POLYEXPOSITIONS AU TRAVAIL
Enjeux pour la prévention, méthodes & perspectives

Exposition aux substances chimiques et travail en horaires atypiques

Laurence Weibel
Département EAM, INRS

12 octobre 2023

PLoS one

Does the Clock Make the Poison? Circadian Variation in Response to Pesticides

Louisa A. Hooven*, Katherine A. Sherman, Shawn Butcher, Jadwiga M. Giebultowicz

Department of Zoology, Oregon State University, Corvallis, Oregon, United States of America

Travail de nuit et substances chimiques : prévalence ?

Sumer 2010, une exposition à au moins une substance chimique au cours de la dernière semaine travaillée :

Nuit fixe	40 %
3 x 8 ou 4 x 8	61 %
2 x 12	48 %
2 x 8	42 %
Soir	29 %
Jour	31 %

HST 265

D'après Martins Caetano

Travail de nuit et co-exposition chimique

Exposition à au moins un CMR : plus **fréquente**, plus **intense** et plus **longue**

- Havet et al., 2017 (France)

Probabilité d'exposition à un CMR (aPR = 1.16;95% 1.06-1.26)

- El-Zaemey et al. 2019 (Australia)

1.5x co-exposition à des substances chimiques

- Safe Work Australia 2015 (Australia)

Plus susceptibles d'être exposés à d'autres risques et à des risques multiples (OR = 2.45, 95%CI = 2.01-3.0)

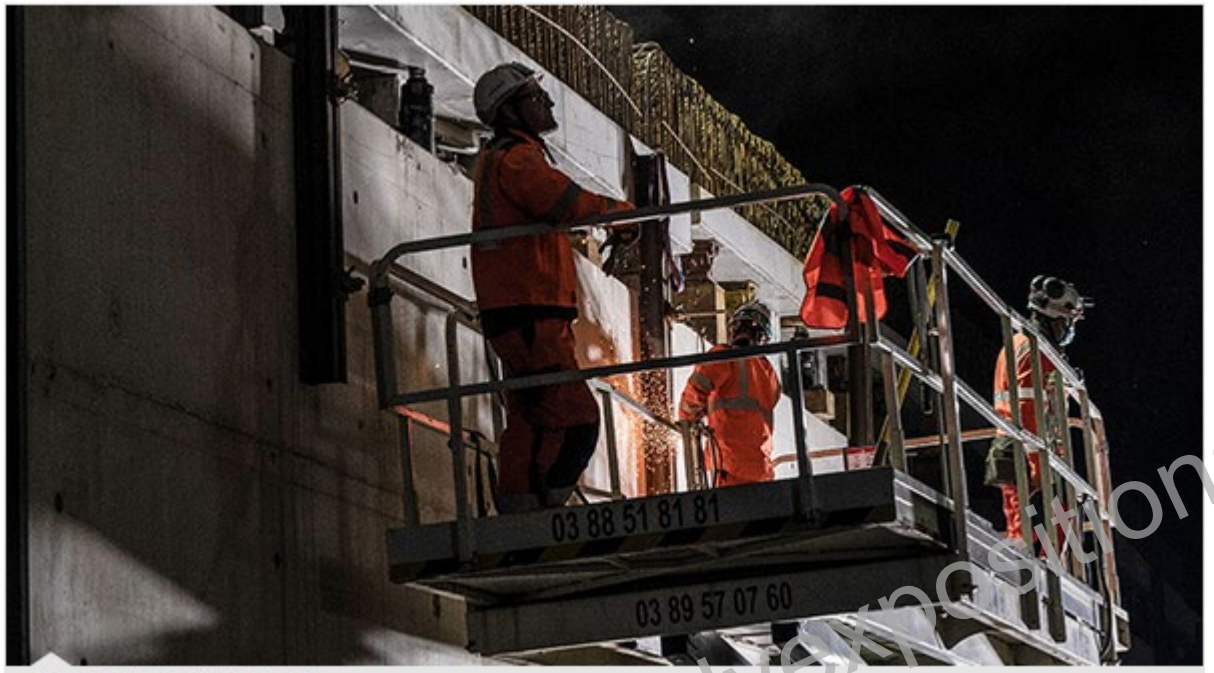
- Jay et al. 2017 (New Zealand)

