitive to food intake, but also depends on the time of the day.[14-18]. Eating at night may further deteriorate the already low alertness levels [11, 19]. However, not eating at night is associated with increased hunger and cravings for food around the circadian nadir [11]. It is suggested that a small snack could ensure good alertness levels and reduce hunger during the night shift [11].

Also the digestive system follows a circadian rhythm. At night the digestive system is in a resting state and metabolic processes such as stomach and intestinal peristalsis, production of gastric juices and insulin secretion are diminished compared to daytime [20]. When working the night shift, workers redistribute their food intake from day to night [21, 22], while total energy intake remains the same [23]. In addition, night shift workers tend to snack more frequently instead of eating a full meal [22]. As the digestive system is in a relative resting state, it is not surprising that shift workers

experience gastro-intestinal complaints (e.g. abdominal pain, diarrhoea and heartburn) during the night [11, 24, 25].

Until now it is not clear what the best advice for night shift workers is with respect to eating frequency and energy intake to optimize cognitive performance and reduce gastrointestinal complaints. In this study we investigated the association of the number of eating occasions and energy intake with alertness levels and gastrointestinal complaints in nurses during the night shift. The results of this study could be used to develop nutrition intervention strategies and inform dietary guidelines that can be applied as a vital part of occupational health and safety management programs in shift work.

Methods

Participants

Nurses working the night shift were recruited in three hospitals located in the surrounding of Wageningen, the Netherlands. Nurses were invited to participate via email and advertisements posted at the intranet site for employees of the concerning hospital. To obtain a homogenous study population, nurses were included in the study when they were working the night shift for at least 6 months, were not using drugs that could cause or reduce sleep problems, were not using daylight lamps on the workplace during the night shift, were eating according to a Dutch eating pattern (2 cold meals and 1 hot meal) and were not donating blood one week before and during the data collection period as donating blood could cause fatigue [26]. In total, we screened and included 164 nurses, aged 18 to 61 year, of whom 24 dropped out of the study before data on dietary intake was collected. We additionally excluded 11 male nurses, and 8 smokers and 3 nurses with missing data on smoking from the data analysis, as they formed a minority of the study population and could affect the study results. Male nurses, for example, had a different eating pattern than female nurses, and smokers were exposed to fresh air during the night shift during their cigarette breaks which could have affected the PVT results. Sample size calculations were performed on the parameter dietary intake in order to obtain a reliable estimate of the usual dietary intake, where energy and all macro- and micro nutrients were covered. It allowed us to detect differences among dietary intake and to perform subgroup analysis. All nurses gave written consent before the start of the study.

Study design

This observational study was conducted between April 2015 and July 2018. At the start of the data collection period, nurses had their height and body weight measured, and they filled out a demographic questionnaire. Thereafter, based on night shift timetables, measurements in nurses were scheduled and nurses were asked to complete an alertness test once between 2:00 h and 5:00 h during the night shift. At 17:00 h the same day, nurses were invited via email to complete a 24-hour dietary recall and a questionnaire including questions about quality and duration of day sleep, and gastrointestinal complaints during that night shift. We always measured the first night shift in a serie of night shifts, and this was repeated over three series of night shifts with at least one month in between. A night shift serie is defined as a row of consecutive night shifts. The study was approved by the Medical Ethical Committee of Wageningen University and Research (ABR: NL54414.081.15) and was conducted according to the principles of the Declaration of Helsinki.

Anthropometrics and demographics

Height was measured without shoes using a stadiometer to the nearest 0.5 cm. Body weight was measured without shoes to the nearest 0.5 kg using analogue, or to the nearest 0.1 kg using digital weighing scales, depending on the hospital. Height and body weight were used to calculate body mass index (BMI) in kg/m2. The demographic questionnaire included questions about e.g. education, smoking, and working hours.

Dietary intake

Dietary intake was assessed by three 24-hour dietary recalls. Each 24-hour dietary recall was completed on the day after the first night shift. The 24-hour dietary recalls were self-administered via Compleat, a web-based program. Compleat is based on a validated technique to increase the accuracy of dietary recalls [27], and includes foods used in a Dutch food pattern [28]. Portion sizes of foods or recipes were reported by using household measures, standard portion sizes, or weights in grams. Nurses were asked to record all the foods and drinks they consumed during 24 hours; from the evening meal prior to the night shift until the evening meal after the night shift. They

were also asked to write down the time of day when each food or drink was consumed. All foods and drinks reported at one moment in time were considered as the intake of one eating occasion. An eating occasion was defined as a new eating occasion if it was at least 15 minutes apart from the previous one [29]. For the eating occasions count, we excluded all eating occasions where only drinks were consumed to avoid over-estimation of the total number of eating occasions [30]. Average daily energy intake per night shift and average energy intake per eating occasion were calculated by first multiplying the frequency of each food or drink by portion size and energy content using the 2013 Dutch Food Composition Table [31][84] Thereafter, we calculated energy intake per eating occasion, per night shift and total daily energy intake by adding up the energy intake of each food and drink. Drinks were included in the caffeine and energy intake calculations. All intake reported between the start and end times of the night shift was classified as consumption during the night shift.

Objective and subjective alertness

Objective alertness was assessed by the Psycho Vigilance Task (PVT). The PVT is a validated 10-minute visual reaction time task that evaluates sustained attention [10]. This task was carried out on a desktop between 2:00 h and 5:00 h during the night shift. Nurses were asked to respond to the appearance of a visual stimulus, a white circle on a black screen, by pressing the space bar as quickly as possible. The visual stimulus appeared every 2 to 10 seconds for 10 minutes at a fixed point on the screen. When nurses were interrupted while performing the PVT, either by a patient or a colleague, they were asked to take the PVT again. For each completed PVT, we determined the median reaction time (RT; ms), mean reciprocal response time (1/RT), and number of lapses (RT > 500 ms). As the number of lapses were not normally distributed we used log transformation for the number of lapses and added 1 lapse to compensate for the nurses that had 0 lapses (log(number of lapses+1)).

Subjective alertness was assessed by the 7-point Samn-Perelli Scale (SPS). Nurses were asked to complete the SPS before the start of the PVT. The SPS asks the level of fatigue at that moment. The answer scores range from 1 ("fully alert, wide awake") to 7 ("completely exhausted, unable to function effectively") [32].

Gastrointestinal complaints

Gastrointestinal complaints were assessed using a 5 item self-rating questionnaire. Each item was scored using a 5 point Likert-type rating scale. The score of each item was summed up to get a total gastrointestinal complaint score (5 items; α = 0.842). Intestinal complaints include gastric pain, diarrhoea/constipation, growling intestines, heartburn and bloating. The answer scores ranged from 1 ("completely disagree") to 5 ("completely agree").

Statistical Analysis

All analyses were performed in SPSS statistics 25. P-values of <0.05 were considered statistically significant. Raw data were checked for quality (outliers, omissions) and normality. Data are presented in mean ± SD. in n (%) or as median and interquartile range in case of skewness. Differences in subjective and objective alertness over the three non-consecutive night shifts were assessed by a Wilcoxon rank test. Pearson correlations were used to investigate the correlation between subjective alertness and reciprocal reaction time and log transformed number of lapses. To analyse the association between the number of eating occasions (= eating frequency) or energy intake with alertness during the night shift, we used linear mixed models with alertness as dependent variable (objective and subjective measures separately) and additionally adjusting for eating frequency or total energy intake, respectively, in kcal during the night shift, and for caffeine, age, and BMI. We also controlled for dependence amongst the repeated measurements for each nurse and controlled for cluster effects within the three hospitals. To analyse the association between the number of eating occasions or energy intake during the night shift and gastrointestinal complaints we used similar linear mixed models with total score for gastrointestinal complaints or the separate intestinal complaints as dependent variable and adjusted for the same variables. When outliers were present, we performed the analysis with and without the outliers. If an outlier did not result in different associations and conclusions, we kept the outlier in the analysis.

Results

Participant characteristics

About half (55.1%) of the nurses were classified as having normal body weight and 44.0% as being overweight or obese (**Table 5.1**). Body weight remained stable throughout the data collection period. The start time of the night shift was between 22:00 h and 23:15 h and on average the night shift started at $22:54 \pm 0:23$. The end time of the night shift was between 7:00 h and 8:30 h and on average ended at $7:26 \pm 0:17$. Nurses worked on average 2.6 ± 2.0 night shifts series per month and 2.6 ± 1.0 night shifts per series. This means that nurses worked on average 6.4 ± 5.0 night shifts each month. This number differed significantly between the three hospitals. Anthropometric and demographic data did not differ significantly between the hospitals.

Table 1. Anthropometrics and demographics of female night shift working nurses (n=118) in mean ± SD, median (IQR) or n (%).

Characteristic	\	/alue
Age, median years (IQR)	44.2	(30.1-51.6)
Body weight, mean kg ±SD	71.9	±12.88
Height, mean cm ±SD	169.3	±5.87
Body Mass Index, mean kg/m ² ±SD	25.0	±4.10
- Underweight (<18 kg/m²), n (%)	1	(0.8)
- Normal (18-25 kg/m²), n (%)	65	(55.1)
 Overweight (25-30 kg/m²), n (%) 	43	(36.4)
- Obese (>30 kg/m²), n (%)	9	(7.6)
Education		
- Intermediate education, n (%)	61	(51.7)
- Higher education, n (%)	55	(46.6)
Married/cohabiting		
- Yes, n (%)	98	(83.1)
Children		
- Yes, n (%)	64	(54.2)
Hours of employment, mean per week ±SD	28.4	±5.71
Night shifts series/month, mean series ±SD	2.6	±1.98
Night shifts/serie, mean nights ±SD	2.6	±0.97
Night shift experience, mean years ±SD	17.5	±11.62

Subjective and objective alertness

The PVT was on average started at $3:09 \pm 0:48$ h. Nurses had a median reaction time of 414.4 [IQR: 382.5-463.1] ms (**Figure 5.1**), a mean reciprocal reaction time of 2.52 ± 0.32 ms and 9.8 [IQR: 4.3-19.4] lapses (**Figure 5.2**) on the PVT during the night shifts.

They scored on average 3.2 ± 0.8 out of a score of 7 on the SPS, which is considered as 'Okay, somewhat fresh' [32]. The subjective and objective alertness levels did not differ significantly between the three study periods. Subjective alertness was not correlated with reciprocal reaction time (r=-0.107, p=0.320) nor number of lapses (r=0.136, p=0.143).

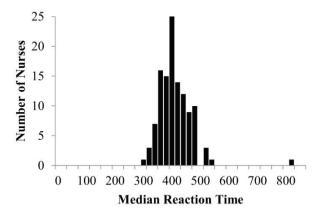


Figure 5.1. Histogram of average median reaction time (ms) of nurses (n=118)

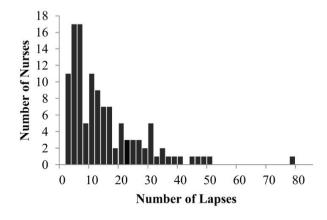


Figure 5.2. Histogram of average number of lapses of nurses (n=118)

Gastrointestinal complaints

Seventy-nine percent (79.0%) of the nurses experienced at least one gastrointestinal complaint during one of the night shifts. The most prevalent gastrointestinal complaints nurses reported were growling intestines and bloating. Growling intestines was experienced during 54.0% of the night shifts and bloating during 45.7% of all night

shifts. Diarrhoea or constipation was experienced during 23.3%, gastric pain during 11.0%, and heartburn during 8.6% of the night shifts. In 22.4% of the cases at least three gastrointestinal complaints were experienced to a greater or lesser extent during the same night shift.

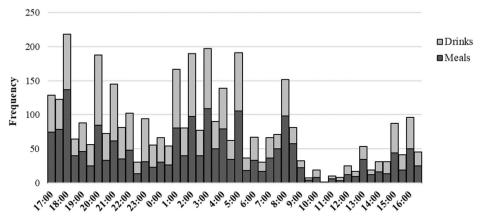


Figure 5.3. Distribution of meals and drinks consumed by nurses (n=118) before, during and after the night shift, measured by three 24-hour dietary recalls

Dietary intake

All included nurses completed at least one 24-hour dietary recall. Seven nurses completed only one 24-hour recall, 14 nurses completed two 24-hour recalls, and 97 nurses completed all three 24-hour recalls. Foods and drinks were consumed throughout the day (**Figure 5.3**). All nurses consumed foods or drinks during the night shift.

The nurses had on average 6.0 (IQR: 5.0-7.3) eating occasions between the evening meal prior to the night shift until the evening meal after the night of which 2.5 (IQR: 2.0-3.0) eating occasions were during the night shift. They consumed on average 1656 ± 450 kcal between the evening meal prior to the night shift until the evening meal after the night, of which 610 (IQR: 455-737) kcal were consumed during the night shift. An eating occasion during the night shift consisted on average of 175 (IQR: 82-343) kcal. The nurses consumed on average 37.3 (IQR: 0.0-100.5) mg caffeine during the night shift. This corresponds to one cup of green or black tea or half a cup of coffee.

Eating frequency, energy intake and alertness

Table 5.2 shows the associations of number of eating occasions and total energy intake during the night shift with objective and subjective alertness. The number of

eating occasions was positively associated with alertness levels. This was shown by the number of eating occasions that was inversely associated with median reaction time (β =-4.81 ms, 95% CI: -9.14 - -0.43, p=0.030), and log transformed number of lapses (β =-0.04, 95% CI: -0.07 - -0.00, p=0.030), and was positively associated with reciprocal reaction time (β =-0.03 1/ms, 95% CI: 0.00 - 0.05, p=0.018). Total energy intake during the night shift was not associated with alertness levels. The number of eating occasions as well as energy intake were not associated with subjective alertness. More caffeine was associated with slower reaction times and deteriorated subjective alertness levels, but not with more lapses. Age was associated with deteriorated subjective alertness levels.

Table 5.2. Association between number of eating occasions and energy intake with objective and subjective alertness in 118 female nurses during the night shift.

	Median ^a /	(IQR)/	Median reaction time (ms)		Rec	Reciprocal reaction time (1/ms)		
	meanb	±SD	ß	95% CI	p-value	ß	95% CI	p-value
Number of EO	2.5a	(2.0 - 3.0)	-4.81	(-9.140.48)	0.030	0.03	(0.00 - 0.05)	0.018
Energy per 100 kcal	609.8ª	(454.6 - 736.5)	1.43	(-0.19 - 3.06)	0.084	-0.01	(-0.01 - 0.00)	0.233
Caffeine per 100 mg	37.3a	(0.0 - 100.5)	8.78	(3.53 - 14.03)	0.001	-0.04	(-0.070.01)	0.004
Age, years	44.2a	(30.1 - 51.6)	0.20	(-0.63 - 1.02)	0.639	0.00	(-0.00 - 0.00)	0.996
BMI, kg/m2	25.0 ^b	±4.1	0.86	(-1.50 - 3.22)	0.472	-0.01	(-0.02 - 0.01)	0.386

EO=eating occasions, ^a Median is provided when data was not normally distributed, ^b Mean is provided when data was normally distributed.

Table 5.2. Continued

	Number of lapses (log)			Samn-Perelli Scale		
	ß	95% CI	p-value	ß	95% CI	p-value
Number of EO	-0.04	(-0.070.00)	0.030	-0.01	(-0.11 - 0.08)	0.779
Energy per 100 kcal	0.00	(-0.01 - 0.02)	0.575	-0.02	(-0.06 - 0.02)	0.291
Caffeine per 100 mg	0.02	(-0.02 - 0.07)	0.354	0.16	(0.04 - 0.29)	0.008
Age, years	0.00	(-0.01 - 0.00)	0.438	-0.01	(-0.02 - 0.00)	0.027
BMI, kg/m2	0.00	(-0.01 - 0.02)	0.681	-0.01	(-0.04 - 0.03)	0.746

Eating frequency, energy intake and gastrointestinal complaints

The number of eating occasions was not associated with the total gastrointestinal complaints score (β =-0.13, 95% CI: -0.51 - 0.25, p=0.493) (**Table 5.3**). However, when looking at the separate gastrointestinal complaints, the number of eating occasions was associated with less heart burn (β =-0.11, 95% CI: -0.19 - -0.02, p=0.017), and not with any of the other single complaints. Total energy intake (per 100 kcal) during the

night shift was not associated with the total gastrointestinal complaints score (β =-0.12, 95% CI: -0.27 - 0.02, p=0.099).

Older age was associated with less total gastrointestinal complaints (β =-0.02, 95% CI: -0.03 - 0.00, p=0.048), i.e. less constipation/diarrhoea and growling intestines. Caffeine use was associated with more heartburn and bloating but not with gastric pain, constipation/diarrhoea or growling intestines.

Table 5.3. Association between number of eating occasions and energy intake with total score of gastrointestinal complaints in 118 female nurses during the night shift.

	Median ^a /	(IQR)/	Gastrointestinal complaints			
	meanb	±SD	ß	95% CI	p-value	
Number of EO	2.5ª	(2.0 - 3.0)	-0.13	(-0.51 - 0.25)	0.493	
Energy per 100 kcal	609.8ª	(454.6 - 736.5)	-0.12	(-0.27 - 0.02)	0.099	
Caffeine per 100 mg	37.3a	(0.0 - 100.5)	0.28	(-0.2 - 0.76)	0.251	
Age, years	44.2a	(30.1 - 51.6)	-0.08	(-0.140.01)	0.019	
BMI, kg/m2	25.0 ^b	±4.1	0.04	(-0.14 - 0.22)	0.678	

EO=eating occasions, ^a Median is provided when data was not normally distributed, ^b Mean is provided when data was normally distributed.

Discussion

This present study examined the association of the number of eating occasions and energy intake with objective and subjective alertness and gastrointestinal complaints in female nurses during the night shift. We showed that more eating occasions during the night shift was associated with faster reaction times and fewer lapses (delayed reaction time > 500 ms). However, the number of eating occasions was not associated with subjective alertness or gastrointestinal complaints. Also, total energy intake during the night shift was not associated with both objective and subjective alertness and gastrointestinal complaints.

