ALINEA

NUTRITION

NOVEMBER 2021

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Koopman ADM, Rauh SP, van 't Riet E, Groeneveld L, van der Heijden AA, Elders PJ, Dekker JM, Nijpels G, Beulens JW, Rutters F. The Association between Social Jetlag, the Metabolic Syndrome, and Type 2 Diabetes Mellitus in the General Population: The New Hoorn Study. J Biol Rhythms. 2017 Aug;32(4):359-368.

What We Know, Think We Know, or Are Starting to Know

When was the last time you had jetlag? You may have noticed, depending on how many time zones you crossed, that for a few days your sleep was disturbed, and your gut felt really out of sorts when you ate. What you wouldn't have noticed would have been what was going on 'under the hood', including the fact that you would likely be experiencing some glucose intolerance and insulin resistance [1,2].

Why can't you just fly to Sydney, hop off the flight and get on with your day as if you'd always been there? The reason is because all of your internal biological rhythms would have been synchronised to what the monitor in your aircraft seat called the "local time at origin".

After arriving at your destination, while your watch may now be set to 9am, the "local time at origin" is 2am, and your body is an anticipatory machine: it has synchronised your internal physiology to run according to that local time. It expects you to be asleep, so at 9am in Sydney you are exhausted, not hungry, reaching for caffeine, and wondering whether everyone in Bondi is vegan. But, after a few days you adjust. Not to everyone talking about Bali, you never adjust to that. But you do adjust to the local time, and you now sleep when its dark, get up when its light, drive a Holden Commodore, and drink VB.

Ok, 'Straya puns aside, life on Earth is governed by the interaction of three 'clocks'. The first is the 'solar clock', this is based on the daily light-dark cycle wherever you are in the world; the second is the 'social clock', which is related to the solar clock because humans are diurnal mammals [meaning we are active and awake during the day], and the social clock involves working hours, school start times, etc. [3]. Finally, we have the 'biological clock', which in which our body synchronises the timing of internal processes, like digestion and metabolism, alertness and sleepiness, with the external environment [3].

Many of these biological rhythms are known as 'circadian rhythms', which are rhythms that fluctuate with the same pattern over a 24hr period [4]. If we put you in a pitch-black cave with no light, these rhythms would actually run slightly longer or shorter than 24hrs [5,6]. To synchronise these internal biological rhythms to the precise 24hr day, we rely on external signals from the environment [known in the literature by the beautiful German word, Zeitgeber, meaning 'time giver'] [4,6]. Light is the most important daily signal for these rhythms to synchronise, however, meal timing has also emerged as a signal to rhythms in metabolism [7,8]. Hence, when we change the timing of these signals, we can end up with jetlag.

But what of 'social jetlag' *? Social jetlag describes the differences between sleep timing and duration on work days, with enforced wake times, and free days or weekends, creating a discordance between internal biological time and social timing that can lead to a chronic form of jetlag [9]. Some prior smaller cohort studies have found a relationship between social jetlag, increased adiposity, and metabolic disease risk factors [10–12]. The present study investigated associations between social jetlag and metabolic risk in a Dutch cohort.