Dans aucun des lieux de travail, le travail de nuit n'est une exposition unique

- Pepłońska et al. 2013 (Poland)

D'après Martins Caetano

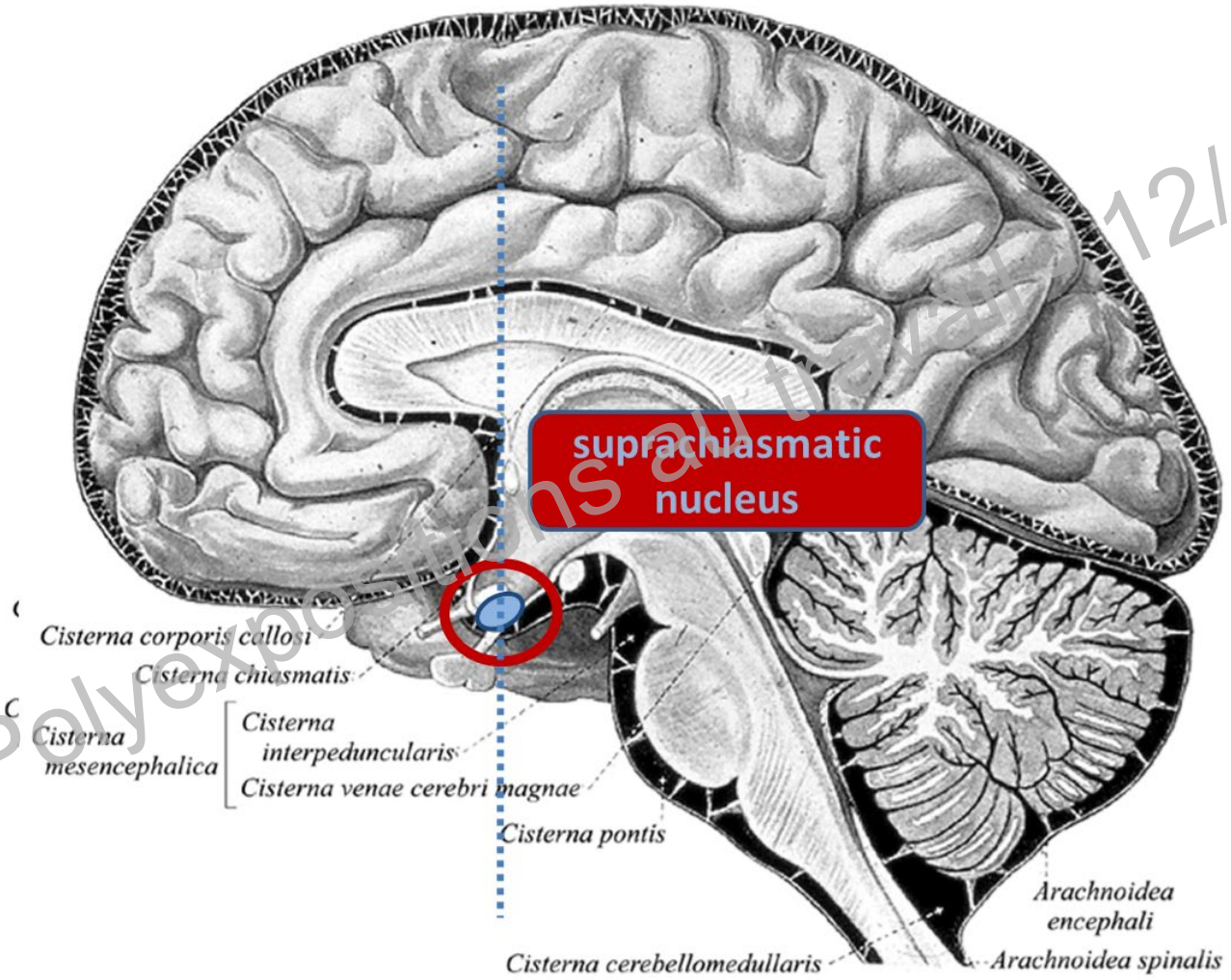
Pourquoi le moment de l'exposition pose problème?