To our knowledge this is the first study that investigated the association between the number of eating occasions with objective and subjective alertness and gastrointestinal complaints in nurses during a night shift in a real-life setting. Our finding that more eating occasions during the nightshift was associated with faster reaction times and fewer lapses gives additional insight to the findings of other studies. Earlier studies focused on the difference between eating either a small or large meal or not eating at all [11, 19, 33]. These studies found that eating one large meal resulted in a worsening of objective alertness levels during the circadian nadir [11, 19, 33], and a small snack

resulted in the best objective alertness levels during a sustained driving task [33]. They also suggested that other options, such as eating multiple snacks or eating a snack later during the night shift, could improve alertness levels and should be investigated as hunger feelings are especially present at the end of the night shift. As our study had an observational study design, it allowed us to investigate the number of eating occasions. Although total energy intake during the night shift in our study was comparable with that provided by the large meals in the studies of Grant et al. and Gupta et al. [11, 19, 33], the amount was distributed over several eating occasions. Hence our results support their hypothesis that smaller meals could prevent a deterioration in alertness levels.

Our present study did not find an association between subjective alertness and the number of eating events. Similar results were found in the studies of Grant et al. and Gupta et al. [11, 19, 33, 34]. They did not find differences in subjective alertness of their participants in eating a large meal versus eating no meal during the night [11, 19]. 33, 34]. Interestingly, Gupta et al. (2019) found that eating a small meal, however, led to the best subjective alertness levels [33, 34]. The exact mechanism behind it is not yet clear. Eating at night is used by some night shift workers as one of the strategies to keep alert during the night [23, 35, 36]. It is shown that the immediate effect of consuming food seems to reduce sleepiness [17]. However, this effect seems to disappear after half an hour. This could explain why we, but also Grant et al. and Gupta et al. [11, 33], did not find differences in subjective alertness between a large meal and no meal as we did not investigate immediate effects. However, it does not explain why a small meal would result in the best subjective alertness compared to a large meal during the night shift around 4:00 h. It is suggested that subjective alertness overestimates actual objective measures of alertness [37, 38]. Furthermore, differences found in subjective alertness during sleep deprivation, as happens during a night shift, are expected to be smaller than differences in objective alertness compared to a nonsleep deprived state [38]. This could be another explanation why we did not find explicit differences in subjective alertness when we analysed the association between subjective alertness and the number of eating occasions. In addition, sleep before the nightshift may have influenced subjective alertness and dietary intake. Nurses could have had a poor night's sleep prior to the first night shift or could have taken a nap. Although we observed that half of the nurses took a nap prior to the night shift we do

not know when they took a nap or how they slept the night prior to the first night shift. Although associations between diet and subjective alertness are not evident, it might still be useful to include these measurements. Improving subjective alertness can be seen as a perceivable benefit which consequently could lead to higher motivation to comply with a dietary intervention. Nevertheless, better and more sensitive methods are needed to assess subjective alertness, specifically over a longer time period.

For gastrointestinal complaints we observed an association between the number of eating occasions with heart burn but not with total score of gastrointestinal complaints, which was unexpected. It was hypothesized that more eating occasions would have been associated with relative more gastrointestinal complaints as the digestive system is in a relative resting state during the night. More eating occasions were expected to disrupt this resting state. However, it could be that eating at night result in different types of gastrointestinal complaints compared to not eating at night. In the study of Grant et al. (2017), not eating at night resulted in increased stomach upset, especially around 4:00 h [11]. This was not the case in the eating at night group. On the other hand, eating at night resulted in increased bloating compared to not eating at night [11]. Additionally, a small meal resulted in fewer complaints. As in our study population every nurse consumed some food to a greater or lesser extent, we cannot draw any conclusions on whether not eating is associated with less gastrointestinal complaints compared to eating.

However, we found an association between caffeine use and heart burn and bloating, and an association between age and constipation/diarrhoea and growling intestine. These results suggest that other factors, such as caffeine intake and age, are involved as well. It is suggested that caffeine contributes to the development of gastrointestinal complaints [39], however, there is no clear evidence available in literature. For age it is likely that nurses who experience less gastrointestinal complaints will work the night shift at a later age than nurses with complaints. Moreover, other studies found associations between gastrointestinal complaints and sleep disturbances [40, 41]. However, these studies were cross-sectional and therefore causal relationships could not be assessed. In addition, sleep disturbances could also be related to changed meal times or the other way around and not necessarily directly to the gastrointestinal complaints. Sleep disturbances were not taken into account in the present study.

This present study has several strengths. It has a relatively large sample size and included multiple measurements per nurse, which increases the power. We included nurses from three different hospitals which increases the external validity to other female health professionals. However, these results cannot be generalized to other night shift working populations, because the type of work might affect alertness levels. In addition, other night shift working populations may have different dietary intake patterns that can influence alertness levels as well as the prevalence and extent of gastrointestinal complaints. Also, we only included women in the data analysis because the number of men was rather low and could bias the results. The studies of Grant et al. (2017) and Gupta et al. (2016) included men only, because the menstrual cycle and oral contraceptives of women could influence the results of the PVT [42, 43]. We did not collect data on the phase of the menstrual cycle of the nurses or contraceptives, and therefore could not analyse the influence of hormonal changes.

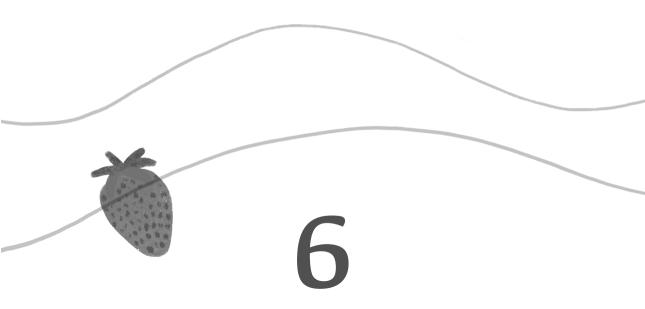
Although the observational study design allowed us to investigate multiple dietary factors that could affect objective and subjective alertness and gastrointestinal complaints, we cannot draw any conclusions about the causal relationships between the found associations in this study. We also have to interpret the results with caution as the found regression coefficients are rather small. Another limitation related to the observational design is that we observed a large variation in the amount of energy per eating occasion that nurses consumed during the night shift. Therefore it was not possible to draw conclusions about the size of an eating occasion in relation to alertness levels. Although the results showed that more eating occasions are associated with better objective alertness, it is hypothesized that the consumption of only one or more small meals during the night shift could further improve alertness levels and probably decrease the experienced gastrointestinal complaints during the night shift [11]. However, this should be further investigated [33, 34].

In conclusion, this study showed that eating frequency is positively associated with objective alertness levels in female nurses during the night shift. The results need to be confirmed in an intervention study, where also the timing, size and composition of the meal is taken into account. In practice, optimizing nutritional guidelines in terms of timing, frequency, size and composition of a meal could lead to faster responses, less (medical) errors and a better well-being of night shift workers.

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The effect of meal frequency and glycaemic load during the night shift on alertness, hunger feelings and gastrointestinal complaints in female health care workers – a two-armed randomized cross-over trial

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Abstract

Background: Nutrition strategies in night shift workers could optimize alertness, and minimize hunger and gastrointestinal complaints, thereby contributing to safety and perceived well-being.

Objective: To investigate the effect of 1 or 3 small meals either with a low or high glycemic load, compared to no meal during the night shift, on alertness levels, hunger feelings, and gastrointestinal complaints during the night shift.

Design: Fifty-one female healthcare workers, aged 18 to 61 years, participated in a 2-armed randomized cross-over design. Each study arm consisted of three intervention periods during the night shift. Participants received either 1 or 3 portions of yoghurt depending on the study arm. For the three interventions, either carbohydrates with a low glycemic load (1LGL or 3LGL) or a high glycemic load (1HGL or 3HGL) were added to the yoghurts, or participants received no yoghurt at all as a control (0NGL). Participants completed a validated brief psychomotor vigilance task (PVT-B) to assess objective alertness, the Samn-Perelli scale to assess subjective alertness and filled out questionnaires about gastrointestinal complaints and hunger feelings.

Results: Participants in the 1LGL (ß -4.6; 95% CI 0.0, 9.3) and 3LGL (ß -3.4; 95% CI 0.0, 6.8) condition had less lapses during the PVT-B than in the 3HGL condition. Participants in all four meal conditions reported less hunger feelings than if consuming no meal. Participants in the 3LGL condition experienced more rumbling intestines than in the 3HGL (ß 1.1; 95% CI 0.4, 1.7) and 0NGL (ß 0.74; 95% CI 0.11, 1.37) condition. **Conclusions**: Three small meals with a low glycemic load during the night shift was the only condition that resulted both in the best alertness levels *and* the least hunger feelings. However, this condition appeared to lead to more gastrointestinal complaints. https://www.trialregister.nl/trial/8715

Introduction

Working hours of health care workers can be scheduled both during the day and at night to ensure continuous health care. In the Netherlands, about 26 percent of health care workers regularly work night shifts [1]. However, working during night hours goes against natural rhythms of sleep during the night and wakefulness during the day, resulting in reduced well-being and increased health and safety risks [2-4].

By working instead of sleeping, night shift workers are susceptible to the effects of sleep deprivation and reduced alertness levels [5]. Especially between 2:00 and 6:00 AM alertness levels are at their lowest, which may lead to more errors, especially in tasks requiring sustained attention [6, 7]. Therefore, it is not surprising that night shift workers are up to a 30 percent higher risk of making (medical) errors or having accidents than day shift workers [5, 8, 9]. Optimizing alertness levels of staff is therefore crucial in healthcare because patient safety could be compromised.

Nutrition interventions could be one of the strategies in optimizing alertness levels. Cognitive performance, including alertness, is shown to be sensitive to food intake. Several aspects of nutrition, such as food and meal composition, timing of intake, and meal size and frequency, can play a role in this. Regarding composition and timing, alucose intake is associated with improved short-term cognitive performance, while carbohydrate intake, in general, is associated with poorer long-term alertness [10-12]. The exact mechanisms of these associations are yet unclear. Small variations in blood glucose levels may be an explanation, because a lower postprandial glycemic response has been shown to be beneficial to cognitive performance [13, 14]. The glycemic response depends on the rate at which carbohydrates are absorbed in the blood represented by the glycemic index (GI) and additionally the amount of carbohydrates represented by the glycemic load (GL) of carbohydrate-containing foods [15]. While the GI only takes into account the quality of the carbohydrate, the GL also includes their quantity. Thus, a lower postprandial glycemic response may be obtained by consuming carbohydrates with a low GI as reflected in a low GL meal. Moreover, not eating at all at night would theoretically result in even more stable blood glucose levels and consequently better alertness levels. However, it may increase hunger and cravings for food [7].

The size of a meal, in terms of energy intake, seems also to be associated with alertness levels and hunger feelings [7, 16-19]. Eating a large meal (~30% of estimated daily energy requirement (EER)) during the night shift resulted in lower alertness during the circadian nadir [7, 16, 17], while a smaller meal (~10% EER) showed the best alertness compared to a large meal or no meal at all [7, 16, 17, 20]. However, it is unknown what the effect is of eating multiple small meals compared to no meal or one small meal [20-22].

Eating several small meals or snacks during the night may have consequences for the digestive system, as this system also follows a natural day and night rhythm [23]. Eating one or multiple meals at night may disrupt the relative resting state of the digestive system at night, and result in gastrointestinal complaints. Night shift workers indeed experience more gastrointestinal complaints than day shift workers [7, 24, 25], which is likely the result of a shift in food intake from day to night including a higher meal frequency [26, 27]. On the other hand, a previous study in which nurses consumed on average 2 to 3 small meals during the night did not find an association between meal frequency and gastrointestinal complaints [28].

Altogether, it is important to investigate which nutrition strategies, in terms of meal frequency, timing, size and composition (including GL), would result in the best alertness levels and the least hunger feelings and gastrointestinal complaints, thus contributing to safety and perceived well-being of health care workers. Therefore, the aim of the present study was to investigate the effect of 1 or 3 small meals, either with a low or high glycemic load, compared to no meal during the night shift on alertness levels, hunger feelings and gastrointestinal complaints. It was expected that eating multiple meals with a low glycemic load will maintain or optimize alertness levels while reducing hunger feelings and having no negative effect on gastrointestinal complaints.

Methods

Participants

Nurses, midwives and other hospital staff with similar night shifts in hospital Gelderse Vallei (ZGV), Ede, received an e-mail from the care managers of their department, and advertisements were posted at the intranet site for employees of ZGV on behalf of the

research team. When participants were interested in the study an information meeting was scheduled.

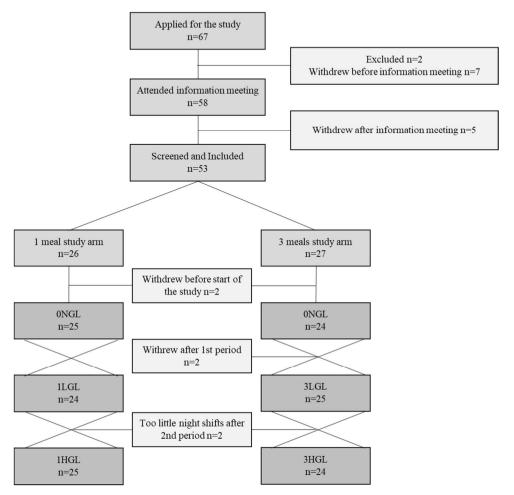


Figure 6.1. Flow diagram of participant randomized two-armed cross-over design of the study.

In total, we screened and included 53 female healthcare workers, aged 18 to 61 year, of whom 2 dropped out before any data was collected, resulting in a final study sample of 51 participants (**Figure 6.1**). Participants were eligible if they were working night shifts for at least 3 months and between 10:00 PM and 8:00 AM, not using daylight lamps on the workplace, not using drugs related to sleep problems, willing to reduce caffeine containing beverages, and not smoking during the night shift (smoking outside

the night shift was allowed). Participants were excluded when they were diagnosed with diabetes mellitus type 1 or 2, hypoglycemia, or lactose or fructose intolerance. Sample size calculations were performed on the main study parameter objective alertness using G*Power, based on the results of two similar studies performed by Gupta (2016) and Grant (2017) who found differences with respect to alertness in mean lapses (delayed responses) [7, 17]. They found a η p2 of 0.29 and based on this the effect size Cohen's f was 0.64. Using this effect size, a probability α =0.05 divided by 3, as we compared 3 meal conditions per study arm, a power (1-ß) of 80%, and a df of 4 ((3-1)*(3-1)) we calculated that a sample size of 44 participants was needed. To account for the 6 meal condition groups, at least 48 participants were needed to detect differences in mean lapses between meal conditions.

Study design

This study comprised of a 2-armed randomized cross-over design. Each study arm consisted of three intervention periods, and each intervention period lasted 3 or 4 days and included 2 or 3 consecutive night shifts depending on the schedule of the participant (**Figure 6.1**). Participants were randomly assigned to one of the two study arms and the order of the three intervention periods.

In the first study arm, participants received a medium sized meal prior to the night shift and one small test meal during the night shift. During one of the three intervention periods this test meal contained carbohydrates with a high glycemic load (1HGL meal condition) and during another intervention period it contained carbohydrates with a low glycemic load (1LGL). During the third intervention period participants were asked to abstain from eating during the night shift as a control, but they received a meal prior to the night shift (0NGL).

In the second study arm participants received no meal before the night shift and three small meals during the nights. Here too, during one of the three intervention periods these test meals contained carbohydrates with a high glycemic load (3HGL) and during another intervention period with a low glycemic load (3LGL). During the third intervention period and similar as in the first study arm, participants were asked to abstain from eating during the night shift as a control (0NGL).

Ethics

The study was approved by the Medical Ethical Committee of Wageningen University and Research and was conducted according to the principles of the Declaration of Helsinki. This study was registered at www.trialregister.nl (Trial NL8715). All participants gave written consent before the start of the study.

Dietary conditions

Nutrition protocol

Participants followed a nutrition protocol during and around the 2 or 3 consecutive night shifts during each intervention period (**Figure 6.2**). The nutrition protocol started with dinner before the first night shift and lasted until breakfast after either the second or third night shift depending on the night shift schedule of the participant. All meals were provided and, except for the test meals, based on the Dutch Dietary Guidelines for a healthy diet [29]. The total daily energy requirement per participant was based on the Estimated Energy Requirement (EER) which was calculated using the Oxford equation to estimate basal metabolic rate [30] and multiplied by the Physical Activity Level (PAL) [31]. The EER was rounded to the nearest 100 kcal. Based on this EER value and participants' preference (small, medium or large eater), participants received meals with a total daily energy amount of one of four energy levels (1900 kcal, 2100 kcal, 2300 kcal or 2500 kcal).

After the evening snack, all participants were provided with meals that contained in total a fixed amount of 582 kcal (2.43 MJ, \sim 10% EER) to consume just before or during the night shift depending on their meal condition. In the no meal condition, the total amount of 582 kcal (2.43 MJ) was consumed in a meal before the night shift around 9:30 PM. In the one meal condition, the total amount of 582 kcal was divided over a meal containing 388 kcal (1.62 MJ) consumed before the night shift, and one test meal (194 kcal, 0.81 MJ) consumed around 2:45 \pm 0:15 AM. In the 3 meal condition, no meal was provided before the night shift and the total amount of 582 kcal was divided over the three test meals, each containing 194 kcal (0.81 MJ). These meals were consumed around 0:15 \pm 0:15, 2:45 \pm 0:15 and 5:15 \pm 0:15 AM.

Participants were allowed to drink ad libitum water, non-caffeinated coffee and herbal tea, and other non-energy drinks. Participants were also permitted to consume a maximum of 2 glasses of carbonated water and 3 cups of coffee or 6 cups of black or

green tea per day, of which only 1 cup of coffee or 2 cups of black or green tea between 7:00 PM and 7:00 AM and no coffee or black or green tea between 3:00 AM and 5:00 AM. Before the start of each intervention period, participants were asked to maintain their habitual lifestyle (e.g. their exercise regime, sleep patterns) but to refrain from any type of extreme physical activity the evenings before the night shift.

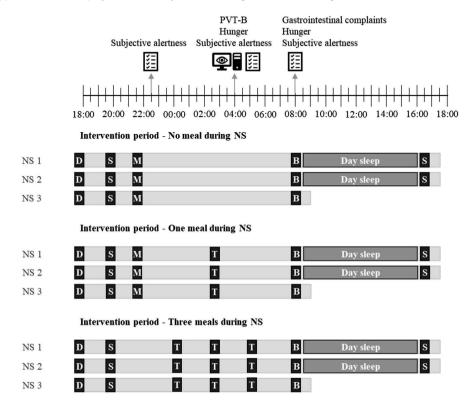


Figure 6.2. Nutrition protocol and the timing of the Brief Psychomotor Vigilance Task (PVT-B) and other questionnaires around the 2-3 night shifts (NS). D: Dinner, S: Snack, M: Meal before NS, T: Test meal, B: Breakfast.