*Geek Box: Chronotype & Social Jetlag

To grasp these concepts a bit more, let's dig into two distinct, but highly related, concepts: your 'chronotype' and 'social jetlag'. Your "chronotype" (essentially meaning 'time type') is a behavioural representation of your internal biological 'clock' timing. It is important to note that a chronotype is a biological construct, not a psychological construct or trait. Our current scientific understanding shows a strong genetic influence on this time of day preference. This genetic foundation interacts with our modern environment – artificial light, work schedules, trans-meridian air travel, social life timing – to influence our behavioural preferences for morning or evening. Think of it this way: we are all exposed to the same light-dark cycle in a given time zone, but the timing of our internal biological processes will synchronise to this external time with different phases. For example, I might have a desired sleep phase from 9pm to 5am, while you might prefer to sleep from midnight to 8am. To determine our chronotypes, we would calculate the midpoint of sleep. In this example, my midpoint of sleep would be 1am and yours would be 4am. In this example, I have an earlier sleep phase, and would also likely feel most alert and active earlier in the day, while you would have a later sleep phase and would feel most alert and active in the evening or at night. But let's say we both have to be up at 6am on workdays. This is fine for me; but this is cutting your sleep short by 2hrs. The research shows that late chronotypes do not compensate by going to bed earlier, so the effect is that having to wake up earlier results in curtailed sleep. As a result, late chronotypes accumulate sleep debt during the working week. This is where social jetlag comes in. As highlighted above, social jetlag arises when our sleep-wake timing on workdays is different to our preferred sleep-wake timing. Check out the graph below: you can see the dark grey bars represent workdays, with red dots showing the midpoint of sleep on workdays. The light grey bars represent free days, when people can sleep according to personal preference, with the green triangles being the midpoint of sleep on free days. Social jetlag is calculated by subtracting the midpoint of sleep on workdays from that on free days, i.e., the difference between the two, and is expressed in hours:minutes. The difference between social jetlag and jetlag from air travel, is that you eventually adjust to your new time zone with air travel; with social jetlag, it is chronic, occurring week after week over time.

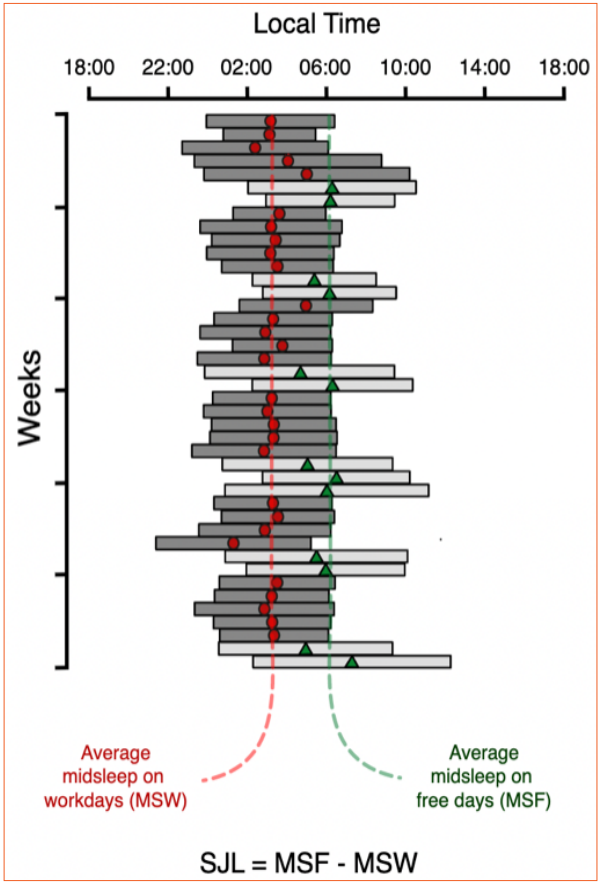

Figure *from Roenneberg et al.* [3].

The Study

The New Hoorn Study cohort is a population-based cohort in the Netherlands. The present study was a cross-sectional study* of 1,585 participants from the cohort who had completed questionnaires on social jetlag [SJL]. Participants were divided into tertiles of SJL: <1hr, >1hr but <2hr, and >2hr.

Participants were classified as having either the metabolic syndrome [MetSx], prediabetes, or type-2 diabetes [T2D]. All participants attended for clinical measurements of glucose, blood cholesterol and triglyceride levels, blood pressure, and waist circumference.

The analysis investigated whether levels of social jetlag were associated with risk of MetSx or T2D, and the associations with metabolic risk factors.

