Project: Z/340001/12/AB

Adverse effects of Circadian disruption

Project definition and approach

Project description

Introduction and motivation

Shift work and lifestyle factors disrupt the physiological circadian rhythm which leads to a variety of adverse health effects. In this project these reported adverse health effects are reviewed, subpopulation(s) at risk are identified, and missing data are collected via experimental studies in humans and rodents.

Modern society is characterized by the 24-hour economy. Currently, approximately 17% of the population in Europe works in night-shifts and in the next decades this type of work will only increase. Night-shift work is associated with the increased incidence of burn-out, cancers, cardiovascular disease, obesity, and premature birth.

The WHO, IARC acknowledged the adverse effects of shift work and addressed in a report from 2007 the relation between shift work and (breast) cancer. Further studies to the adverse health effects of shift-work, notably breast and prostate cancer and cardiovascular disease is required, because evidence is lacking for a mechanism that could explain the observed associations. The present project focuses on 1) the association between shift work and breast cancer, and 2) mechanisms of circadian disruption in humans.

Human studies for biomarkers

The general aim of this project is to investigate whether working in night shifts leads to chronic health effects via disturbance of the physiological circadian rhythm. Experimental studies carried out at RIVM are aimed at unravelling hormonal and circadian gene expression changes in mice with disturbed day/night rhythm. We aim to develop biomarkers that can, at early time points, predict adverse effects of circadian rhythm disturbances. Moreover, the

effect of different shift work schedules on these predictive biomarkers will be analyzed. Predictive biomarkers identified in mice must be validated in humans.

Study goal

Validate mouse biomarkers for circadian rhythm in human blood samples collected under control situation; every 4 hours during 24-hours.

Experimental set-up

Blood will be collected from 10 females and 10 men during 24-hours at 4-hour intervals. Serum, EDTA-plasma and erythrocytes will be stored for biomarker analysis and buffy coat for RNA isolation.

In addition saliva will be obtained by Salivettes.

From each time point, 4 portions of plasma, 4 portions of serum, 1 portion of buffy coat, 2 portions of erythrocytes and 1 portion of saliva will be aliquotted and stored at -80 C until analysis.

Timetable for realization of the protect

2012 – Organization of research team and sampling

2013 – Laboratory analyses

2014/15 – Statistical analysis and preparation of publications

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