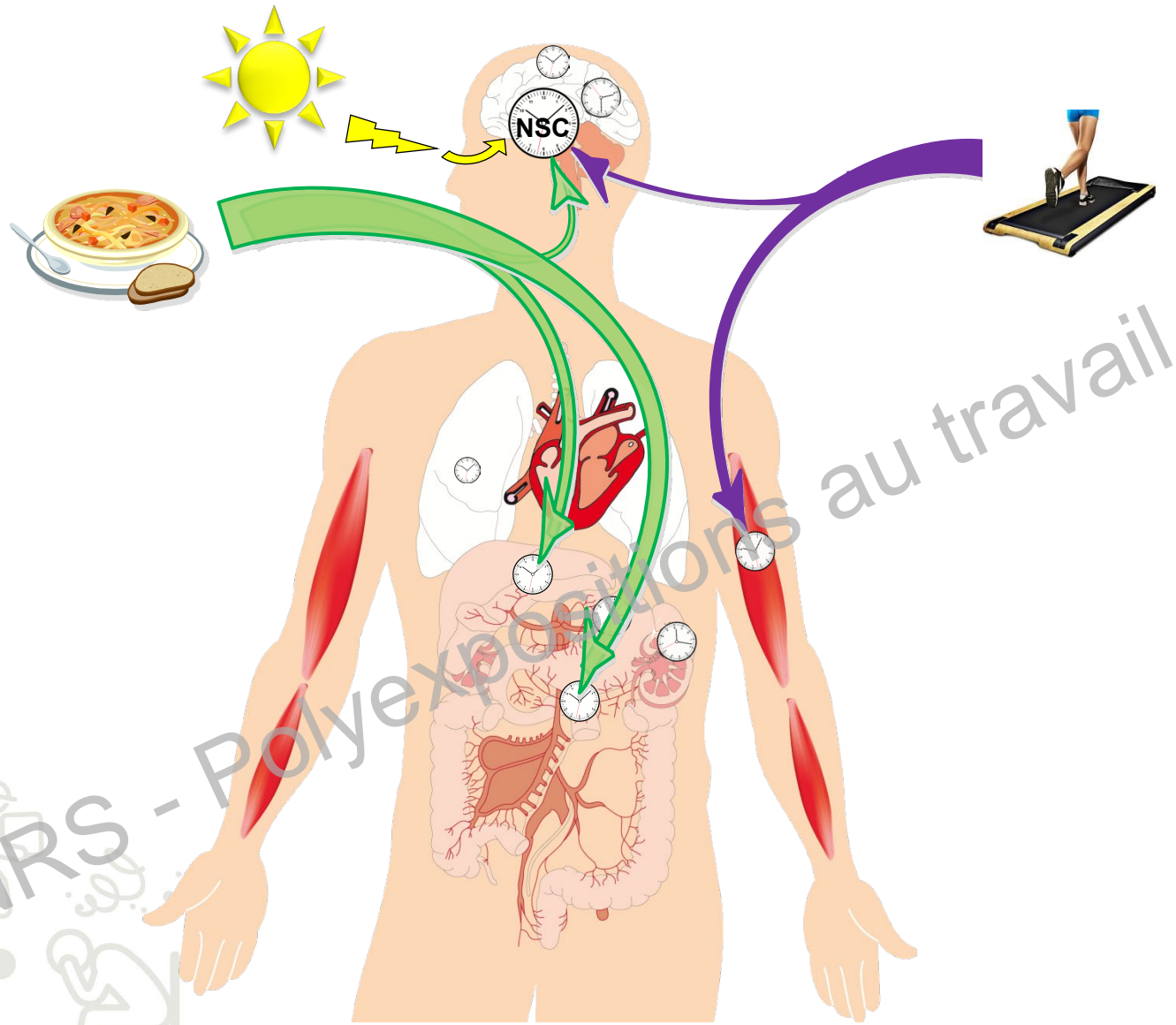
© Gael Kerbaol / INRS / 2015


© Gaël Kerbaol/INRS/2015

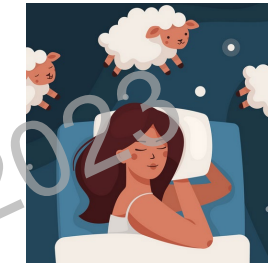
La rythmicité circadienne dépend d'une horloge dans le cerveau