*Geek Box: Cross-Sectional Study

A cross sectional study is a type of observational study design, where data is analysed from a sample population at a specific moment in time [i.e., a 'cross-section' of a group]. The researchers are interested in looking at a particular exposure and outcome and investigating whether the prevalence of the outcome differs based on levels a particular exposure. For example, does the prevalence of type-2 diabetes differ between levels of dietary fat intake? In effect, a cross-sectional study is a snapshot in time, evaluating the relationship between the exposure [in this study, levels of social jetlag] and outcome [MetSx T2D, and risk factors]. Cross-sectional studies can be very useful to look at specific characteristics of a population with a relevant exposure, and compare with healthy or non-exposed populations, to identify differences. In a cross-sectional study, results are presented as 'prevalence ratios' [PR], which are used in cross-sectional studies and analogous to risk ratios in a prospective study. They are prone to certain biases, for example recall bias, or selection bias. However, they are useful for identifying prevalence of an exposure and outcome in a population.

Results: Participants had an average age of 60yrs, and 53% were female. For SJL levels, 61% of participants had <1hr, 31% had 1-2hrs, and 8% had >2hrs. Participants with either 1-2hrs or >2hrs SJL were younger compared to those with <1hr [57yrs compared to 64yrs].

- ***Relationship Between SJL and MetSx & T2D*:** In the overall analysis, compared to <1 SJL, those with >2hr SJL exhibited a significant 62% higher risk of MetSx. Risk of T2D or prediabetes was 10% higher, which was not significant.
- ***Modifying Effect of Age*:** As the prevalence of SJL was clearly modified by age, the analysis also investigated the associations stratified by participants <61yrs of age vs. >61yrs. In participants <61yrs of age, the prevalence ratio of both MetSx and T2D/prediabetes was significantly greater: 106% higher risk of MetSx and 73% higher risk for T2D/prediabetes. There was no significant associations with any outcome in participants >61yrs of age.
- ***Relationship Between SJL and Metabolic Risk Factors*:** In participants <61yrs of age, , SJL of >2hrs was associated with a 0.33mmol/L higher fasting glucose levels and a 2.94cm higher waist circumference. There were no significant associations with blood cholesterol, triglycerides, or blood pressure.

The Critical Breakdown

Pros: Social jetlag was measured using the Munich Chronotype Questionnaire [MCTQ], which is the best validated instrument to determine both chronotype and social jetlag, and the midpoint of sleep from this questionnaire has been shown to correlate strongly with objective laboratory measures of sleep phase [13]. Because age is a strong modifying factor for sleep-wake timing, chronotype and SJL, the analysis included age as a potential effect modifier [more under ***Key Characteristic***, below]. The analysis also adjusted for multiple relevant potential confounders, e.g., education level, employment, BMI.

Cons: As a cross-sectional study, we are looking at a snapshot in time. Participants already have a diagnosis of the relevant outcome of interest, so we cannot determine what relationship an exposure like SJL may have over time. For a population-based cohort, the sample size was modest at ~1,500 participants. The majority of participants also exhibited what would be considered no SJL, being <1hr of weekly SJL on average, and lower numbers in the other groups may have overinflated the effects. Using the MCTQ, chronotype could have been calculated, which would have been useful given the strong correlation between chronotype and SJL. Diet was not analysed, so we cannot infer any potential relationship between diet and the metabolic outcomes.

Key Characteristic

As you may have noticed from the results, there seemed to be a clear association between age and SJL levels. The finding that jumps off the pages of this paper is the effect of age as a modifying factor. Let' s discuss some whys and wherefores of this. The first point is that, although chronotype was not calculated in the present study, SJL is most pronounced in later chronotypes, and there is usually very little SJL in people who sleep at roughly the same times on workdays and weekends [9].

So what might this have to do with age? Well, everything. The three main factors that influence chronotype are genetics, the strength of time-cues [e.g., how much natural light exposure someone gets during the day], and age [14]. Age is a major factor. During our adolescent years, there is a delay in sleep phase which shifts teenagers to naturally delaying sleep by 3hrs on average [14]. This decreases as we age, so on average adults >31yrs delay sleep by around 1hr [14]. However, this continues over time, i.e., there is less and less difference in sleep phase with age [14].