Glycemic load test meals

The selected foods and served portion size were determined based on the amount of energy content (≤10% of EER) and glycemic load of the foods [32]. Thus, the test meal consisted of 225 g semi skimmed yoghurt with either 22.5 g dextrose as a high glycemic load (HGL) or a combination of 10 g β-lactose and 12.5 g fructose as a low glycemic load (LGL). The proportions of 90 weight percent (wt%) yoghurt and 10 wt% sugar were based on standard proportions of sugar added to yogurt [33]. Both the HGL and LGL test meal were comparable in sweetness, taste and texture and similar in

appearance. Thus, participants were blinded regarding the test foods they received. The test meals were prepared by the researchers and packed per served portion (247.5 gram).

For each test meal, we calculated the glycemic load (GL) according to the following formulae [15]:

GL (g) = \sum (carbohydrate content of each food item (g) × Glycemic Index (%)) / 100.

A glycemic load below 10 g is considered as low glycemic load, while a glycemic load above 20 g is considered as high glycemic load [15]. In this study, the glycemic load of the LGL test meals was 8.3 g and the glycemic load of the HGL test meals was 24 g.

Meal compliance

Compliance to the nutrition protocol was checked via assessment of intake by a food record via the mobile app 'Traqq' [34, 35]. Traqq® included an extensive food list, based on the Dutch food composition table [36], and all the provided foods and (test)meals were added to this list. In this way, participants could easily select the right meal or food and report the actual time of consumption. Moreover, drinks were not provided and participants were asked to report all consumed drinks during each intervention period.

Study outcomes

Anthropometrics and demographics.

Before the start of the first intervention period, participants filled out a demographic questionnaire. Height was measured using a stadiometer to the nearest 0.5 cm and body weight was measured using a digital weighing scale to the nearest 0.1 kg, both without shoes. Height and body weight were used to calculate body mass index (BMI) in kg/m2 and together with age to calculate the EER for each participant [30].

Alertness levels

Objective alertness was assessed by the brief Psychomotor Vigilance Test (PVT-B). The PVT-B is a validated 3-minute visual reaction time task that evaluates sustained attention [37]. This task was carried out on a computer during each consecutive night shift between 4:00 AM and 5:00 AM (**Figure 6.2**). The participants were asked to

respond to the appearance of a white circle on a black screen by pressing the spacebar as quickly as possible. The circle appeared every 2 to 6 seconds for 3 minutes at a fixed point on the screen. Each PVT-B provided median rection time (RT), reciprocal reaction time (RRT; ms), and number of lapses (RT >355 ms). For calculating mean RRT, each RT was divided by 1000 and then reciprocally transformed and subsequently averaged for each participant and night shift separately [6]. If the task had to be interrupted because of patient care, the participant was asked to restart the PVT at a later time point but before 5:00 AM.

Subjective alertness was assessed using the 7-point Samn-Perelli Scale (SPS). The SPS asks the level of fatigue at a specific moment. The answer scores range from 1 ("fully alert, wide awake") to 7 ("completely exhausted, unable to function effectively") [38]. Participants were asked to complete the SPS before and after the night shift and before and after the PVT-B.

Hunger feelings

Feelings of hunger and satiety, desire to eat and the amount of desired consumption were rated on a 100 point visual analogue scale (VAS). The questions about hunger feelings were administered via an online questionnaire around 4:00 AM and around 8:00 AM.

Gastrointestinal complaints

Gastrointestinal complaints were assessed using a 6 item self-rating questionnaire and was based on the VAS-IBS [39]. Each item was rated using a 100mm point visual analogue scale (VAS). A score of 0 represented absence of problems and 100 represented very severe problems. Gastrointestinal complaints included abdominal cramps, growling intestines, bloating, flatulence, diarrhea, and constipation. The questions about gastrointestinal complaints were administered via an online questionnaire around 8:00 AM.

Diet quality

The Eetscore Food Frequency Questionnaire (FFQ) [40] was used to get insight in participant's general dietary pattern in terms of diet quality. The Eetscore FFQ is a screener of diet quality, assessing adherence to the fifteen components of the Dutch dietary guidelines [41] using the Dutch Healthy Diet 2015 index (DHD2015-index) [42] and one additional component 'Unhealthy choices' [40]. The fifteen components are

vegetables, fruit, wholegrain products, legumes, nuts, dairy, fish, tea, fats and oils, coffee, red meat, processed meat, sweetened beverages and fruit juices, alcohol and salt. For each component a maximum of 10 points can be allotted, which means complete adherence to the Dutch dietary guideline for that specific component. Together this resulted in a total score ranging between 0 (no adherence) and 160 (complete adherence with the guidelines). The Eetscore FFQ was administered online via the Eetscore tool and completed before the start of the intervention periods.

Statistical analysis

All analysis were performed in SPSS statistics 25. P-values below 0.05 were considered statistically significant. Data are presented in mean ± SD, in n (%) or as median and interquartile range in case of skewness. Univariate Analysis of Variance (ANOVA) was used to detect differences in energy and caffeine intake during the night shift between the 5 conditions. Linear mixed models were used to analyze the effect of meal condition on median reaction time, reciprocal reaction time, mean number of lapses, SPS, hunger feelings and gastrointestinal complaints. We used fixed effects of condition (0NGL, 1LGL, 1HGL, 3LGL and 3HGL), night shift (1, 2, 3), age (vr) and BMI (kg/m²) and a random effect of participant ID. In addition, we adjusted for caffeine intake 2 hours before the PVT when analyzing effects on median reaction time, reciprocal reaction time, mean number of lapses and SPS, and adjusted for caffeine intake during the whole night shift when analyzing the effect on gastrointestinal complaints. Differences in SPS before and after the night shift and before and after the PVT were also analyzed with linear mixed models with an additional fixed effect of time. The 2-way interaction effect between condition and nightshift showed no significant effect and was therefore excluded from the model. Residuals were checked for normality for each model.

Results

Participant characteristics

Median age of the participants was 31.8 years, and median BMI was 25.1 kg/m^2 (**Table 6.1**). They had on average 10 (IQR 3.2-22) years of experience in working night shifts and worked on average 3.9 (SD 1.5) night shifts a month. Participants started their night shift between 10:45 PM and 11:15 PM and ended it between 7:15 AM and 8:30

AM. Most participants (20 out of 48) indicated that they prefer having 2 eating occasions during the night shift, some preferred only 1, some 4 or more and 1 preferred to snack continuously. In general, participants experienced various gastrointestinal complaints while working night shifts. The most common complaint was bloating with an median score of 3.9 (IQR 1.0-6.2) out of 10, followed by flatulence (median 3.1, IQR: 0.9 - 5.8), rumbling intestines (median 3.0, IQR: 1.6 - 4.7) and stomach cramps (median 1.3, IQR: 0.1 - 5.0). Constipation (median 0.5, IQR: 0 - 2.9) and diarrhea (median 0.0, IQR: 0.0 - 0.4) were less often mentioned as complaints. Participants scored 107 ± 14.5 out of 160 points on the DHD2015-index (**Table 6.1**). They scored highest on the components red meat and sodium, indicating a good compliance to these guidelines, and lowest on the components nuts, tea, and unhealthy choices.

Meal compliance

Between 9:00 PM and 6:00 AM, participants consumed similar amounts of energy across the 5 conditions (**Table 6.2**). Although the provided meals were fixed in terms of energy content, the energy intakes varied slightly in practice. Some meals were not consumed or more likely were consumed but not reported. In some cases participants consumed foods that were scheduled to be eaten before 9:00 PM but were actually eaten after 9:00 PM or participants consumed foods or drinks outside the nutrition protocol. This could, for example, be a splash of milk in coffee or tea. Nevertheless, the meals scheduled between 9:00 PM and 6:00 AM were consumed within the given time slots in 75.4% to 89.8% of the cases. Even though drinks with caffeine were not allowed between 3:00 AM and 5:00 AM, participants consumed on average between 1.5 mg and 8.7 mg of caffeine during this time period. Moreover, participants in the 1 meal condition consumed 8.4 (95% CI 3.3, 13.5) mg more caffeine 2 hours before the PVT than participants in the 3 meal condition.

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Table 6.1. Participant characteristics, number of night shifts, and diet quality of 51 female night shift workers in mean ± SD. median (IQR) or n (%).

Characteristic	Mean/Median	SD/(IQR)
Age, median, years (IQR)	31.8	(24.3-46.6)
Body weight, median kg (IQR)	69.7	(63.0-78.0)
Height, mean cm	169.7	±5.83
Body Mass Index, median kg/m²	25.1	(22.2-26.7)
- Normal (18-25 kg/m²), n (%)	25	(49.0)
- Overweight (25-30 kg/m²), n (%)	21	(41.2)
- Obese (>30 kg/m²), n (%)	5	(9.8)
Basal Metabolic Rate, kcal	1399	(1352-1489)
Estimated Total Energy Expenditure,		
kcal	2229	(2105-2403)
Vegetarian, n (%)	7	(13.2)
Night shifts per month, mean series	3.9	±1.5
Night shifts per serie, mean nights	3.1	±0.8
Night shift experience, mean years	10.0	(3.2-22)
DHD2015-index score ¹ , mean	107	±14.5
- Vegetables, mean ±SD	7.0	±2.6
- Fruit, mean ±SD	7.6	±2.7
- Whole grains, mean ±SD	7.9	±2.2
- Legumes, mean ±SD	6.4	±4.0
- Nuts, mean ±SD	4.9	±3.6
- Dairy, mean ±SD	6.2	±3.1
- Fish, mean ±SD	5.2	±3.7
- Tea, mean ±SD	4.8	±4.0
- Fats and oils, mean ±SD	6.9	±4.5
- Coffee, mean ±SD	7.6	±2.5
- Red meat, mean ±SD	9.5	±1.4
- Processed meat, mean ±SD	5.9	±3.0
- Sweetened beverages, mean ±SD	8.1	±2.6
- Alcohol, mean ±SD	8.2	±3.2
- Sodium, mean ±SD	8.4	±2.0
- Unhealthy choices, mean ±SD	2.6	±3.9

¹ The score ranges between 0 and 160 points, and between 0-10 points per component.

Table 6.2. Compliance to meal intake and timing between 9:00 PM and 6:00 AM for the different conditions, 51 participants.

	0NGL	1LGL	1HGL	3LGL	знег
	n=29	n=24	n=25	n=25	n=24
Energy, in kcal	565.5 ± 104.6	563.5 ±72.5	552.4 ±117.3	585.9 ±83.6	574.4 ±86.6
- Energy outside nutrition protocol, in kcal	19.7 ± 57.9	10.6 ± 28.8	20.5 ±39.6	16.5±61.6	12.8 ±33.2
Caffeine, in mg	36.4 ± 48.9	40.7 ±53.3	36.2 ±47.9	25.9 ±40.7	25.8 ±43.2
- 1 hour before PVT	2.9 ±11.8	4.7 ± 13.2	3.8 ±13.6	0.0 ±0.0	1.5 ±6.9
- 2 hours before PVT	6.3 ±19.2	12.0 ± 21.7	8.8 ±20.4	2.8 ± 11.6	2.4 ±9.7
- between 3:00 – 5:00 AM	5.1 ±14.7	8.7 ±19.6	4.3 ±14.1	2.8 ±11.3	1.5 ±6.9
Time meal before NS	$9.45 \pm 0.14 \text{ PM}$	$9.46 \pm 0.15 \text{PM}$	9:48 ± 0:14 PM	n.a.	n.a.
- % within time slot	88.7	85.7	89.8	n.a.	n.a.
Time test meal 0:00 – 0:30 AM	n.a.	n.a.	n.a.	$0.29 \pm 0.32 \text{ AM}$	$0.27 \pm 0.30 AM$
- % within time slot	n.a.	n.a.	n.a.	79.7	80.0
Time test meal 2:30 – 3:00 AM	n.a.	$2:58 \pm 0:34 \text{ AM}$	$2:50 \pm 0:26 \text{ AM}$	$2:50 \pm 0:25 \text{ AM}$	$2.53 \pm 0.36 \text{AM}$
- % within time slot	n.a.	70.0	78.9	82.8	75.4
- time between test meal and PVT, min	n.a.	94.3 ±31.6	93.0 ±31.3	99.6 ±20.8	95.6 ±45.5
Time test meal 5:00 – 5:30 AM	n.a.	n.a.	n.a.	$5:12 \pm 0:14 \text{ AM}$	$5:19 \pm 0:28 \text{ AM}$
- % within time slot	n.a.	n.a.	n.a.	86.4	84.4

Abbreviations: 0NGL, no meal and no glycemic load condition; 1LGL, 1 meal with a low glycemic load condition; 1HGL, 1 meal with a high glycemic load condition; 3LGL, 3 meals with a low glycemic load condition; 3HGL, 3 meals with a high glycemic load condition; 3HGL, 3 meals with a low glycemic load condition; 3HGL, 3 meals with a high glycemic load condition; 0.8, night shift; PVT, psychomotor vigilance

Objective alertness levels and eating conditions

Participants started the PVT on average at 4:23 (SD 0:20) AM. In the 0NGL condition, participants had on average an estimated median RT of 379.9 (95% CI 366.7, 393.1) ms, a reciprocal RT of 2.7 (95% CI 2.6, 2.7) and 35.4 (95% CI 31.5, 39.3) lapses. These were not significantly different from the other conditions (**Table 6.3 and Suppl. Figure 6.1A & 6.1B**). However, there was a significant difference in lapses of the condition 3HGL with the 1LGL and 3LGL conditions. Participants in the 3HGL condition had 4.6 (95% CI 0.0, 9.3) more lapses than the 1LGL condition and 3.4 (95% CI 0.0, 6.8) more lapses than the 3LGL condition.

The estimated median RT varied to some extent during the night shifts. During night shift 1 (NS1) was 384.7 (95% CI 371.8, 397.6) ms and was 10.3 (95% CI -18.8, -1.8) ms slower than during NS2, but not different from NS3.

Subjective alertness levels and eating conditions

The Samn-Perelli scale (SPS) before the night shift was on average started at 10:41 (SD 01:03) PM, the SPS after the nightshift was started at 08:16 (IQR 07:56, 08:42) AM. The SPS before the PVT was started on average at 4:23 (SD 0:20) AM and the SPS after the PVT 3 minutes later. In the 0NGL condition, participants scored at the start of the night shift 2.6 (95% CI 2.4, 2.9) out of 7 on the SPS, which is between 'Very lively, but not at peak' and 'Okay, somewhat fresh' [38]. This score increased significantly (p<0.001) during the night shift; before the start of the PVT participants scored 3.3 (95% CI 3.0, 3.5) points, after the PVT 3.5 (95% CI 3.3, 3.7) points and after the night shift 3.9 (95% CI 3.5, 4.0) points on the SPS, which is considered as 'A little tired, less than fresh'. This was similar to the other four conditions, although participants in the 3HGL condition were borderline more tired after the PVT (ß 0.29 95% CI -0.01, 0.59 p=0.056) and after the night shift (ß 0.28 95% CI -0.03, 0.59 p=0.074) than those in the 0NGL condition (**Table 6.4** and **Suppl. Figure 6.2**). Moreover, participants in the 3HGL condition were 0.28 (95% CI -0.03, 0.59 p=0.073) points and borderline more tired after the PVT than the 3LGL condition.

Overall, there was a time effect over the three consecutive night shift days; participants were less tired after the PVT and after the NS on NS3 than on NS1 or NS2.

Table 6.3. Results of Linear Mixed Models for objective alertness levels assessed by the Psychomotor Vigilance Test (PVT) during the night shift in 51 participants showing the effects of meal condition, night shift, and the covariates age, BMI and caffeine intake 2 hours before the PVT.

		Me	Median Reaction Time	ime	Recip	Reciprocal Reaction Time	Time	ž	Number of Lapses	Se
		ß	95% CI	P-value	ß	95% CI	P-value	ß	95% CI	P-value
Condition	ONGL	0			0			0	,	
	1LGL	-4.43	-4.43 (-16.92, 8.07)	0.486	0.05	(-0.02, 0.11)	0.187ª	-1.88	(-5.14, 1.39)	0.259
	1HGL	-3.43	(-15.70, 8.84)	0.582	0.02	(-0.05, 0.08)	0.611	-0.32	(-3.53, 2.89)	0.845
	3LGL	-2.95	(-15.97, 10.07) 0.656	0.656	0.02	(-0.05, 0.09)	0.601 ^b	-0.65	(-4.07, 2.77)	0.708 ^d
	3HGL	6.97	6.97 (-6.02, 19.96)	0.292	-0.04	(-0.11, 0.03)	0.229ab	2.77	(-0.64, 6.18)	0.111 ^{cd}
Night shift	1st	0	ı		0	ı		0		
	2nd	-10.27	.10.27 (-18.76, -1.78)	0.018	0.04	(-0.01, 0.09)	0.083	-2.19	(-4.39, 0.02)	0.052
	3rd	-6.43	(-16.41, 3.54)	0.205	0.04	(-0.02, 0.09)	0.189	-1.14	(-3.73, 1.45)	0.388
Age	years	0.71	(-0.31, 1.74)	0.166	00.00	(-0.01, 0.00)	0.198	0.23	(-0.08, 0.54)	0.142
BMI	kg/m^2	1.92	(-1.06, 4.90)	0.202	-0.01	(-0.03, 0.01)	0.172	0.59	(-0.31, 1.49)	0.191
Caffeine intake mg	mg	0.04	0.04 (-0.20, 0.28)	0.736	0.00	(0.00, 0.00)	0.984	0.03	(-0.03, 0.09)	0.377

Abbreviations: 0NGL, no meal and no glycemic load condition; 1LGL, 1 meal with a low glycemic load condition; 1HGL, 1 meal with a high glycemic load condition; 3LGL, 3 meals with a low glycemic load condition; 3HGL, 3 meals with a high glycemic load condition. and Conditions with similar letters indicate significant differences (p-value < 0.05).