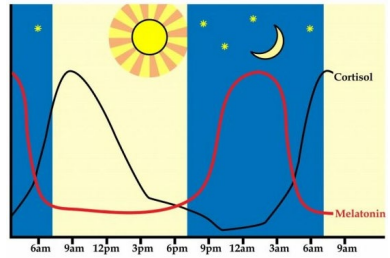


Le système circadien

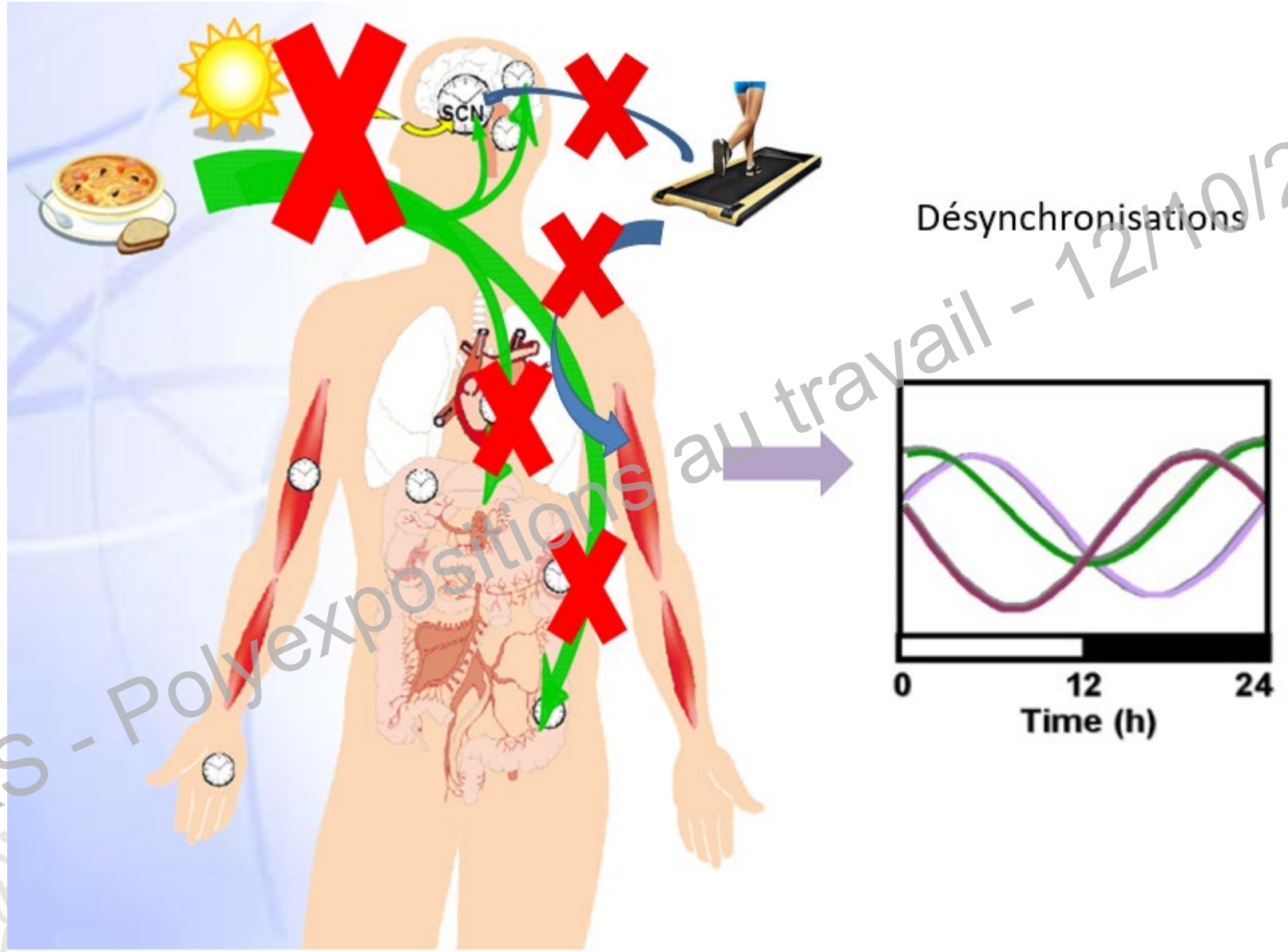


D'après E Challet, 2023





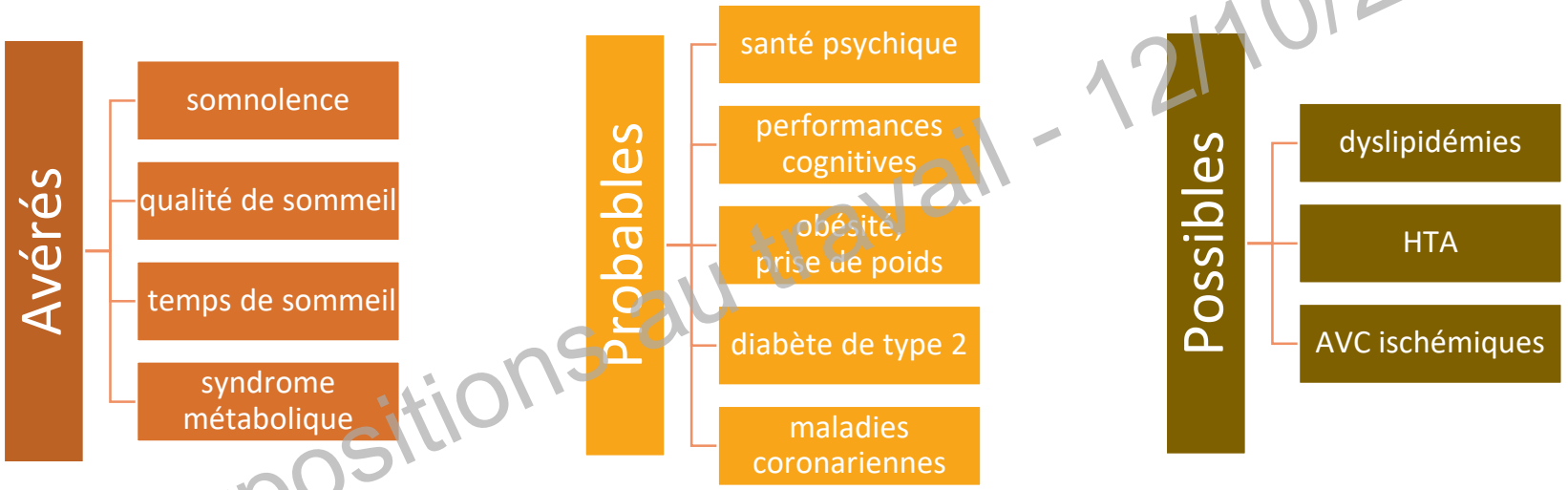
Le système circadien du travailleur de nuit



Adapté de Challet, 2023

Effets du travail de nuit

anses
agence nationale de sécurité sanitaire
alimentation, environnement, travail



International Agency for Research on Cancer
World Health Organization

Agent	Group	Volume	Year	Additional information
Night shift work	2A	98, 124	2020 online	NB Volume 98 evaluated shiftwork that involves circadian disruption

