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PAPER TITLE:
Social Jetlag, Obesity and Metabolic Disorder: Investigation in a Cohort Study

THE FINDINGS:
We studied whether there is an association between social jetlag, a measure of chronic circadian disruption caused by a discrepancy between our internal versus social clocks, and measures of obesity, clinically assessed measurements of metabolic phenotypes and indicators of obesity-related disease; specifically, for inflammation and diabetes. Our findings come from the Dunedin Multidisciplinary Health and Development Study. The study has followed a group of 1,037 children born in 1972-73 in Dunedin, New Zealand, from birth to age 38 years, with 96% of the sample taking part at age 38. This study assessed the height, weight, fat mass and waist circumference of participants in the clinic, as well as measuring C-reactive protein (hsCRP) and glycated haemoglobin levels in their blood, biomarkers for inflammation and diabetes respectively. It then compared these findings with results from a questionnaire, which assessed participants' sleep duration and chronotype - their preference in sleep timing. All measures investigated were tested at age 38. Our analysis was restricted to the non-shift workers in our cohort (n=815).

We found that:
1. As little as two hours of social jetlag can increase the risk of an elevated BMI and biomarkers for inflammation and diabetes.
2. Social jetlag was associated with numerous clinically assessed measures of metabolic dysfunction and obesity, including obesity (BMI>=30), fat mass, and metabolic syndrome.
3. Metabolically unhealthy obese individuals had higher social jetlag levels than those who were obese but metabolically healthy.

WHY ARE THESE FINDINGS IMPORTANT?
Obesity is one of the leading causes of preventable death worldwide. Circadian rhythms are known to control both sleep timing and energy homeostasis, and disruptions in circadian rhythms have been linked to metabolic dysfunction and obesity-associated disease. In previous research, social jetlag was associated with elevated self-reported Body Mass Index (BMI), possibly indicative of a more generalized association with obesity and metabolic dysfunction.

This is the first study to find broader associations of increased social jetlag with increased measurements of obesity and increased risk for obesity related-disease. Unlike travel jetlag, which can cause temporary problems with metabolism, social jetlag can occur chronically throughout an individual's working life, so is likely to have more serious, chronic consequences for metabolism.

The findings are consistent with the possibility that "living against our internal clock" may contribute to metabolic dysfunction and its consequences. Further research aimed at understanding the physiology of and contributory social factors for social jetlag may inform obesity prevention and have ramifications for policies and practices that could increase social jetlag, such as work schedules and daylight savings time.

SUPPORTING DETAILS:

How we measured social jetlag.

At age 38, the Munich Chronotype Questionnaire was used to assess social jetlag as well as sleep duration and chronotype (29). Social jetlag, the discrepancy between our internal timing and external timing, was measured by subtracting each participant's midpoint of sleep on work days (MSW) from their midpoint of sleep on free days (MSF). Sleep duration was calculated by averaging the sleep duration on work days and free days, assuming 5 work days and 2 free days a week as standard.

Measures of being overweight.

Height was measured to the nearest millimeter using a portable Harpenden Stadiometer (Holtain, Crymych, UK). Weight was recorded to the nearest 0.1kg using calibrated scales. Individuals were weighed in light clothing. BMI was computed as weight (kg)/height (m^2). Obesity was defined as BMI≥30. Of the participants, 23.4% (n=192) were obese. Waist circumference (girth) was measured in centimeters. Fat mass was measured using a body composition analyser (Tanita BC 418, Tokyo, Japan) to assess bio-electrical impedance.

Measures of disease markers.

Inflammation. Elevated systemic inflammation was assessed using high sensitivity assays of C-reactive protein (hsCRP) in blood. HsCRP was measured on a Hitachi 917 analyzer (Roche Diagnostics, GmbH, D-68298, Mannheim, Germany) using a particle enhanced immunoturbidimetric assay. The CDC/AHA definition of high cardiovascular risk (hsCRP>3 mg/L) was adopted to identify the risk group (Pearson et al., 2003).

Glycated hemoglobin. Glycated hemoglobin concentrations (expressed as a percentage of total hemoglobin) were measured by ion exchange high performance liquid chromatography (Variant II; Bio-Rad, Hercules, Calif) (coefficient of variation, 2.4%), a method certified by the US National Glycohemoglobin Standardization Program. The American Diabetes Association definition of "pre diabetes" high glycated hemaglobin (>=5.7) was adopted to identify the risk group (ADA, 2012).

Measuring metabolic syndrome.

Metabolic syndrome was assessed from measurements of five biomarkers: (i) high waist circumference (≥88cm for women, ≥102cm for men), (ii) high blood pressure (≥130/85 mmHg), (iii) low high density lipoprotein (HDL) cholesterol (<50mg/dl for women, <40mg/dl for men), (iv) high glycated hemoglobin (≥5.7%), and (v) high triglycerides (≥200 mmol/l). Biomarker assessments have been described in detail previously (Belsky et al., 2013). Cohort members with high-risk values on three or more biomarkers were defined as having metabolic syndrome (Alberti et al., 2009). Of the participants, 15.9% met criteria for metabolic syndrome.

WHAT ADDITIONAL RESEARCH IS NEEDED?

Controlled experiments where we specifically vary the amount of social jetlag and see if it has molecular and physiological consequences on the metabolic system, and whether minimizing the degree of social jetlag can reduce obesity and its health consequences. Determine if other factors that cause circadian strain have similar effects on obesity, metabolism and obesity-related disorders.

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