Table 6.4. Results of Linear Mixed Models for subjective alertness levels assessed by the Samn-Perelli scale before and after the night shift and before and after the PVT in 51 participants, showing the effects of condition, night shift, age, BMI and caffeine intake 2 hours before the test.

		3,	SPS before NS	NS	Ø	SPS before PVT	5	0,	SPS after PVT		S	SPS after NS	
		В	95% CI	95% CI P-value	В	B 95% CI P-value	P-value	В	B 95% CI P-value	P-value	В	B 95% CI P-value	P-value
Condition	ONGL	0		,	0		,	0	,	,	0		
	1LGL	0.02	(-0.22, 0.26) 0.867) 0.867	-0.06	-0.06 (-0.36, 0.24) 0.697	269.0	0.09	0.09 (-0.20, 0.38) 0.532	0.532	0.10	0.10 (-0.22, 0.42) 0.530	0.530
	1HGL		(-0.15, 0.33) 0.448	0.448	0.01	0.01 (-0.28, 0.31) 0.944	0.944	0.01	0.01 (-0.28, 0.29) 0.947	0.947	0.25	0.25 (-0.07, 0.57) 0.120	0.120
	31.GL	0.11	(-0.13, 0.35) 0.381	0.381	-0.05	-0.05 (-0.35, 0.26) 0.767	0.767	0.01	0.01 (-0.29, 0.31) 0.953	0.953	0.18	0.18 (-0.14, 0.49) 0.263	0.263
	3HGL		(-0.09, 0.38) 0.220	0.220	0.24	0.24 (-0.07, 0.54) 0.129	0.129	0.29	0.29 (-0.01, 0.59) 0.056	0.056	0.28	0.28 (-0.03, 0.59) 0.074	0.074
Night shift	1st	0			0			0			0		
	2nd	0.03	(-0.14, 0.19) 0.740) 0.740	0.05	0.05 (-0.16, 0.26) 0.664	0.664	0.02	0.02 (-0.18, 0.22) 0.849a	0.849ª	-0.39	-0.39 (-0.61, -0.17) 0.001b	0.001₺
	3rd	_	(-0.38, 0.01) 0.061) 0.061	-0.29	-0.29 (-0.54, -0.05) 0.019	0.019	-0.36	-0.36 (-0.59, -0.12) 0.003ª	0.003ª	-0.87	-0.87 (-1.13, -0.61) 0.000 ^b	00000
Age	years	0.00	(-0.02, 0.01) 0.814	0.814	0.01	0.01 (-0.01, 0.03) 0.208	0.208	0.01	0.01 (-0.01, 0.02) 0.548	0.548	0.01	0.01 (-0.01, 0.03) 0.265	0.265
BMI	kg/m^2		(-0.05, 0.05) 0.992	0.992	0.00	0.00 (-0.05, 0.04) 0.866	998.0	0.01	0.01 (-0.04, 0.06) 0.662	0.662	-0.01	-0.01 (-0.06, 0.04)	0.726
Caffeine intake	md		(-0.01, 0.00) 0.345	0.345	0.00	0.00 (-0.01, 0.00) 0.699	0.699	0.00	0.00 (-0.01, 0.00) 0.510	0.510	0.00	0.00 (-0.01, 0.00) 0.386	0.386

Abbreviations: 0NGL, no meal and no glycemic load condition; 1LGL, 1 meal with a low glycemic load condition; 1HGL, 1 meal with a high glycemic load condition; 3LGL, 3 meals with a low glycemic load condition; 3HGL, 3 meals with a high glycemic load condition. a.b Conditions with similar letters indicate significant differences (p-value < 0.05). Higher values indicate more tiredness.

Hunger feelings and eating conditions

The questions about hunger feelings *during* the night shift were filled in at 4:23 (IQR 4:08 –5:03) AM and *after* the night shift at 8:16 (IQR 7:56 – 8:42) AM.

During the night shift participants scored in the 0NGL condition 5.5 (95% CI 5.0, 6.0) out of 10 points on the hunger scale, 2.0 (95% CI 1.5, 2.5) on the satiety scale, 6.3 (95% CI 5.8, 6.9) on the desire to eat scale and 6.1 (95% CI 5.7, 6) on the how much they want to eat scale. After the night shift they scored 6.6 (95% CI 6.0, 7.1) on the hunger scale, 1.4 (95% CI 1.0, 1.8) on the satiety scale, 6.9 (95% CI 6.3, 7.5) on the desire to eat scale and 6.0 (95% CI 5.5, 6.6) on the how much they want to eat scale. The eating condition had an effect on hunger, satiety, desire to eat and how much participants wanted to eat both during and after the night shift (Table 6.5 & 6.6 and Suppl. Figure 6.3 & 6.4). In general, participants in all four meal conditions (1LGL, 1HGL, 3LGL, 3HGL) experienced less hunger feelings during the night shift than in the no meal condition (0NGL), but no differences were observed between the one meal and three meals conditions. However, after the night shift only participants in the three meal conditions experienced less hunger feelings than the no and one meal conditions. Moreover, no differences were found between no meal and one meal conditions after the night shift.

Overall, there was no time effect over the three consecutive night shift days on the four hunger outcomes *during* the night shift, but some time effects were visible on these outcomes *after* the night shift. Especially after the NS3 participants were less hungry, had less desire to eat and wanted to eat less than NS1.

Gastrointestinal complaints and eating conditions

During the night shift, participants suffered the most from rumbling intestines, bloating and flatulence, while less from flatulence and diarrhea. In the 0NGL condition, participants scored 1.1 (95% CI 0.7, 1.5) out of 10 on stomach cramps, 2.1 (95% CI 1.5, 2.7) points on rumbling intestines, 2.1 (95% CI 1.5, 2.7) on bloating, 1.9 (95% CI 1.4, 2.5) on flatulence, 0.5 (0.95% CI 0.3, 0.8) on diarrhea and 0.9 (95% CI 0.5, 1.3) on constipation. All other four conditions did not differ significantly from the 0NGL condition, except for participants in the 3LGL condition who experienced more rumbling intestines and the 1LGL condition suffering from less diarrhea (**Table 6.7** and **Suppl. Figure 6.5**).

Table 6.5. Results of Linear Mixed Models for hunger feelings *during* the night shift, assessed by a 10 cm visual analogue scale (VAS), in 51 participants, showing the effects of condition, night shift, age, and BMI.

		Hunger	Satiety	Desire to eat	How much want to eat
		B 95% CI P-value	B 95% CI P-value	B 95% CI P-value	B 95% CI P-value
Condition	ONGL	0	- 0	- 0	- 0
	1LGL	-0.57 (-1.19, 0.05) 0.071	0.40 (-0.19, 1.00) 0.182	-0.67 (-1.30, -0.05) 0.036	-0.92 (-1.47, -0.37) 0.001
	1HGL	-0.69 (-1.29, -0.09) 0.024	0.35 (-0.23, 0.93) 0.240	-0.59 (-1.20, 0.02) 0.058	-0.88 (-1.42, -0.35) 0.001
	3LGL	-1.24 (-1.85, -0.63) <0.001	0.96 (0.37, 1.54) 0.002	-1.12 (-1.74, -0.49) <0.001	-1.09 (-1.64, -0.55) <0.001
	3HGL	-1.19 (-1.80, -0.59) <0.001	0.56 (-0.02, 1.15) 0.060	-0.92 (-1.53, -0.30) 0.004	-0.90 (-1.44, -0.36) 0.001
Night shift	1st	0	0	0	- 0
	2nd	0.15 (-0.27, 0.58) 0.471	-0.07 (-0.47, 0.34) 0.749	0.22 (-0.21, 0.64) 0.314	-0.10 (-0.47, 0.27) 0.586
	3rd	0.02 (-0.47, 0.51) 0.926	-0.09 (-0.57, 0.38) 0.696	0.05 (-0.44, 0.55) 0.830	-0.11 (-0.54, 0.32) 0.624
Age	years	-0.05 (-0.08, -0.01) 0.019	-0.03 (-0.07, 0.00) 0.070	-0.04 (-0.08, 0.01) 0.094	-0.02 (-0.06, 0.02) 0.275
BMI	kg/m²	0.01 (-0.09, 0.12) 0.789	0.08 (-0.03, 0.18) 0.144	-0.02 (-0.14, 0.11) 0.799	0.04 (-0.07, 0.14) 0.478
Abbreviations: 0NGL, no meal and no	0NGL, no r	meal and no glycemic load condit	llycemic load condition, 1LGL, 1 meal with a low glycemic load condi	and no glycemic load condition; 1LGL, 1 meal with a low glycemic load condition; 1HGL, 1 meal with a high glycemic load	neal with a high glycemic load

condition; 3LGL, 3 meals with a low glycemic load condition; 3HGL, 3 meals with a high glycemic load condition.

Table 6.6. Results of Linear Mixed Models for hunger feelings after the night shift, assessed by a 10 cm visual analogue scale (VAS), in 51 participants, showing the effects of condition, night shift, age, and BMI.

			Hunger			Satiety			Desire to eat	t	Hov	How much want to eat	o eat
		В	95% CI P-value	P-value	В	95% CI P-value	P-value	В	B 95% CI P-value	P-value	В	95% CI P-value	P-value
Condition	ONGL	0	,	,	0	,	,	0			0		,
	1LGL	0.05	(-0.5, 0.6) 0.855ab	0.855ab	-0.03	-0.03 (-0.53, 0.47) 0.897f	0.897	0.30	0.30 (-0.3, 0.91) 0.323gh	0.323gh	-0.42	-0.42 (-0.99, 0.16) 0.157	0.157
	1HGL	0.07	(-0.48, 0.61) 0.813°d	0.813 ^{cd}	0.05	0.05 (-0.45, 0.55) 0.837	0.837	-0.14	-0.14 (-0.74, 0.47) 0.656	0.656	-0.20	-0.20 (-0.78, 0.37) 0.483	0.483
	3LGL	-1.15	(-1.69, -0.61) <0.001ac	<0.001 ^{ac}	0.65	(0.15, 1.15) 0.010 ^f	0.010 ^f	-1.19	-1.19 (-1.79, -0.59) <0.001 ^{gi}	<0.0019	-0.95	-0.95 (-1.52, -0.38) 0.001	0.001
	3HGL	-0.90	(-1.43, -0.37) 0.001 ^{bd}	0.001 ^{bd}	0.59	(0.1, 1.08)	0.019	-0.78	-0.78 (-1.37, -0.19) 0.010h	0.010 ^h	-0.97	-0.97 (-1.54, -0.41) 0.001	0.001
Night shift	1st	0			0			0			0		
	2nd	-0.26	(-0.63, 0.1)	0.158e	0.41	0.41 (0.07, 0.75) 0.019	0.019	-0.25	-0.25 (-0.66, 0.15) 0.219	0.219	-0.30	-0.30 (-0.69, 0.09) 0.128	0.128
	3rd	-0.73	(-1.16, -0.3) 0.001e	0.001€	0.38	0.38 (-0.02, 0.78) 0.063	0.063	-0.70	-0.70 (-1.18, -0.23) 0.004	0.004	-0.57	-0.57 (-1.02, -0.11) 0.014	0.014
Age	years	-0.06	(-0.1, -0.02) 0.002	0.002	-0.01	-0.01 (-0.04, 0.02) 0.710	0.710	-0.06	-0.06 (-0.1, -0.01) 0.012	0.012	-0.04	-0.04 (-0.08, 0) 0.060	090.0
BMI	kg/m²	0.02	(-0.1, 0.13) 0.789	0.789	0.08	0.08 (-0.01, 0.17) 0.095	0.095	0.00	0.00 (-0.13, 0.13) 0.998	0.998	0.04	0.04 (-0.07, 0.16) 0.458	0.458

Abbreviations: 0NGL, no meal and no glycemic load condition; 1LGL, 1 meal with a low glycemic load condition; 1HGL, 1 meal with a high glycemic load condition; 3LGL, 3 meals with a low glycemic load condition; 3HGL, 3 meals with a high glycemic load condition. ^{a-j} Conditions with similar letters indicate significant differences (p-value < 0.05).

Table 6.7. Results of Linear Mixed Models for gastrointestinal complaints assessed by a 10 cm visual analogue scale (VAS), in 51 participants, showing the effects of condition, night shift, age, BMI, and caffeine intake during the night shift.

))				,		
		S	Stomach cramps		Rur	Rumbling intestines	S		Bloating	
		В	95% CI	P-value	В	95% CI	P-value	В	95% CI	P-value
Condition	ONGL	0	•		0			0		
	1LGL	-0.22	(-0.74, 0.31)	0.419	-0.02	(-0.65, 0.62)	0.955	0.47	(-0.22, 1.15)	0.179°
	1HGL	-0.20	(-0.72, 0.32)	0.454	-0.04	(-0.67, 0.60)	0.905	-0.44	(-1.12, 0.24)	0.205⊶
	3LGL	0.29	(-0.23, 0.81)	0.272 ^a	0.74	(0.11, 1.37)	0.021b	0.51	(-0.16, 1.18)	0.138^{d}
	3HGL	-0.31	(-0.82, 0.20)	0.238ª	-0.35	(-0.97, 0.28)	0.274 ^b	-0.09	(-0.76, 0.58)	0.793
Night shift	1st	0	•		0			0	,	
	2nd	-0.42	(-0.78, -0.06)	0.023	-0.39	(-0.82, 0.04)	0.073	-0.55	(-1.02, -0.09)	0.019
	3rd	-0.33	(-0.76, 0.09)	0.124	-0.40	(-0.91, 0.10)	0.119	-0.50	(-1.04, 0.05)	0.074
Age	years	-0.02	(-0.05, 0.01)	0.221	-0.05	(-0.1, -0.01)	0.017	-0.02	(-0.07, 0.02)	0.307
BMI	kg/m^2	-0.04	(-0.13, 0.04)	0.305	0.02	(-0.11, 0.15)	0.745	-0.02	(-0.15, 0.10)	0.720
Caffeine intake	mg	0.00	(-0.01, 0.00)	0.505	00.00	(-0.01, 0.00)	0.239	0.00	(-0.01, 0.00)	0.099
			Flatulence			Diarrhea			Constipation	
		В	95% CI	P-value	В	95% CI	P-value	В	95% CI	P-value
Condition	ONGL	0			0	•		0	•	
	1LGL	-0.02	(-0.70, 0.66)	0.950	-0.42	(-0.81, -0.03)	0.035	-0.28	(-0.70, 0.14)	0.186
	1HGL	0.17	(-0.51, 0.85)	0.623	-0.13	(-0.53, 0.26)	0.507	-0.19	(-0.61, 0.23)	0.373
	3LGL	0.31	(-0.36, 0.98)	0.359	-0.26	(-0.64, 0.13)	0.193	0.03	(-0.38, 0.45)	0.876
	3HGL	-0.38	(-1.04, 0.29)	0.266	-0.03	(-0.42, 0.35)	0.860	0.15	(-0.26, 0.56)	0.479
Night shift	1st	0			0	•		0	•	
	2nd	-0.46	(-0.93, 0.01)	0.056	-0.07	(-0.36, 0.21)	0.619	0.22	(-0.07, 0.50)	0.132
	3rd	-0.43	(-0.98, 0.12)	0.125	0.01	(-0.32, 0.35)	0.937	0.56	(0.23, 0.90)	0.001
Age	years	-0.03	(-0.06, 0.01)	0.115	0.00	(-0.01, 0.02)	0.502	-0.01	(-0.04, 0.01)	0.327
BMI	kg/m^2	-0.03	(-0.13, 0.08)	0.574	00.00	(-0.04, 0.04)	0.970	0.01	(-0.07, 0.10)	0.760
Caffeine intake	mg	0.00	(-0.01, 0.01)	0.933	0.00	(-0.01, 0.00)	0.178	0.00	(0.00, 0.00)	0.654

Abbreviations: 0NGL, no meal and no glycemic load condition; 1LGL, 1 meal with a low glycemic load condition; 1HGL, 1 meal with a high glycemic load condition; 3LGL, 3 meals with a high glycemic load condition. and Conditions with similar letters indicate significant differences (p-value < 0.05).

Furthermore, there were some differences within the four meal conditions (1LGL, 1HGL, 3LGL and 3HGL). Participants in the 3LGL condition experienced 0.6 (95% CI 0.1, 1.1) points more stomach cramps and 1.1 (95% CI 0.4, 1.7) points more rumbling intestines than in the 3HGL condition. Moreover, participants in the 1HGL condition experienced 0.91 (95% CI 0.2, 1.6) less bloating than the 1LGL condition and 1.0 (95% CI 0.0, 1.9) less bloating than in the 3LGL condition.

Time effects of the three consecutive night shifts on stomach cramps and bloating were seen; participants were suffering less from these gastrointestinal complaints during NS2 than NS1. During NS3 participants experienced more constipation than during NS1.

Discussion

This study investigated the effect of 1 or 3 small meals, either with a low (1LGL and 3LGL) or high glycemic load (1HGL and 3HGL), compared to no meal (0NGL) during the night shift on alertness levels, hunger feelings and gastrointestinal complaints. No differences were found for alertness levels and gastrointestinal complaints between the no meal with the LGL and HGL meal conditions. However, the least hunger feelings during and after the night shift were reported when three meals were consumed during the night shift. With respect to alertness, consuming one or three LGL meals during the night shift resulted in less lapses than three HGL meals, but not than one HGL meal. Results for subjective levels of alertness were overall in line with this, although these were not statistically different. Health care workers experienced gastrointestinal complaints in varying degrees in all meal conditions, but scored on average highest on stomach cramps, rumbling intestines and bloating in the 3LGL condition compared to the other meal conditions.

Similar to our results, a study by Gupta et al (2019) showed no differences between not eating and eating a small meal during the night shift [16]. However, they found that, at the end of the night shift and after a 40-minute task that required prolonged sustained attention, eating a small meal resulted in less lapses than eating no meal [16]. This suggests that the effect of eating a small meal during the night shift might be strengthened by a task that increases fatigue, which is of particular interest in night shift professions that involve driving for example.

Our results regarding the LGL and HGL conditions suggest that the glycemic load of the meals was more important than the number of meals with respect to the number of lapses. However, this was not the case for median reaction time (RT) and reciprocal reaction time (RRT). It must be noted that at the time the PVT-B was conducted participants had only consumed two of the three test meals, but this probably did not affect the results between the LGL and HGL conditions. There are only a few other studies that investigated the effect of GL on cognitive performance in the short term. However, these studies had different GLs, were performed during day time either in children or older diabetic people and are therefore not comparable to the current study [43]. Also, results of previous studies investigating the effect of GI on blood glucose levels and its association with cognitive performance are also not consistent and their results seem to depend on time of day, type of cognitive test and size and composition of the meal (especially of carbohydrates) [13, 44].