Thus, it may be that the potential for discordance between preferred sleep phase and 'social clocks' are more pronounced in middle age.

Interesting Finding

In the analysis that investigated associations with risk factors, SJL of >2hrs was associated with a 0.33mmol/L higher fasting glucose levels and a 2.94cm higher waist circumference. Again, this was only observed in participants younger than 61yrs of age. In the literature, the most consistent effect of interventions inducing circadian disruption is in relation to glucose tolerance [1,15]. Why could this be? Recall that circadian rhythms follow the same rhythmic pattern over a 24hr period. The rhythms in glucose tolerance are strongly amplified in the early part of the day [the "biological morning"], and lower later in the day [the "biological evening"] [16]. SJL represent as continued strain on the circadian system to shift and adapt biological timekeeping, which desires consistency, to a constantly changing social timing between workdays and free days [3]. The evidence would suggest that this constant disruption primarily impacts on glucose tolerance and insulin resistance [1,15].

Relevance

It' s important to stress that cross-sectional studies are descriptive studies, providing useful insight into the proportion of a population with a disease and a particular exposure. But we are always left with the question, did the chicken or egg come first? It may be that SJL is associated with a *worsening* of current symptoms of a condition, but we don' t know whether SJL adds up over time to increase risk for the outcome occurring in the first place. Unfortunately, nearly all studies in this area to date are cross-sectional, and there is no prospective data following participants over time to determine whether, indeed, the SJL chicken comes before the diseased egg.

It is also important that we think about what it is exactly that SJL represents, i.e., what is SJL as an exposure? SJL was originally proposed as a measure of circadian misalignment, similar to air travel jetlag [9]. However, it may in fact be more akin to shift work, with constantly changing time-cues, i.e., sleep-wake patterns, meal timing, and light-dark exposure [3]. Simply put; the system is out of whack.

Glucose tolerance appears to be the process most consistently knocked out of whack [1,15]. Although not measured in this study, chronotype has been independently associated with T2D, and may explain some of the observational associations between breakfast skipping and T2D risk [17,18]. Previous research has shown that each hour later in the midpoint of sleep was associated with a 2.5% higher HbA1c, a marker of longer term blood glucose control [17].

And what of diet? Also not assessed in this study, but the wider evidence evening chronotype has been associated with lower diet quality, and a redistribution of energy and macronutrient intake to later in the evening [19–21]. Several authors have suggested that the relationship between chronotype and timing of eating may be mediated by SJL [9,10,22]. And higher SJL has previously been shown to correlate with lower diet quality [12].

There is a long way to go in establishing a more robust evidence-base in relation to these factors, which represent a complex interaction between biology and the modern environment. However, the evidence from human interventions does provide biological plausibility for the risk of metabolic impairment and glucose intolerant states like T2D when biological 'clocks' clash with social 'clocks' [1,2,23].

Application to Practice

The effects of sleep on human health are seldom disputed. Concepts like SJL evolve our consideration of sleep from an absolute view, i.e., a certain number of hours a night, to one which factors the timing when that sleep occurs. This timing is strongly influenced by our genetics, and the important point to note is that the standard '8hrs a night' advice assumes that this 8hrs would be the same for all of us independent of its timing. But this is not the case.

It is difficult for later chronotypes in particular in modern society, because all of our social timing is geared toward the morning, from work start times [which may include even earlier rising for commutes] to school start times. While 'work from home' may have benefitted the schedules of adults, the evidence continues to accumulate that kids perform better in school with a 10am start time, which allows adolescents to sleep in line with their naturally shifted pattern [24].

There is a lot of scope for nutrition professionals to consider sleep related factors in the nutritional context. For SJL, this is something that can be reduced by aiming for more consistent sleep-wake timing, in closer alignment with individual preferences, between work days and free days. But social timing does not always allow for this in all individuals. The main take-home point is to aim for consistency in sleep phase, as much as that is possible.

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