Altogether, consuming three small meals during the night shift does not seem to cause lower alertness levels compared to not eating or eating one small meal during the night shift, but the composition of the meal should be considered especially in terms of GL. Moreover, it would be interesting to know whether the effect of the meal conditions on even longer prolonged alertness tasks will be similar or stronger.

Similar patterns were seen for subjective alertness levels as for objective alertness; although no significant differences were found between the conditions which could be due to too little power to detect these differences. However, participants felt significantly more tired at the end than at the beginning of the night shift. Also other studies did not find differences between not eating and eating a small meal but observed increased levels of sleepiness across the night shift [17, 22]. A possible explanation given for why no difference was found between the eating conditions in the study of Gupta et al (2019), was the carbohydrate content of meals [22], which were presumably higher than in our study. Meals high in carbohydrates or fat are associated with increased feelings of sleepiness [22, 45-47]. On the other hand, night shift workers indicate that one of the reasons they eat, preferably something sweet, is to improve alertness [48]. Associations between the composition of the meal and subjective alertness levels are not yet clear [45-47], but may be linked to the

postprandial glucose response and thus also the time period between consumption and measuring subjective alertness [22, 49].

Not surprisingly, we showed that participants in the three-meal conditions experienced the least hunger feelings compared to the no meal condition and the one meal conditions, especially *after* the night shift. *After* the night shift participants were equally hungry during the one meal condition as during the no meal condition. However, participants in the no meal condition were allowed to consume their breakfast earlier, if they felt hungry, which might have slightly biased these results. In addition to previous studies, we showed that eating three small meals further reduced hunger feelings compared to one small meal and that, depending on the glycemic load, it did not result in unwanted decreased alertness levels as was the case with the consumption of a large meal [7, 22]. Participants indicated that they prefer to have two meals during the night shift, a number that may already be sufficient to prevent hunger feelings, even until the end of the night shift. Future research should explore the effects of two small meals during the night shift and meal timing to confirm this.

Participants experienced gastrointestinal complaints in varying degrees and, not surprisingly, scored on average highest on rumbling intestines and bloating. These complaints were also scored higher in the 3LGL condition than in the other meal conditions. Since participants during the 3HGL condition did not report more gastrointestinal complaints than during the no meal and one meal conditions, these higher gastrointestinal complaints scores were probably caused by the type of monosaccharides used and not the meal frequency. For the LGL meals we used a combination of fructose and lactose, monosaccharides that are known to be tolerated differently in humans [50-52] and therefore could explain the high variance in gastrointestinal complaint scores. Although participants were not fructose and lactose intolerant, the amount of these monosaccharides could have been higher than what they usually consume throughout the day or night [50, 53]. On the other hand, on average the complaints were relatively mild, and less than normally experienced during their night shifts. In our study participants scored between 1.6 and 2.6 for bloating depending on the meal condition, which is comparable to the study of Gupta et al (2019) [22]. Furthermore, our test meals mainly consisted of yogurts, which could be seen as a probiotic in itself and may have had beneficial effects on the microbiome and

ensured a better digestion of lactose [50, 54]. Thus, it should be investigated whether the higher prevalence of gastrointestinal complaints in the 3LGL condition remains the same when the monosaccharides are replaced by more mainstream foods low in GL.

Adherence to the nutrition protocol was relatively high and therefore, even though we did not adjust for meal compliance, we expect that non-compliance with the nutrition protocol had minimal impact on the results. Also the difference in caffeine intake two hours before the PVT between the one and three meal condition is expected to have affected the results to limited extent, as the consumed amounts where rather low and incidental, and in any case were taken into account as covariate in the statistical analyses.

This intervention study was performed in a real life setting, which also supports its feasibility and relevance in daily life. However, this real life setting also comes with some limitations. We had some missing data and were not able to adjust for all types of confounders, such as sleep duration and quality, menstrual cycle, chronotype, work load and the effect of COVID-19 measures (special work clothes equipment) on participants and thus the results. However, by using linear mixed model analysis and randomization, we expect that these confounders did not have much influence on the results. Another consequence of our real live setting may be the relative high number of lapses we found compared to other studies (35 versus 4 to 12)[16, 17, 37]. It would have been interesting if we could have investigated to what extent the number of lapses affected the functioning of the participants, including number of mistakes, and accidents.

Moreover, we did not investigate what the effects of the meal conditions were compared to a habitual night shift when a usual diet was consumed. The test meals we used are usually not eaten in daily life and could be replaced by more healthier foods, for example by increasing the diet fiber content by adding fruit or muesli to the yoghurt. However, as consuming dietary fibers during the night shift may irritate the bowel and may result in more gastrointestinal complaints, effects of consuming other foods during the night shift should be first investigated before recommendations can be made. In addition, further research is needed to determine to what extent differences in effects on alertness of LGL and HGL meals are mediated by their impact

on blood glucose levels, and whether these extend to longer-term effects on mental capacity.

This study population consisted mainly of a female study sample working in a health-promoting work environment and therefore probably with a higher interest in nutrition and health compared to other night shift working populations. Yet, participants had a lower Dutch Healthy Diet-2015 index score than a general, a bit older, female population, 107 (SD 14.5) versus 114 (SD 16.0), indicating a poorer diet quality [40]. However, it must be noted that older people generally have higher diet quality scores than younger people [42, 55]. Nevertheless, we must be careful in generalizing our results to other night shift working populations. Besides being health conscious and female, participants in this study worked irregular work schedules and in a health care setting. The type of working schedule (irregular vs regular) and of work (e.g. nursing or working in a factory) could also affect alertness levels. Therefore, it would be interesting to see whether our results hold true for night shift workers with regular forward rotating shift work schedules and other work professions.

In conclusion, this study showed that three small meals with a low glycemic load during the night shift resulted in the best alertness levels in combination with the least hunger feelings. However, three small meals with a low glycemic load can lead to more gastrointestinal complaints. Based on these results it is recommended to consume a maximum of three small meals with a low glycemic load, when hungry, during the night shift. Night shift workers can best experience themselves whether or not this leads to more gastrointestinal complaints.

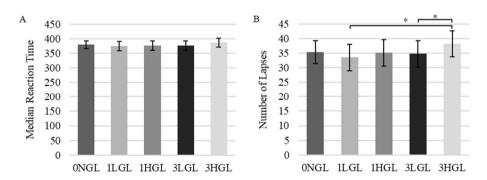
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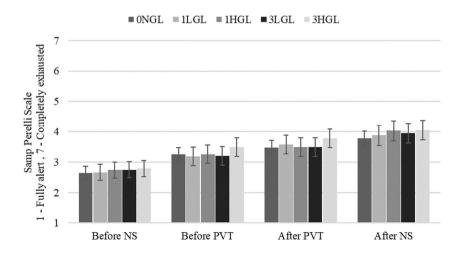
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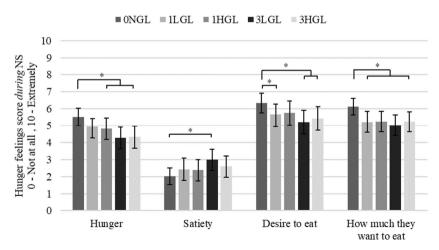
Supplementary materials



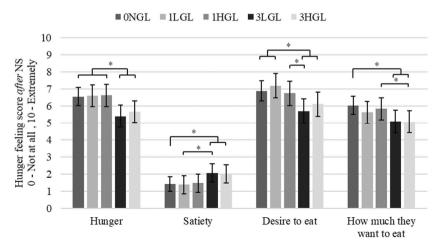
Supplemental figure 6.1A and 6.1B. Median reaction time and number of lapses across meal conditions with 95% CI and adjusted for night shift, age, BMI, caffeine intake 2 hours before psychomotor vigilance test. *Indicate significant differences (p-value < 0.05).



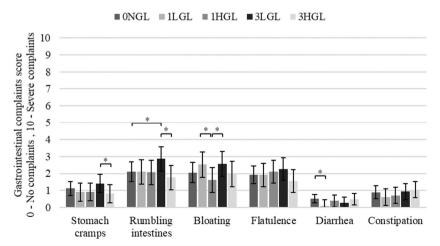
Supplemental figure 6.2. Subjective alertness levels of the meal conditions (mean with 95% CI), assessed by the Samn-Perelli scale (SPS) before and after the night shift (NS) and before and after the psychomotor vigilance task (PVT) in 51 participants and adjusted for night shift (NS1-NS3), age, BMI and caffeine intake 2 hours before the test.



Supplemental figure 6.3. Hunger feeling score (mean with 95% CI) during the night shift of the meal conditions, in 51 participants, and adjusted for night shift (NS1-NS3), age, and BMI. *Indicate significant differences (p-value < 0.05).



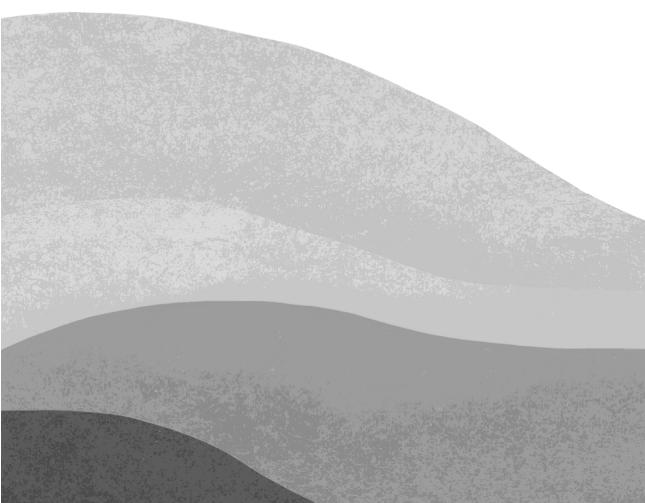
Supplemental figure 6.4. Hunger feeling score (mean with 95% CI) after the night shift of the meal conditions, in 51 participants, and adjusted for night shift (NS1-NS3), age, and BMI. *Indicate significant differences (p-value < 0.05).



Supplemental figure 6.5. Gastrointestinal complaint scores (mean with 95% CI) during the night shift of the meal conditions, in 51 participants, and adjusted for night shift (NS1-NS3), age, BMI and caffeine intake 2 hours before the test. *Indicate significant differences (p-value < 0.05).



General Discussion



The overall aim of this thesis was to investigate which nutrition strategies can be applied to night shift workers in health care resulting in the most optimal alertness levels and the least hunger feelings and gastrointestinal complaints, or in other words that provide the best safety and perceived well-being. To this aim, the following research questions were defined:

- 1. How is *meal composition* associated with alertness levels during the night shift? (Chapters 4 and 6)
- 2. Is the impact of a meal on alertness time-dependent? (Chapter 4)
- 3. How is *meal frequency* associated with alertness, hunger, and gastrointestinal complaints in night shift workers? (**Chapters 5 and 6**)
- 4. What is the *diet quality* of night shift working nurses and how can it be validly assessed? (**Chapters 2, 3 and 6**)
- 5. Do dietary *taste* patterns of night shift working nurses differ from those of a general population? (**Chapter 3**)
- 6. How are dietary *taste* patterns related to *diet quality* in night shift working nurses? (**Chapter 3**)

In this final chapter, the main findings are summarized in **Table 7.1** and discussed in the first paragraphs. This is followed by methodological considerations, (practical) implications and suggestions for further research.

Discussion of main findings

This thesis showed that several dietary factors (i.e. meal frequency, meal composition, meal size) play a role in the relationship between nutrition, health and safety. All these factors should be considered when developing dietary guidelines for night shift workers for the best alertness, lowest health risks and the best benefits (i.e. less gastrointestinal complaints and hunger feelings during the night shift).

Dietary guidelines for night shift workers should ultimately provide an answer to how often, what, how much and when these workers can eat best during the night shift. First, it is important to know *why* night shift workers eat during the night shift since from a biological point of view, it is probably better not to eat during the night shift [1, 2]. One of the reasons for eating during the night shift is having feelings of hunger [5], which

were reduced after eating multiple small meals (**Chapter 6**). In addition, most health care workers preferred to consume two or three meals during the night shift (**Chapter 6**) which was in line with the number of meals usually consumed by nurses during the night shift (**Chapter 5**).

Therefore, the next question is *whether* the number of meals (meal frequency) consumed during the night shift affects alertness levels and gastrointestinal complaints. In **Chapter 5** we showed, in an observational study, that meal frequency was positively associated with alertness levels but not associated with the total gastrointestinal complaints score in female night shift working nurses. This finding was tested in a dietary intervention study (**Chapter 6**), where we observed no difference between meal frequency (0, 1 or 3 meals) and alertness or gastrointestinal complaints in female health care workers.

For alertness, the findings in Chapters 5 and 6 seem contradictory at first sight, but this could be explained by the difference in study design. In Chapter 5, there was little variation in the number of meals reported and because of the observational character of the study, no causal relationship could be determined, while in the intervention study (Chapter 6), the meals were standardized for size, composition and time between meals and alertness test, all factors that may influence alertness, as discussed later. With respect to *gastrointestinal complaints*, the results were similar in both **Chapters** 5 and 6 but contradictory to our hypothesis. It was expected that more eating occasions would be associated with more gastrointestinal complaints as the digestive system would be triggered more often while being in a relative resting state during the night. Therefore, it was expected that not eating would result in the least gastrointestinal complaints. Also here, the size and composition of the meals can influence the number or severity of gastrointestinal complaints during the night shifts [3]. To the best of our knowledge, until now no other dietary intervention study has been performed investigating the effect of meal frequency on gastrointestinal complaints in night shift workers.

In summary, meal frequency, up to three meals, does not (negatively) influence alertness levels and gastrointestinal complaints in female health care workers during the night shift.

Table 7.1 Overview of the studies and main findings of this thesis.

ç	Dietary aspect	Study design	Study sample	Methods	Main findings
7		Cross-sectional study	EetMeetWeet research	DHD2015-index, Eetscore FFQ, full-length FFQ	The Eetscore FFQ was considered acceptable in ranking participants according to their diet quality
	(methodological)		population		compared with the full-length FFQ and showed good to excellent reproducibility.
က	Dietary taste patterns, diet quality	Observational study	Etmaal study; female night shift working nurses, DNFCS 2012-2016; healthy	Taste database, 3-day 24hR, DHD2015-index	During night shift higher En% 'sweet and sour', 'sweet and fat', and 'fat' and lower 'En% 'fat', and 'bitter' tasting foods were consumed than outside night shift.
			general female population (reference)		Night shift workers consumed higher En% sweet and sour' and lower En% bitter' than reference population.
					Higher En% 'fat' tasting foods was associated with lower diet quality ($r=-0.31$) in night shift workers.
4	Macronutrient composition,	Observational study	Etmaal study; night shift working nurses	3-day 24hR, PVT, Samn-Perelli Scale	Fat intake 0-1 hour prior to PVT was associated with lower alertness, CHO intake with higher alertness.
	timing of meals				Fat intake 2-3 hours prior to PVT was associated with higher alertness, carbohydrate intake with lower alertness.
					No associations with subjective alertness were observed.
2	Meal frequency,	Observational	Etmaal study; female night	3-day 24hR, PVT, Samn-Perelli	Eating frequency was associated with higher alertness.
	energy intake	study	shift working nurses	Scale, gastrointestinal complaints questionnaire	No associations between gastrointestinal complaints and alertness were observed.
9	Meal frequency, glycaemic load, diet quality	Two-armed randomized cross-over trial	Time to Eat study; female night shift working nurses and midwives	Nutrition protocol, food diary, PVT-B, Samn-Perelli Scale, hunger and castrointestinal	Three small meals with a low glycaemic load during the night shift resulted in the best alertness levels and the least hunder feelings.
				complaints questionnaire DHD2015-index, Eetscore FFQ	Three small meals with a low glycaemic load can lead to more gastrointestinal complaints.

Abbreviations: DHD2015-index: Dutch Healthy Diet 2015-index, FFQ: Food Frequency Questionnaire, En%: energy percentage, 24hR: 24-hour dietary recall, DNFCS: Dutch National Food Consumption Survey, PVT: Psychomotor Vigilance Task, CHO: carbohydrates.

However, other dietary factors may contribute to alertness or gastrointestinal complaints. Therefore, we investigated *what* nurses should eat during the night shift for optimal alertness levels and the least gastrointestinal complaints. Several factors were considered, including macronutrient composition, glycaemic load (GL), and timing of the meal.

In **Chapter 4** we showed that the associations between macronutrients and alertness depend on the time between consuming a meal and alertness testing. This was especially the case for carbohydrate and fat intake, but not for protein intake. Fat intake was associated with lower alertness levels shortly after consumption but associated with better alertness levels 2 to 3 hours after intake. Opposite time-dependent associations were found for carbohydrate intake. These time-dependent associations between macronutrient intake and cognitive performance, including alertness, were also observed in two other studies [1, 2]. Moreover, differences in timing may explain why some studies showed positive effects of carbohydrates on alertness while others showed negative effects [4-6].

Nonetheless, carbohydrates seem to influence alertness more than fat or protein [5], but this effect could depend on the type of carbohydrates. In **Chapter 6** we showed that consuming one or three low glycaemic loaded (LGL) meals during the night shift resulted in better alertness than three high glycaemic loaded (HGL) meals. Other studies that have investigated the effect of GL on alertness are limited. In addition, the results of these few other studies were inconsistent and could be due to differences in the time, size and composition of the meal [7, 8]. In our study the time, size and composition of the meals were similar across meal conditions, indicating that GL indeed could affect alertness levels.

Interestingly, the standardized test meals, either high or low in GL and consumed 1 to 2 hours before the alertness test (**Chapter 6**) did show differences in alertness between LGL and HGL, while in **Chapter 4** macronutrient intake 1 to 2 hours before the alertness test was not associated with alertness. On the other hand, overall energy intake 1 to 2 hours before the alertness test was associated with better alertness levels (**Chapter 4**). Besides the differences in study design (observational versus intervention), a possible explanation could be the differences in postprandial glucose response. So far, the exact underlying mechanisms of the relationship between macronutrient intake and alertness (performance) are not clear. However, some studies suggest that it is the significant rise and fall of glucose levels after food intake,

while others suggest that it is the stability of blood glucose levels [4, 6-8]. For both mechanisms, the food matrix plays an important role because it determines the absorption rate of glucose in the blood.

While the LGL meals provided better alertness levels than HGL meals, they also resulted in more *gastrointestinal complaints* when three LGL meals were consumed (**Chapter 6**). These higher scores may be explained by the use and amount of lactose and fructose in the LGL meals. These monosaccharides are known to induce gastrointestinal complaints to varying degree [9-11]. The total amount of these monosaccharides in the three LGL meals could have been more than what some nurses usually consume and therefore may have increased their gastrointestinal complaints [12, 13].

All in all, both **Chapters 4 and 6** contribute to understanding the association between macronutrient intake, as part of a mixed meal, and alertness levels during the night shift. Macronutrient intake during the night seems to be associated with alertness but this effect appears to be time-dependent. Moreover, LGL meals result in better alertness levels than HGL meals but could lead to more gastrointestinal complaints.

A final question is how *meal size*, in terms of energy intake, affects alertness levels during the night shift. In **Chapters 4 and 5** we observed that the frequency, timing, and macronutrient composition of the meals varied between nurses, but we could not analyse meal size separately from meal composition and the time between meals and alertness testing. Therefore, we could not draw any conclusions about the association between meal size and alertness, hunger feelings and gastrointestinal complaints.

Previous studies showed that a larger meal (~30% of estimated daily energy requirement (EER)) resulted in lower alertness levels, less hunger feelings and more gastrointestinal complaints than no meal or one small (~10% EER) meal. Given that a large meal decreased alertness and could compromise the safety of participants and patients, it was not ethically justified to offer a large meal in a real-life intervention study. Therefore, we only provided participants with small meals in our intervention study (**Chapter 6**). We also showed that compared to no meal, one or three small meals did not result in lower alertness levels and more gastrointestinal complaints, but reduced hunger feelings. Thus, multiple small meals appear to be an effective strategy in reducing hunger feelings while alertness levels and gastrointestinal complaints are not affected.

Eventually, these dietary factors should be translated into foods that fit within the (Dutch) dietary guidelines for a healthy diet and that are aligned with the taste preferences of night shift workers. Therefore it is imperative to know what the diet quality of the health care workers is and what improvements still can be made.

In this thesis, we assessed diet quality of female night shift workers in **Chapters 3 and 6 (Table 7.2)**. The total diet quality of night shift working nurses around the night shift was similar to the diet quality of a reference population (**Chapter 3**). Other studies also showed no consistent differences in diet quality between day and night shift workers [12-15].

Although the overall diet quality was not different we did find differences for some of the individual component scores. Night shift workers adhered better to the guidelines for fruit, sugar-containing beverages and alcohol, and worse to the guidelines for tea and fat and oils than the reference population (Chapter 3). These differences in the component scores for fruit, oils and fats were also found in some studies, but not all [14]. While we found higher scores (better adherence) for alcohol in **Chapter 3**, most studies found no differences between alcohol intake of night shift workers and day shift workers or reference population [14]. It must be noted that the nurses' score in Chapter 3 reflected diet quality during and around the night shift and it could therefore be expected that no alcohol was consumed during this time frame. However, the alcohol score obtained in Chapter 6 was similar to that of the reference population, as it reflected diet quality (including alcohol intake) over the last month. In contrast to our results (Chapters 3 and 6), other studies showed unfavourable scores for soft drinks for night shift workers compared to day shift workers [14]. However, this difference may be explained by underreporting of drinks in our studies (see the section about dietary assessment methods).

In summary, assessing diet quality may serve as a complementary approach when studying other dietary factors such as nutrient intake and meal frequency because it evaluates the total diet pattern [16]. It is especially interesting to investigate the underlying components. This provides insight into which components are of particular interest in specific shift work populations and enables targeted nutrition intervention strategies for the greatest health gain. For example, both the components 'Nuts' and 'Unhealthy choices' can be improved in our health care workers. (Chapters 3 and 6).

The component 'Unhealthy choices' consists of foods that are high in energy, saturated fat and sugar, and includes small cookies, large cookies and pastries, cakes, chips or pretzels, chocolate and savoury snacks (Chapter 2). In Chapter 3 we showed that especially the large cookies and pastries were eaten during the night shift and the small cookies outside the night shift. To determine why certain food choices were made, we investigated dietary taste patterns of night shift workers and compared those with a reference population (Chapter 3). It was expected that, due to fatigue, the nurses would revert their food choices more towards innate taste preferences, e.g. sweet, savoury and fatty foods [17-22]. Although we indeed found that night shift working nurses consumed more energy from 'sweet and fat' tasting foods during the night shift than outside the night shift, this did not result in a higher total daily energy intake of 'sweet and fat' tasting foods than the reference population. It thus remains unknown whether fatigue plays a role in food choices during the night shift.

By understanding these food choices, also from a sensory perspective, we may better guide or advise night shift workers on healthy food choices, that align with their preferences. A nutritional strategy could be to recommend foods *during* the night shift that are perceived as 'sweet and fat', but are healthier than large cookies and pastries, for example, a portion of semi-skimmed yoghurt with fruit. Since these foods were already consumed by some of the nurses, this could be a viable strategy. The yogurt with fruit also has a low glycaemic load (LGL) which corresponds with the LGL meal investigated in **Chapter 6**.

By aligning nutritional guidelines for night shift workers to their preferences it may increase compliance and therefore lead to a healthier diet. Previous studies showed that healthy diets had in general lower taste intensities, reflected by relatively higher energy and gram intakes of 'neutral' tasting foods (such as vegetables) and lower intakes of 'fat, salt and umami' and 'bitter' tasting foods (such as snacks and alcohol) [23, 24]. We found similar associations of diet quality with 'fat, salt and umami' tasting foods, but not with 'neutral' and 'bitter' tasting foods (**Chapter 3**). Thus, associations between dietary taste patterns and diet quality in night shift workers are not necessarily equivalent to the associations found in a general population.

Methodological considerations

Dietary assessment

To study the relationship between nutrition, health and alertness, accurate dietary assessment is crucial to guarantee the quality of studies and outcomes. However. accurately assessing dietary intake is challenging as current methods are prone to measurement errors, such as recall bias, socially desirable answers and participants' ability to correctly estimate portion size. These measurement errors can result in misreporting of daily intake and have probably also occurred in our studies. In addition. recalling dietary intake from the past (i.e. 24-hour dietary recalls (24hR)) could especially be hard when sleep-deprived which was the case with our night shift workers. We indeed identified potential misreporters in our observational study (Chapters 3, 4 and 5) and, in Chapter 3, 26.7% of the night shift workers was identified as a potential low energy reporter, while in the reference population this was 17.9%. This higher percentage among night shift workers may be explained by fatigue, but possibly also by underreporting of drinks. In both the 24hRs (Chapters 3, 4 and 5) and food diaries (Chapter 6) we noticed that drinks in particular were not well reported. For example some participants recorded drinks on one day but not during another day or no drinks were reported at all. Especially when calculating the DHD2015-index score based on the 24hRs this could have resulted in an overestimation of the component score of 'Sugar sweetened beverages' and underestimation of the component score of 'Tea'. This could, consequently, also have affected the results in **Chapter 3**. There we observed that a higher intake of 'sweet and sour' tasting foods was associated (borderline significance) with a higher DHD2015-index score, but a higher intake of 'Sugar sweetened beverages' would have increased energy intake of 'sweet and sour' tasting foods and lowered the diet quality, attenuating the association. Furthermore, in all studies we adjusted for the reported caffeine intake, however, the actual intake of caffeinated drinks could have been higher and thus explain a larger part of the variation in the association between diet and alertness. The actual association between (the different aspects of) diet and alertness may thus have been slightly over- or underestimated.

To deal with underreporting, we have performed sensitivity analysis in **Chapters 3, 4** and **5**. Only in **Chapter 3** this resulted in a minor difference in results as excluding

under reporters reduced the difference in the percentage of energy intake by 'sweet and sour' tasting foods between the night shift workers and the reference population.

Nowadays web-based and smartphone-based tools are widely used for dietary assessment instead of the more traditional paper- or telephone-based methods [25]. In this thesis various web-based and smartphone-based tools were used; FFQs (Chapter 2) were administered via the FFQ-toolTM [26], the Eetscore FFQs (Chapters 2 and 6) via Limesurvey and the Eetscore tool, the 24-hour dietary recalls (Chapters 3, 4 and 5) via Compl-eatTM [27] and the food record (Chapter 6) via Traqq® [28, 29]. Although these tools have been validated, each tool has its strengths and weaknesses [25]. To illustrate, technology-driven tools may be less prone to socially desirable answers due to the absence of a researcher. Yet, reporting errors remain due to the self-report nature of these tools (i.e., incomplete records, unusual amounts). Collected food intake data was thoroughly checked by well-trained research dieticians, errors were identified and corrected according to a standardized protocol (an example being the report of 200 pieces of broccoli instead of 200 grams of broccoli).

Lastly, the 24hR via Compl-eat is based on a normal eating-fasting rhythm and starts with recalling what was eaten during breakfast. However, for night shift workers breakfast is not necessarily breakfast but can also be a warm meal or eaten in the afternoon. We, therefore, adapted Compl-eat and referred to specific time periods instead of using specific meal labels such as breakfast, and the starting point was the evening meal prior to the night shift instead of breakfast. In agreement, the reporting periods in Traqq® (i.e., food diary) were also tailored to the eating-fasting rhythm of night shift workers. Tailoring dietary assessment methods to the population under study allows for a more accurate assessment of respondents' diet. In addition, using an innovative 2-hour recall (2hR) methodology in night shift workers can overcome the memory-related measurement error, which may be enhanced by fatigue [29].

The result for the diet quality scores (DHD2015-index scores) appear to be different across the chapters (**Table 7.2**). While in **Chapter 3** no difference in diet quality was observed between female night shift working nurses and a female reference population, in **Chapter 6** diet quality score of female night shift working nurses was lower than the score of women as assessed in **Chapter 2**. However, several factors contributed to these apparently different scores. First, the female population in

Chapter 2 was on average older than the night shift working nurses (Chapter 6) and as, in general, an older population scores higher on diet quality the results are not comparable. Second, the scores in Chapter 6 were calculated via the Eetscore FFQ, while the scores in Chapter 3 were calculated via two or three 24hR. Although multiple 24hRs will gain insight into the habitual intake of commonly consumed foods, more recalls are needed to capture the habitual intake of episodically consumed foods such as fish and legumes, which are two components of the DHD2015-index [25]. Therefore, the Eetscore FFQ was probably better in capturing the intake of these episodically consumed foods which is also reflected in higher scores for these components in Chapter 6 than in Chapter 3 and resulting in an overall higher diet quality score.

Thus, the used methods, the days (regular day or night shift) that were captured, and the age of participants were all factors that may have influenced the diet quality score. Therefore scores are not completely comparable, but they still provide insight into the overall diet quality and the underlying components.

All in all, measuring diet quality via an index score allows ranking participants according to their diet quality and consequently to investigate relationships with other outcome measures such as dietary taste patterns. When comparing overall diet quality scores between day and night shift workers or nightshift workers and a reference population, it is important to ensure that age, gender and dietary assessment methods are taken into account.

Table 7.2 Overview of the Dutch Healthy Diet 2015-index (DHD2015) scores, in mean ± SD, calculated in this thesis.

	Chapter 2	Chapter 2	Chapter 2	Chapter 2	Chapter 3	Chapter 3	Chapter 6
Study	EetMeetWeet	EetMeetWeet	EetMeetWeet	EetMeetWeet	Etmaal	DNFCS 2012-2017	Time to Eat
z	565	565	514	237	120	307	49
Population	General	General	General	General	Night shift workers	General	Night shift workers
Dietary assessment	FFQ	Eetscore FFQ	Eetscore FFQ	Eetscore FFQ	3x 24hR	2x 24hR	Eetscore FFQ
Gender	Both	Both	Women	Men	Women	Women	Women
Age, years	56.9 ± 15.8	56.9 ± 15.8	53.9 ± 16.2	63.4 ± 12.4	41.4 ± 11.9	38.2 ± 12.0	31.8 (24.3-46.6)
BMI, kg/m ²	24.2 ± 3.8	24.2 ± 3.8	23.7 ± 3.8	25.4 ± 3.6	25.0 ± 4.0	25.9 ± 5.2	25.1 (22.2-26.7)
Smokers, %	6.1 %	6.1%	2.0 %	% 8	7 5%	21.5 %	1.9 %
Day	Regular	Regular	Regular	Regular	Night shift	Regular	Regular
Total energy, kcal					1690 ± 471	1856 ± 532	
DHD2015-index:							
Vegetables	7.1 ± 3.0	6.9 ± 2.9	7.2 ± 2.8	5.7 ± 2.9	6.9 ± 2.7	6.3 ± 3.2	7.0 ± 2.6
Fruit	7.8 ± 3.2	7.6 ± 3.1	7.9 ±2.8	6.7 ± 3.3	7.3 ± 3.4	5.2 ± 3.9	7.6 ± 2.7
Wholegrain products	7.0 ± 3.1	7.7 ± 2.3	7.7 ±2.3	7.4 ± 2.5	5.3 ± 2.7	4.5 ± 2.9	7.9 ± 2.2
Legumes	8.2 ± 3.4	8.0 ± 3.4	8.0 ±3.4	8.3 ± 3.2	1.4 ± 3.4	0.9 ± 2.8	6.4 ± 4.0
Nuts	5.0 ± 4.0	5.6 ± 3.8	5.6 ±3.7	5.3 ± 3.9	2.0 ± 3.6	1.1 ± 2.9	4.9 ± 3.6
Dairy	6.3 ± 3.3	6.1 ± 3.3	5.9 ±3.3	6.6 ± 3.3	6.3 ± 3.2	6.0 ± 3.4	6.2 ± 3.1
Fish	•	6.7 ± 3.4	6.8 ±3.4	6.5 ± 3.5	1.3 ± 2.9	1.6 ± 3.2	5.2 ± 3.7
Теа	7.1 ± 3.6	5.9 ± 4.1	6.5 ±4.1	4.4 ± 4.1	4.7 ± 4.0	6.5 ± 4.1	4.8 ± 4.0
Fat and oils		6.2 ± 4.6	6.0 ±4.6	6.5 ± 4.5	3.3 ± 4.1	6.6 ± 4.4	6.9 ± 4.5
Coffee		7.9 ± 2.7	7.9 ±2.7	7.8 ± 2.8			7.6 ± 2.5
Red meat	9.2 ± 2.0	9.4 ± 1.8	9.6 ±1.4	9.1 ± 2.3	9.0 ± 2.5	9.2 ± 2.1	9.5 ± 1.4
Processed meat	6.0 ± 3.5	5.7 ± 3.5	6.3 ±3.3	4.1 ± 3.6	4.6 ± 3.9	4.7 ± 4.0	5.9 ± 3.0
Sugar-containing beverages	6.9 ± 3.5	7.9 ± 2.9	8.2 ±2.6	7.1 ± 3.3	7.4 ± 3.4	5.3 ± 4.3	8.1 ± 2.6
Alcohol	2.8 ± 4.4	7.9 ± 3.3	8.2 ±3.2	7.3 ± 3.2	9.9 ± 0.9	8.5 ± 3.3	8.2 ± 3.2
Sodium	7.7 ± 2.7	8.1 ± 2.2	8.5 ±1.6	7.1 ± 2.8	7.5 ± 2.9	7.9 ± 2.6	8.4 ± 2.0
Unhealthy choices	1.0 ± 2.6	3.6 ± 4.1	3.9 ±4.1	2.9 ± 4.0			2.6 ± 3.9
Total score 16 comp.		111.3 ± 17.3	114.4 ± 16.0	102.8 ± 18.0			107.0 ± 14.5
Total score 14 comp.					77.0 ± 14.9	74.2 ± 15.8	96.8 ± 13.3
Total score 13 comp.	82.2 ± 15.1	90.5 ± 15.5					

Abbreviations: DNFCS: Dutch National Food Consumption Survey, FFQ: Food Frequency Questionnaire, 24hR: 24-hour dietary recall, comp.: components.

Potential confounders

Caffeine

In Chapter 4. a higher caffeine intake was, unexpectedly, associated with poorer objective alertness levels. In addition, the number of lapses and subjective feeling of alertness were not associated with caffeine intake. Caffeine is known for its stimulating effect on cognitive performance [30] and doses from 32 to 300 mg have been shown to improve the cognitive domains attention, vigilance, and RT in both sleep deprived and well-rested individuals [30, 31]. Lower doses (below ~ 32-40 mg), which were observed in Chapters 4. 5 and 6. could have no effect while higher doses (above ~400mg) could lead to high arousal, thereby negatively impacting cognitive performance [30]. Therefore, explanations for the unexpected associations between caffeine and alertness could be that the intake of caffeine was too low to improve alertness or that individuals that were the most tired had the most caffeine (i.e. reverse causation). Moreover, it is suggested that simple tasks, such as a PVT to measure sustained alertness, are more susceptible to the effects of caffeine [30, 32]. However, in Chapters 4, 5, and 6 the PVT was performed in a real-life setting where nurses could be distracted by colleagues or alerted by patient calls. Therefore, the task was more complex than merely measuring sustained attention, and thus objective alertness levels could have been less affected by caffeine intake. Lastly, although caffeine is able to improve cognitive performance, including alertness, it is less effective in promoting subjective feelings of alertness [33, 34]. This could explain why we failed to observe an association between caffeine and subjective feelings of alertness, especially with the low doses.

Chronotype

Every human follows a sleep-wake cycle. However, there are inter-individual differences on how the sleep-wake cycle is aligned with the dark-light cycle. This preference is commonly referred to as morning or evening chronotype and changes over the lifespan [35, 36]. In general, children are more early (morning) chronotypes and this gradually changes to later (evening) chronotypes in their adolescence and after that chronotype may become earlier again, although some people will never shift back to morning [35, 36].

It is suggested that shift work tolerance depends on chronotype and that evening types tolerate night shifts better than morning types [37, 38]. Although chronotype is

associated with alertness, this does not necessarily lead to more or less errors during the different shifts (day, evening and night) [37].

Evening chronotypes consume foods on average an hour later than morning types while daily energy intake is similar [39]. In addition, they have a poorer diet quality than morning types [40]. However, it is suggested that evening types are not at higher risk of being overweight than morning types [40]. On the other hand, some studies showed that when a higher percentage of energy was consumed later during the day it was associated with overweight, and when it was consumed earlier in the day it was associated with lower odds of being overweight. This latter association was stronger in morning types [41-43]. Moreover, when food intake is not aligned with chronotype, and thus misaligned with the circadian rhythm of the energy metabolism, it is associated with higher risks of being overweight [44]. Since the food intake of night shift workers does not correspond to chronotype anyway, this could explain the higher risk of being overweight.

A way to assess chronotype is via the Munich Chronotype Questionnaire for shift workers (MCTQ^{shift}) [45]. However, to be able to chronotype shift workers, they should wake up without an alarm on free days after evening shifts [45], and this was not the case for most of our shift working nurses in **Chapter 6**. We were therefore not able to include chronotype in our analyses, which could have increased the power of our study. Given the impact chronotype can have on both alertness as well as (timing of) dietary intake, future research and dietary guidelines should consider chronotype.

Menstrual cycle

Women in the follicular phase have been shown to have lower alertness levels than in the luteal phase of the menstrual cycle and also than women using oral contraceptives and men [46, 47]. Menstrual cycle could thus have influenced alertness levels during the night shift.

In the observational study, described in **Chapters 4 and 5**, we did not collect data on the phase of the menstrual cycle and therefore could not analyse the influence of hormonal changes on alertness levels. In the intervention study in **Chapter 6** we did collect data on the menstrual cycle. However, most nurses had an intrauterine device (IUD), were continuously using oral contraceptives or had an irregular menstrual cycle, making it impossible to analyse the impact of the menstrual cycle on alertness levels.

Also, the menstrual cycle could have influenced food intake [48]. Women in the luteal phase may crave more chocolates, desserts and sweets, fried snacks, pastries and sausages [48]. This could have affected the dietary taste patterns in **Chapter 3**. On the other hand, differences *around* and *during* the night shift were assessed in the same participant and the days in both the night shift working study sample and reference population were randomly selected and could have covered all the days during the menstrual cycle and therefore had little impact on the results.

Future research should, when possible, include information about the menstrual cycle and examine the impact on alertness and food intake. Also, nutrition strategies for night shift workers may need to be personalized or aligned to the different phases of the menstrual phase.

Objective versus subjective alertness levels

In this thesis, we focused on alertness, as reduced alertness levels are a major factor in the increased safety risks of night shift workers [49-51]. Alertness can be measured subjectively (i.e., perceived alertness) and objectively (i.e., sustained alertness). A tool that has been proven to be sensitive for measuring objective alertness – or sleepiness – is the psychomotor vigilance task (PVT), which measures sustained attention. Subjective alertness can be perceived as a direct benefit that consequently could lead to higher motivation to comply with dietary intervention strategies. However, it must be noted that agreement between measures of objective and subjective alertness is often low, especially during the biological night [52, 53]. Individuals are likely to overestimate their alertness levels, especially during the night shift [53]. Therefore, with regard to safety, objective alertness is probably the most reliable measurement.

Study design

Setting

All our studies were performed in a real-life setting. Therefore, the obtained results are more relevant for practice. Performing the intervention study (**Chapter 6**) in a real-life setting also supports the feasibility of adhering to the nutritional strategies in daily life. However, this real-life setting also comes with some limitations. Similar to the observational study (**Chapters 3, 4 and 5**) we had some missing data and we were not able to adjust for additional potential confounders or predictors, such as sleep durations and quality, menstrual cycle, chronotype, and workload. However, by using

linear mixed model analysis we were able to deal with missing data and, as discussed earlier, by randomization and the cross-over design we expect that the unmeasured covariates affected the results only to a small extent.

Study populations

Participants in this thesis primarily consisted of women. In general, it is increasingly recognized that sex differences affect health outcomes. This also applies to the effects of circadian misalignment on energy balance and cognitive performance (including alertness) [54]. Women are more prone to the impact of night shift work on health and safety than men and therefore more research is needed on women in particular [54]. Furthermore, men have a relatively higher preference for savoury foods while women in general prefer sweet tasting foods [55, 56]. In addition, women have a better diet quality than men and consume more fruit, vegetables and tea and less red and processed meat, sugar containing beverages and alcohol than men [57] (**Chapter 2**). Therefore, our findings are not directly generalizable to male night shift workers.

Second, the studies performed in this thesis mainly included nurses. The participating nurses might have been more interested in the role of nutrition in health, well-being and safety than other nurses or other night shift professionals, and could therefore be health-oriented. In an unhealthier study sample, there may be more variation in dietary intake and this could potentially result in more significant associations with alertness and gastrointestinal complaints. The type of work might have also affected alertness levels; work that is more monotonous and less distracting (driving or working in a factory) may lead to lower alertness levels and therefore be more susceptible to changes in dietary intake. Therefore, although the results of this thesis cannot be directly generalized to other night shift professions, our results are particularly relevant for taxi drivers, bus drivers and factory workers, as their work requires sustained alertness and dietary interventions could significantly improve alertness levels. Moreover, the work schedule could also affect alertness levels. Participating nurses in this study worked irregular work schedules which could consequently result in more irregular dietary patterns. Therefore, nutrition strategies, including improvements in the dietary pattern could have had greater effects on these nurses than on night shift workers with regular forward rotating shift work schedules. However, future research is needed to investigate whether this is actually the case and whether these findings hold true for other night shift working populations.

(Practical) implications and suggestions for further research

Given the many negative health consequences of night shifts on shift workers and the possible impact of diet on this matter, it is important that specific dietary guidelines are formulated for night shift workers. A recent overview of available dietary advice for shift workers showed that there are several dietary guidelines available, but only a few are supported by evidence [58]. We have added our findings to a European guideline [4] to show what this thesis adds to the level of evidence and what new insights it provides (**Table 7.3**). However there is still a need for more research in this area as, to this day, only a few nutrition intervention studies have been conducted in night shift workers [43, 59-61] or during simulated night shifts [2, 3, 62-65]. In the following paragraphs some suggestions for future research are given.

First, to be able to set up evidence-based dietary guidelines, the results of the intervention study described in **Chapter 6** should be replicated, but also address other night shift populations. Moreover, more research is needed to build on these results and to study the long-term effects on health. This also requires more insight into the underlying mechanisms of the relationship between nutrition and health during the night shift. Therefore, measurements of blood glucose, insulin, free fatty acids and triglycerides should be included. Also, fluid intake should be closely monitored, as dehydration could negatively affect cognitive performance [66]. This is especially important when health care workers have to wear protective suits, such as during the covid-19 pandemic, and thus maintaining a good fluid balance can be compromised by both sweating and not being able to easily consume drinks.

Second, we have shown that a maximum of three small meals will not necessarily result in a deterioration of alertness levels and gastrointestinal complaints. Our results also suggested that a maximum of two meals may already be sufficient to reduce hunger feelings. However, this has yet to be tested. Also, the timing of these meals requires attention. Some studies suggest that a small meal should be eaten at the end of the night shift [3, 62]. On the other hand, alertness levels are lowest around 4:00 AM and, based on the results of **Chapter 4**, consuming food one to two hours before that time (around 2:00 AM) is least likely to further deteriorate alertness levels. This food should be low in fat and HGL carbohydrates. Likewise, the meal at the end of the

night shift could be eaten around 6:00 AM, which is about one to two hours before night shift workers are going home and be on the road.

Another point of attention in future research is the effect of nutrition intervention studies on gastrointestinal complaints of night shift workers. On average the complaints were relatively mild, and the severity was lower than normally experienced during their night shifts (**Chapter 6**). The intervention study itself appeared to already lead to less gastrointestinal complaints than normal during the night shift. It would also be interesting to know how the gastrointestinal complaints during the night shift relate to those during the day shift. Moreover, some nurses usually consume larger meals or unhealthier snacks (**Chapters 3 and 5**) than during the intervention study (**Chapter 6**). These meals and snacks could contain more fat and sugar, which would perhaps trigger the gastrointestinal tract to a larger extent [11].

Moreover, it should also be investigated what has the greatest impact on improving the health and safety of night shift workers; a more *regular* and overall healthier diet with a maximum of two small meals at night, or not eating at night to disrupt the biological clock as little as possible. In addition, it would be interesting to know how this dietary intervention study relates to the shift workers' usual diet or chronotype. It has been suggested that an intervention closely to their habitual dietary patterns will be most effective [4]. This could also be related to their chronotype preference.

Lastly, these nutrition intervention strategies should also be implemented together with other strategies, such as day-light lamps, forward rotating schedules and napping, and investigating which strategies have combined the highest impact on reducing the negative consequences of shift work. Together this can result in evidence-based guidelines for night shift workers and used as a vital part of occupational health and safety management programs in shift work.

Table 7.3 Overview of dietary guidelines presented by Lowden et al [6] and what this thesis adds to the level of evidence

Guidelines from Lowden et al [6]

General guidelines

Avoid eating, or at least restrict energy intake, between midnight and 06.00 hours, and try to eat at the beginning and end of the shift.

Avoid "large meals" (>20% of daily energy intake) 1–2 hours prior to the main daily sleep episode.

Provide a variety of food choices: complete or vegetarian meals and high-quality snacks are recommended. Avoid foods and beverages classified as low-quality snacks.

Maintain a healthy lifestyle with exercise, regular meal times, and good sleep hygiene when not working

Specific guidelines for shift work

Eat breakfast before day sleep to avoid wakening due to hunger.

Stick as closely as possible to a normal day and night pattern of food intake.

Divide the 24-hour intake into eating events with three satiating meals each contributing 20–35% of 24-hour intakes. The higher the energy needs, the more frequent the eating should be.

Avoid over-reliance on (high-energy content) convenience foods and high-carbohydrate foods during the shift. Instead choose vegetable soups, salads, fruit salads, yoghurt, wholegrain sandwiches, cheese or cottage cheese (topped with slices of fruits), boiled egg, nuts, and green tea (promoting antioxidant activity), although this may not be palatable to some.

Avoid sugar-rich products such as soft drinks, bakery items, sweets, and non-fibre carbohydrate foods (high glycaemic load) like white bread.

Additional information from this thesis

Not eating during the night shift is feasible in reallife and will not result in lower alertness levels compared to eating 1 or 3 small meals (~10% of daily energy intake)

Diet quality should be improved in night shift working nurses, eating healthy snacks could fit in a healthy diet.

These high-quality snacks should not contain too much fat or high GI carbohydrates.

Align these foods with taste preferences

Not eating during the night shift is feasible, but when hungry, eating 1 or 3 small meals (10% of daily energy intake) with a low glycaemic load will not result in lower alertness levels than not eating.

The foods listed in the left column fit in a healthy diet

Carbohydrates, especially with a high GI so providing high glycaemic load may result in lower alertness levels during the night shift.

Align provided foods with taste preferences

These products do not fit in the Dutch dietary quidelines (low diet quality)

High glycaemic loaded meals may result in lower alertness levels during the night shift.

Not eating during the night shift is feasible in reallife and will not result in lower alertness levels compared to eating 1 or 3 small meals (~10% of daily energy intake per meal)

Conclusions

To prevent further disruption of the circadian rhythm by food intake it is, theoretically, best to eat as little as possible during the night shift. Not eating during the night shift is feasible in real-life and will not result in lower alertness levels than eating one or three small meals. However, consuming up to three small meals with a low glycaemic load can be an effective strategy in reducing hunger feelings during the night shift, while alertness levels are maintained. This strategy may lead to more gastrointestinal complaints and night shift workers can best experience themselves whether this also applies to them. Future research is needed to investigate how these dietary intervention strategies relates to the shift workers' usual diet and whether these strategies lead to better alertness and fewer gastrointestinal complaints than usual. Moreover, more research is needed to build on the results of this thesis and to study the long-term effects on health. This also requires more insight in the underlying mechanisms of the relationship between nutrition and health during the night shift. These underlying mechanisms may also provide more insight into the time-dependent associations between macronutrient intake and alertness we observed.

The diet quality of night shift working nurses did not differ from a reference population but monitoring dietary quality can still serve as a complementary approach when studying other dietary factors such as nutrient intake and meal frequency because it evaluates the total diet pattern. It is particularly interesting to investigate the underlying components to potentially target nutrition intervention strategies where the greatest health gain can be achieved.

Using a taste database in addition to a diet composition database gave an extra opportunity to not only investigate the diet of night shift working nurses from a nutrient and diet quality perspective, but also from a sensory perspective. Moreover, associations between dietary taste patterns and diet quality in night shift workers are not necessarily equivalent to the associations found in a general population. Shift worker-specific associations can be used to guide development of tailored nutrition interventions. Aligning nutritional interventions for night shift workers to their preferences may increase compliance, invoke dietary behaviour change, and thus lead to a healthier diet.

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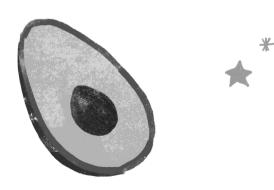
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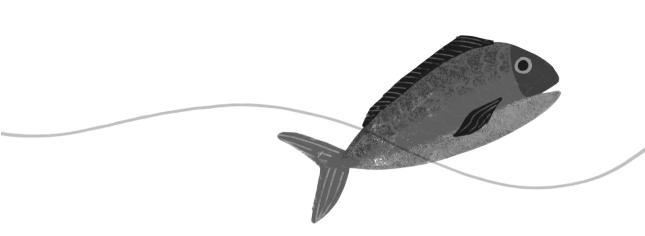
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Summary



Night shift work is associated with increased health and safety risks due to a mismatch between internal biological timing and the sleep-wake schedule. Direct consequences night shift workers could experience during the night shift are reduced alertness levels, increased hunger feelings, and gastrointestinal complaints. Nowadays, there is increased recognition of the relationship between diet, biological rhythms and metabolism, and their association with health and disease. This interaction is also referred to as chrono-nutrition. The field of chrono-nutrition focuses on the influence of meal timing, meal composition, meal size, meal frequency and meal regularity on the biological clock and vice versa. Therefore, nutrition strategies including adaptations in meal composition, meal frequency and meal timing may alleviate the reduced alertness levels and increased hunger feelings and gastrointestinal complaints. However, it is unknown what nutrition strategies work best.

Therefore, the overall aim of this thesis was to investigate which nutrition strategies can be applied to night shift workers in health care resulting in the most optimal alertness levels and the least hunger feelings and gastrointestinal complaints, or in other words, that provide the best safety and perceived well-being.

In **Chapter 2** we described the development and evaluation of the Eetscore FFQ, a short screener specifically developed to assess the DHD2015-index score. This cross-sectional study consisted of 751 participants, aged 19–91 years. Our results showed that, compared to a full-length FFQ, the Eetscore FFQ was considered an acceptable screener to rank participants according to their diet quality, but relatively poor for assessing the level of diet quality for an individual. Moreover, the Eetscore FFQ showed good to excellent reproducibility and is, therefore, suitable to monitor changes in the diet quality of individuals.

In **Chapter 3** we assessed diet quality and studied the dietary patterns of night shift workers from a taste perspective. In an observational study we assessed dietary taste patterns of 120 female night shift workers and compared them to 307 females of a reference population. We observed that *during* night shifts, nurses consumed a significantly higher energy percentage of 'neutral', 'sweet and sour' and 'sweet and fat' tasting foods and a lower energy percentage of 'fat' and 'bitter' tasting foods than *outside* the night shift. Overall, they consumed a larger energy percentage from foods

with a 'sweet and sour' taste and a lower energy percentage from foods with a 'bitter' taste than the reference population, irrespective of age, BMI and smoking status. Moreover, we showed that a higher intake of 'fat' and 'fat, salt and umami' tasting foods were associated with lower diet quality.

In **Chapter 4** we investigated the association between macronutrient composition with objective and subjective alertness, during different time periods throughout the night shift of 128 nurses in an observational study. We found opposite, time-dependent associations with objective alertness levels for fat and carbohydrate intake, with a kind of tipping point 1 to 2 hours before the psychomotor vigilance test (PVT). Although no associations were found between the intake of any of the macronutrients (protein, fat and carbohydrates) 1 to 2 hours before the PVT and objective alertness levels, an overall higher energy intake 1 to 2 hours before the PVT was associated with better alertness levels. We did not find an association between protein intake and alertness levels for any time period. Also, no associations were found between macronutrient intake and subjective levels of alertness.

Subsequently, with data from the same observational study, in **Chapter 5** we examined the association of the number of eating occasions and total energy intake during the night shift with objective and subjective alertness and gastrointestinal complaints in 118 female nurses. A total of 79% of the nurses experienced at least one gastrointestinal complaint during the night shift of which growling intestines and bloating were the most prevalent. We observed that more eating occasions during the night shift were associated with faster reaction times and fewer lapses (delayed reaction time >500 ms). However, the number of eating occasions was not associated with subjective alertness or GI complaints. Also, total energy intake during the night shift was associated with neither objective and subjective alertness nor GI complaints.

In an intervention study, a two-armed randomized cross-over trial (**Chapter 6**), we investigated the effect of 1 or 3 small meals, either with a low (1LGL and 3LGL) or high glycaemic load (1HGL and 3HGL), compared to no meal (0NGL) during the night shift on alertness levels, hunger feelings and gastrointestinal complaints in 51 female health care workers. We found no differences in alertness levels and gastrointestinal complaints between the 0NGL and the other meal conditions. We showed that the LGL

meals during the night shift resulted in the best alertness levels. Results for subjective levels of alertness, although not statistically significant, were overall in line with this. The least hunger feelings were reported when three meals were consumed during the night shift. Nurses experienced gastrointestinal complaints in varying degrees in all meal conditions, but most in the 3LGL condition. Nevertheless, the scores for each gastrointestinal complaint in all meal conditions were relatively low compared to their usual gastrointestinal complaints score.

To summarize, for long-term health, it is theoretically best to eat as little as possible during the night shift. Not eating during the night shift is feasible in real-life and will not result in lower alertness levels than eating one or three small meals. However, consuming up to three small meals with a low glycaemic load can effectively reduce hunger feelings during the night shift, while alertness levels are maintained. This strategy may lead to more gastrointestinal complaints in some night shift workers and therefore they can best experience themselves whether this also applies to them.

The overall current diet quality of night shift working nurses did not differ from a reference population. However, monitoring dietary quality may be very valuable as a complementary approach when studying other dietary factors such as nutrient intake and meal frequency because it evaluates the total diet pattern. It is particularly interesting to investigate the underlying components to potentially target nutrition intervention strategies where the greatest health gain can be achieved. Moreover, to improve the diet quality of night shift workers and to increase compliance to nutrition intervention strategies it seems to be important to include taste preferences in nutrition strategies.

Altogether, this thesis gave more clarity on the relationship of nutrition with alertness and gastrointestinal complaints of night shift workers which can be used to develop evidenced-based dietary guidelines for night shift workers as a vital part of occupational health and safety management programs in shift work.

Future research is needed to investigate how these dietary intervention strategies relate to the night shift workers' usual diet and whether these strategies lead to better alertness and fewer gastrointestinal complaints than usual. Moreover, more research

is needed to build on these results and to study the long-term effects on health. This also requires more insight into the underlying mechanisms of the relationship between nutrition and health during the night shift. These underlying mechanisms may also provide more insight into the time-dependent associations between macronutrient intake and alertness which we observed.

Dutch summary Nederlandse samenvatting

Het werken in de nachtdienst gaat samen met verhoogde gezondheids- en veiligheidsrisico's vanwege een mismatch tussen het interne biologische ritme en slaap-waakschema. Directe gevolgen die nachtdienstmedewerkers tijdens de nachtdienst kunnen ervaren zijn verminderde alertheid, meer hongergevoel en maagen darmklachten. Tegenwoordig is er steeds meer erkenning voor de associatie tussen voeding, biologisch ritme en metabolisme in relatie met gezondheid en ziekte. Deze interactie wordt ook wel chronovoeding (*chrono-nutrition*) genoemd. Het vakgebied van chronovoeding richt zich op de invloed van maaltijdtiming, -samenstelling, -grootte, -frequentie en -regelmaat van de biologische klok en *vice versa*. Daarom kunnen voedingsstrategieën, waaronder aanpassingen in de maaltijdtiming, -samenstelling en -frequentie, verminderde alertheid, verhoogd hongergevoel en maag- en darmklachten verlichten. Het is echter niet bekend welke voedingsstrategieën het best werken.

Daarom was het algemene doel van dit proefschrift om te onderzoeken welke voedingsstrategieën kunnen worden toegepast voor nachtdienstmedewerkers in de gezondheidzorg om te zorgen voor de meest optimale alertheidniveaus en de minste hongergevoelens en maag- en darmklachten met als gevolg om te zorgen voor de beste veiligheid en ervaren welzijn.

In **hoofdstuk 2** beschreven we de ontwikkeling en evaluatie van de Eetscore voedselfrequentievragenlijst (Eetscore FFQ), een korte screener die speciaal is ontwikkeld om de mate waarin men voldoet aan de richtlijnen Gezonde Voeding aan de hand van DHD2015-index score te kunnen vaststellen. Dit werd gedaan in een cross-sectionele studie die bestond uit 751 deelnemers in de leeftijd van 19 tot 91 jaar. Onze resultaten toonden aan dat, in vergelijking met een volledige FFQ, de Eetscore FFQ een acceptabele screener was om deelnemers te rangschikken op basis van hun voedingskwaliteit, maar relatief slecht voor het beoordelen van het niveau van voedingskwaliteit voor een individu. Bovendien toonde de Eetscore FFQ een goede tot uitstekende reproduceerbaarheid en is daarom geschikt om veranderingen in de voedingskwaliteit van individuen te monitoren.

In **hoofdstuk 3** evalueerden we de kwaliteit van de voedingspatronen van nachtdienstmedewerkers en bestudeerden we deze voedingspatronen ook vanuit een smaakperspectief. In een observationele studie beoordeelden we

voedingssmaakpatronen van 120 vrouwelijke nachtdienstmedewerkers door deze te vergelijken met die van 307 vrouwen uit een referentiepopulatie. We merkten op dat verpleegkundigen *tijdens* de nachtdienst een significant hoger energiepercentage van 'neutraal', 'zoet en zuur' en 'zoet en vet' smakende voedingsmiddelen consumeerden en een lager energiepercentage van 'vet' en 'bitter' smakende voedingsmiddelen dan *buiten* de nachtdienst. Over het algemeen consumeerden ze een groter energiepercentage uit voedingsmiddelen met een 'zoetzure' smaak en een lager energiepercentage uit voedingsmiddelen met een 'bittere' smaak dan de referentiepopulatie, ongeacht leeftijd, BMI en rookstatus. Bovendien toonden we aan dat een hogere inname van 'vet' en 'vet, zout en umami' smakende voedingsmiddelen geassocieerd was met een lagere voedingskwaliteit.

In hoofdstuk 4 onderzochten we in een observationele studie de associatie tussen de macronutrientensamenstelling van de voeding met objectieve en subjectieve alertheid van 128 verpleegkundigen gedurende verschillende tijdsperioden tijdens de nachtdienst van . We vonden tegenovergestelde, tijdsafhankelijke associaties tussen objectieve alertheidsniveaus en vet- en koolhydraatinname, met een omslagpunt 1 tot 2 uur voor de alertheidstest (PVT). Hierbij was vetinname geassocieerd met verminderde alertheid direct na consumptie, maar leek geassocieerd met een betere alertheid 2 tot 3 uur na consumptie. Het tegenovergestelde lijkt aannemelijk te zijn voor de inname van koolhydraten. Alhoewel er geen associaties werden gevonden tussen de inname van een van de macronutriënten (eiwitten, vetten en koolhydraten) 1 tot 2 uur vóór de PVT en objectieve alertheidsniveaus, was een algehele hogere energieinname 1 tot 2 uur vóór de PVT geassocieerd met betere alertheidsniveaus. We vonden geen verband tussen eiwitinname en alertheidsniveaus voor een bepaalde tijdsperiode. Ook werden er geen verband gezien tussen de macronutriënteninname en subjectieve alertheidniveaus.

Vervolgens onderzochten we, met gegevens uit hetzelfde observationele onderzoek, in **hoofdstuk 5** de associatie van het aantal eetmomenten en de totale energie-inname tijdens de nachtdienst met objectieve en subjectieve alertheid en maag- en darmklachten bij 118 vrouwelijke verpleegkundigen. In totaal ervoer 79% van de verpleegkundigen tijdens de nachtdienst minstens één maag- en darmklacht waarvan rommelende darmen en een opgeblazen gevoel het meest voorkwamen. We zagen

dat meer eetmomenten tijdens de nachtdienst waren geassocieerd met snellere reactietijden en minder fouten (vertraagde reactietijd >500 ms). Het aantal eetmomenten was echter niet geassocieerd met subjectieve alertheid of maag- en darmklachten. Ook de totale energie-inname tijdens de nachtdienst was noch met objectieve en subjectieve alertheid, noch met maag- en darmklachten geassocieerd.

In een interventiestudie, een tweearmige gerandomiseerde cross-over studie (hoofdstuk 6), onderzochten we het effect van het gebruik van 1 of 3 kleine maaltijden, hetzii met een lage (1LGL en 3LGL) of hoge glycemische last (1HGL en 3HGL), in vergelijking met geen maaltijd (0NGL) tijdens de nachtdienst op alertheidsniveaus. hongergevoelens en maag- en darmklachten klachten bij 51 vrouwelijke gezondheidswerkers. We vonden geen verschillen in alertheidsniveaus en maag- en darmklachten tussen de 0NGL en de andere maaltiidcondities. We toonden aan dat de LGL-maaltiiden tiidens de nachtdienst resulteerden in de beste alertheidsniveaus. De resultaten voor subjectieve niveaus van alertheid, hoewel niet statistisch significant. waren over het algemeen in overeenstemming hiermee. Niet verrassend werden de minste hongergevoelens gemeld wanneer drie maaltijden werden geconsumeerd tijdens de nachtdienst. Verpleegkundigen ervoeren maag- en darmklachten in verschillende mate in alle maaltijdomstandigheden, maar de meeste in de 3LGLconditie. Desalniettemin waren de scores voor elke maag- en darmklacht in alle maaltiidcondities relatief laag in vergeliiking met hun gebruikeliike maag- en darmklachten tiidens de nachtdienst.

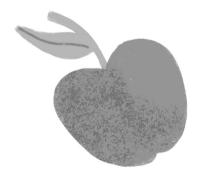
Samenvattend, is het theoretisch het beste om zo min mogelijk te eten tijdens de nachtdienst. Niet eten tijdens de nachtdienst is haalbaar in het echte leven en zal niet resulteren in verminderde alertheidsniveaus dan het eten van een of drie kleine maaltijden. Echter, het consumeren van maximaal drie kleine maaltijden met een lage glycemische last kan effectief het hongergevoel tijdens de nachtdienst verminderen, terwijl de alertheidsniveaus worden gehandhaafd. Deze strategie kan bij sommige nachtploegwerkers echter wel leiden tot meer maag- en darmklachten en daardoor kunnen zij het beste zelf ervaren of dit ook voor hen geldt.

De voedingskwaliteit van nachtdienstwerkende verpleegkundigen verschilde niet van die van een referentiepopulatie. Het monitoren van de voedingskwaliteit kan echter

zeer waardevol zijn voor het bestuderen van andere voedingsfactoren zoals de maaltijdsamenstelling en de maaltijdfrequentie, voor het evalueren van het totale voedingspatroon. Het is daarnaast interessant om de onderliggende voedingscomponenten te evalueren om mogelijk voedingsinterventiestrategieën te richten op waar de grootste gezondheidswinst kan worden bereikt. Bovendien, om de voedingskwaliteit van nachtploegwerkers te verbeteren en de naleving van voedingsinterventiestrategieën te vergroten, lijkt het belangrijk om smaakvoorkeuren op te nemen in voedingsstrategieën.

Al met al gaf dit proefschrift meer duidelijkheid over de relatie tussen voeding en alertheid en maag- en darmklachten van nachtdienstmedewerkers. Deze informatie kan worden gebruikt om evidence-based voedingsrichtlijnen voor nachtdienstmedewerkers te ontwikkelen. Deze richtlijnen kunnen dan vervolgens als essentieel onderdeel opgenomen worden in het beleid van bedrijven om de gezondheid en veiligheid van ploegendienstmedewerkers te optimaliseren.

Toekomstia onderzoek nodia te onderzoeken is om hoe deze voedingsinterventiestrategieën zich verhouden tot de gebruikelijke voeding van de nachtdienstmedewerkers en of deze strategieën leiden tot een betere alertheid en minder maag- en darmklachten dan normaal. Bovendien is meer onderzoek nodig om op deze resultaten voort te bouwen en de langetermijneffecten op de gezondheid te bestuderen. Dit vraagt ook om meer inzicht in de onderliggende mechanismen van de relatie tussen voeding en gezondheid tijdens de nachtdienst. Deze onderliggende mechanismen kunnen ook meer inzicht geven in de tijdsafhankelijke associaties tussen de macronutriënteninname en alertheid die we hebben waargenomen.



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Marc, I am glad we are still in touch! Thank you for your friendship and interest. Hopefully, we can meet again in real life soon!

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About the author



Curriculum Vitae

Mariëlle was born on the 22nd of May 1988 in Alphen aan den Rijn, the Netherlands. After completing secondary school (Voortgezet Wetenschappelijk Onderwijs) at Hondsrug College in Emmen (2006), she studied Nutrition and Dietetics at the Hanze University of Applied Sciences in Groningen. During her BSc. she followed a minor in Applied Psychology. In 2011 she started her MSc. Nutrition and Health at Wageningen University and Research (WUR). In 2014, she



completed her MSc. with an internship at Erasmus Medical Centre where she guided dietitians in conducting research into the effectiveness of their dietary consultations in various patient groups.

After graduating she continued working at WUR. First as a student assistant where she provided support for several educational courses, and later on as a research assistant in several projects. Two of those projects included the development and evaluation of the Eetscore tool and the Nutriprofiel tool. In 2015, she was appointed on the project 'Shiftwork and Nutrition' where she set up and carried out an observational study in night shift workers. This study investigated the association of diet composition, meal timing and frequency with alertness, gastrointestinal complaints and sleep in night shift working nurses. In 2017, she continued working on this topic by starting a PhD in the Time to Taste project at the WUR. This project aimed to set up a dietary intervention to improve the wellbeing and fitness of people with a disrupted circadian rhythm.

During her PhD project, Mariëlle attended several courses and presented at national and international conferences. In 2018, she was awarded with the prize for best oral presentation at the meeting of the British Feeding and Drinking Group (BFDG). In 2022, she won the poster pitch prize at the VoedingNL conference. Furthermore, she was involved in teaching and supervising BSc. and MSc. students and was part of the PhD committee where she, among other things, organized and cooked, together with fellow PhDs, a Christmas diner. Moreover, she was part of the organisation committee of the International Conference on Diet and Activity Methods (ICDAM) (online) conference in 2020. Mariëlle is currently working as a public health researcher at the Municipal Health Service (GGD) in the Utrecht region.

List of publications

Publications in peer-reviewed journals

- de Rijk, M.G., van Doorn, G., van Egmond, A., Visser, W., & de Roos, N.M. (2016). Veranderingen in serumfosfaat bij chronische hemodialysepatiënten met verschillende etnische achtergronden al dan niet na een dieetconsult. Nederlands Tijdschrift voor Dietisten, 71(6).
- Looman, M., Feskens, E.J., **de Rijk, M.**, Meijboom, S., Biesbroek, S., Temme, E.H., de Vries, J., & Geelen, A. (2017). Development and evaluation of the Dutch Healthy Diet index 2015. Public Health Nutr, 1-11. doi:10.1017/S136898001700091X
- de Vries, R., Morquecho-Campos, P., de Vet, E., **de Rijk, M.**, Postma, E., de Graaf, K., Engel, B., & Boesveldt, S. (2020). Human spatial memory implicitly prioritizes high-calorie foods. Sci Rep, 10(1), 15174. doi:10.1038/s41598-020-72570-x
- Brouwer-Brolsma, E.M., Lucassen, D., **de Rijk, M.G.**, Slotegraaf, A., Perenboom, C., Borgonjen, K., Siebelink, E., Feskens, E. J. M., & de Vries, J.H.M. (2020). Dietary Intake Assessment: From Traditional Paper-Pencil Questionnaires to Technology-Based Tools. Paper presented at the IFIP Advances in Information and Communication Technology, Cham.
- de Rijk, M.G., van Eekelen, A.P.J., Kaldenberg, E., Boesveldt, S., te Woerd, W., Holwerda, T., Lansink, C.J.M., Feskens, E.J.M., & de Vries, J.H.M. (2021). The association between eating frequency with alertness and gastrointestinal complaints in nurses during the night shift. J Sleep Res, 30(5), e13306. doi:10.1111/jsr.13306
- de Rijk, M.G., Slotegraaf, A.I., Brouwer-Brolsma, E.M., Perenboom, C.W.M., Feskens, E.J.M., & de Vries, J.H.M. (2021). Development and evaluation of a diet quality screener to assess adherence to the Dutch food-based dietary guidelines. Br J Nutr, 1-11. doi:10.1017/S0007114521004499

Expected publications

- de Rijk, M.G., van Eekelen, A.P.J., Boesveldt, S., Kaldenberg, E., Holwerda, T., Lansink, C.J.M., Feskens, E.J.M., & de Vries, J.H.M. (2022). Macronutrient intake and alertness during night shifts the time interval matters. Human Nutrition & Health. Wageningen University & Research. Wageningen.
- de Rijk, M.G., de Vries, J.H.M., Mars, M., Feskens, E.J.M., & Boesveldt, S. (2022). Dietary taste patterns and diet quality of female nurses around the night shift. Human Nutrition & Health. Wageningen University & Research. Wageningen.
- de Rijk, M.G., Boesveldt, S., Feskens, E.J.M., & de Vries, J.H.M. (2023). The effect of meal frequency and glycaemic load during the night shift on alertness, hunger feelings and gastrointestinal complaints in female health care workers – a twoarmed randomized cross-over trial. Human Nutrition & Health. Wageningen University & Research. Wageningen.

Overview of completed training activities

Discipline specific activities	Organizer and location	Year
Good Clinical Practice course	HNH, Wageningen, NL	2016
Werkgroep Voeding	WeVo, Wageningen, NL	2016
Voeding Nederland 2016	AVZ, NAV, DCN, NVD, NVVL, Utrecht, NL	2016
Voeding Nederland 2018	VoedingNL, Utrecht, NL	2018
Sensory Perception and Food Preference	VLAG, Wageningen, NL	2018
Exposure Assessment in Nutrition Research	VLAG, Wageningen, NL	2018
Nutritional Science Days	NAV, Heeze, NL	2018
Symposium Geef Slaap de Ruimte	ZGV, Ede, NL	2018
Voeding Nederland 2019	AVZ, NAV, DCN, NVD, NVVL, Utrecht, NL	2019
British Feeding and Drinking Group	BFDG, Swansea, GB	2019
TiFN retreat	TiFN, Hilvarenbeek, NL	2019
Nutritional Science Days	NAV, Heeze, NL	2019
13th European Nutrition Conference FENS	FENS, Dublin, IE	2019
Nutrition 2020	ASN, Online	2020
International Conference on Diet and Activity Methods	ICDAM, Online	2020
Pangborn Sensory Science Symposium	Pangborn, Online	2021
VoedingNL 2022	AVZ, NAV, DCN, NVD, NVVL, Utrecht, NL	2022

General courses	Organizar and leastion	Year
General courses	Organizer and location	Tear
PhD week	VLAG, Baarlo, NL	2017
PhD Workshop Carousel	WGS, Wageningen, NL	2017
Scientific Writing	WGS, Wageningen, NL	2018
Masterclass Mixed Models	HNH, Wageningen, NL	2017
Modelling of Habitual Dietary Intake	VLAG, Wageningen, NL	2017
Workshop Teaching and Supervising Thesis Students	VLAG, Wageningen, NL	2018
Speaking Skills	WGS, Wageningen, NL	2019
Career Perspectives	WGS, Wageningen, NL	2021

Other activities	Organizer and location	Year
Preparation of research proposal	HNH, Wageningen, NL	2017
PhD study tour to UK	HNH, GB	2017
Biweekly meetings Chair group Global Nutrition	HNH, Wageningen, NL	2017-2021
Biweekly meetings Chair group Sensory Science	HNH, Wageningen, NL	2017-2021
Bimonthly project meetings	TiFN, Wageningen, NL	2017-2021

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