Les voies physiologiques du métabolisme sont régulées par les rythmes circadiens

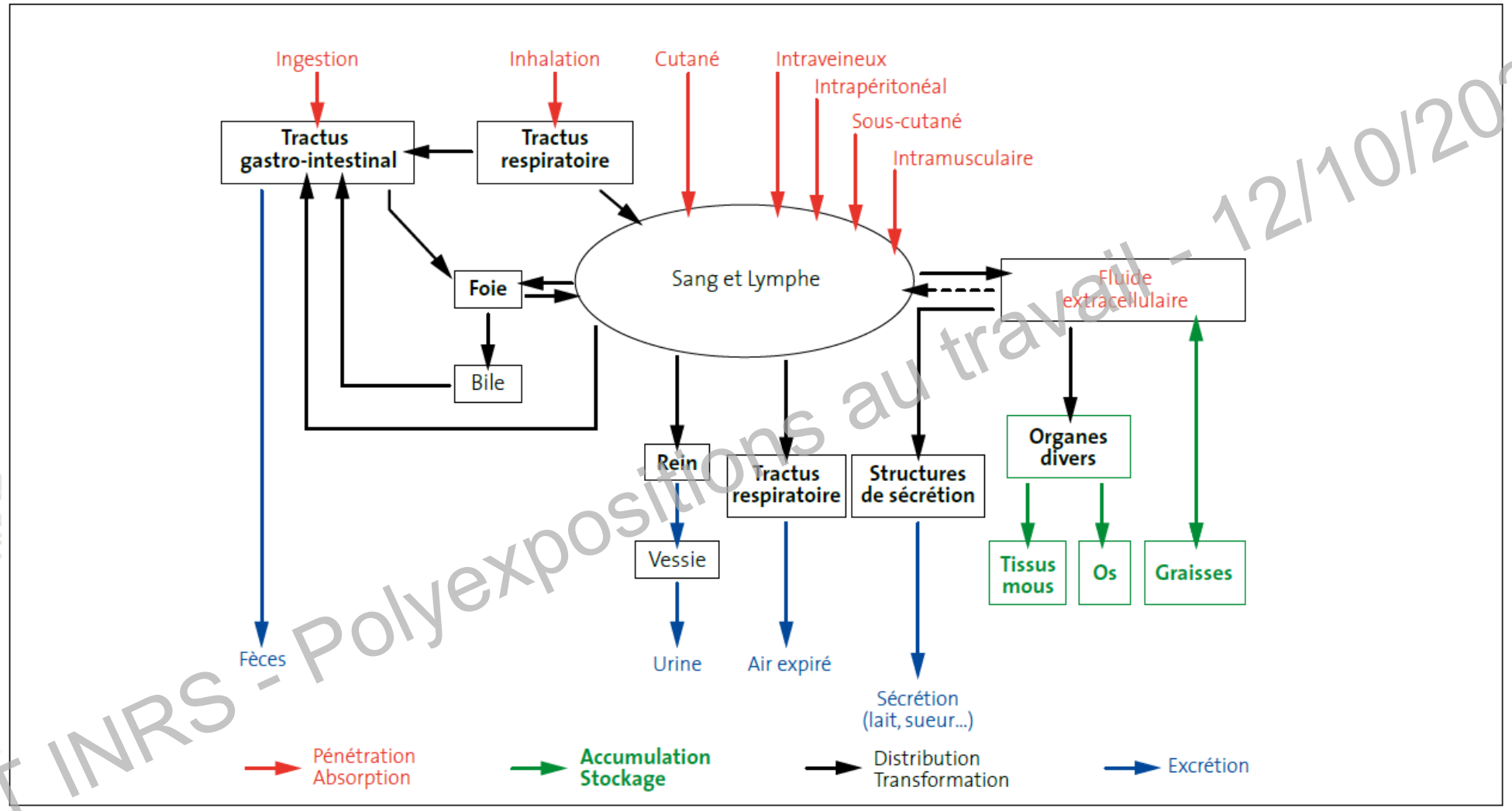
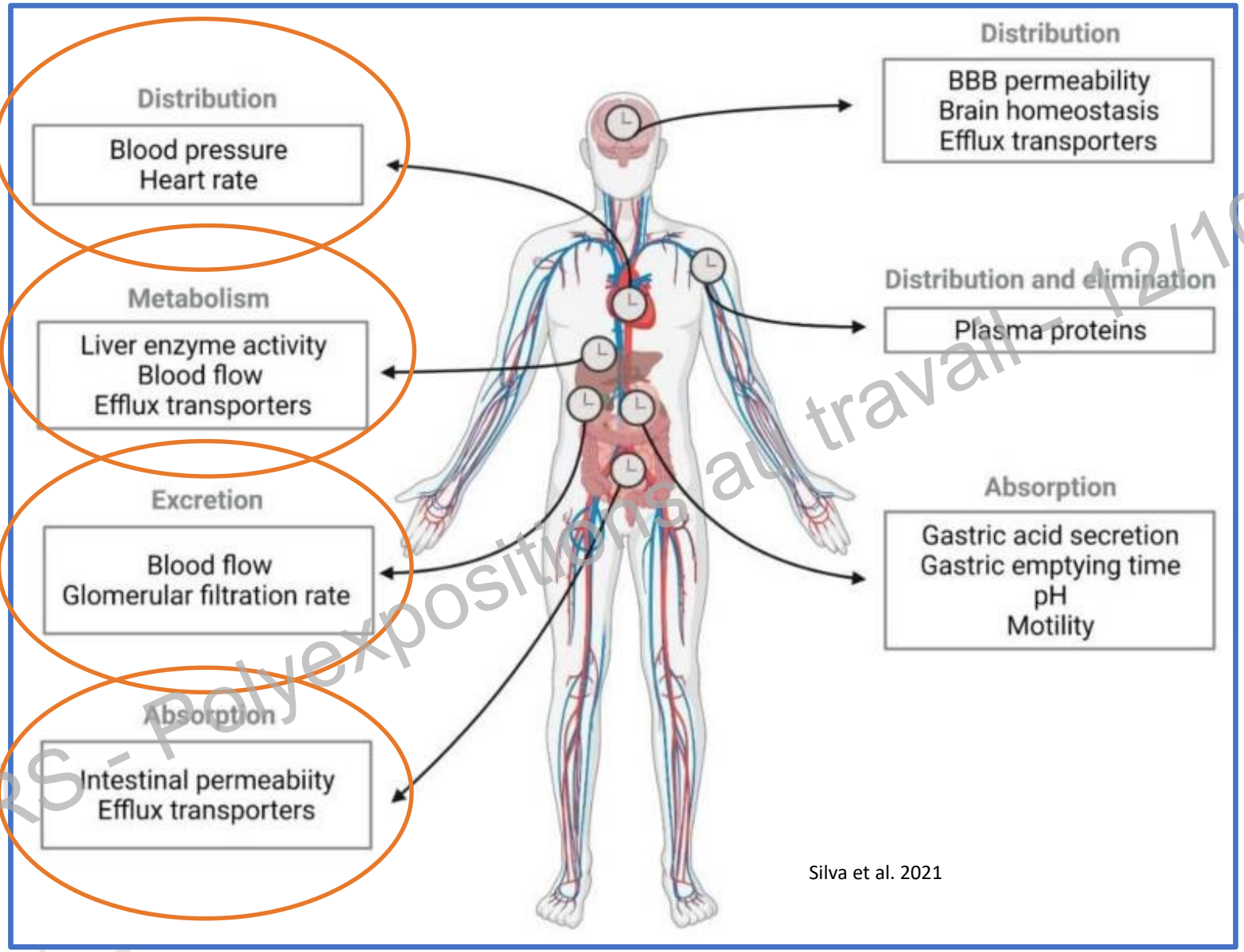


Fig. 1. Métabolisme des substances chimiques dans l'organisme.

Adapté de Martins Caetano

FTO. https://www.inrs.fr/publications/bdd/fichetox.html

Les voies physiologiques du métabolisme sont régulées par les rythmes circadiens

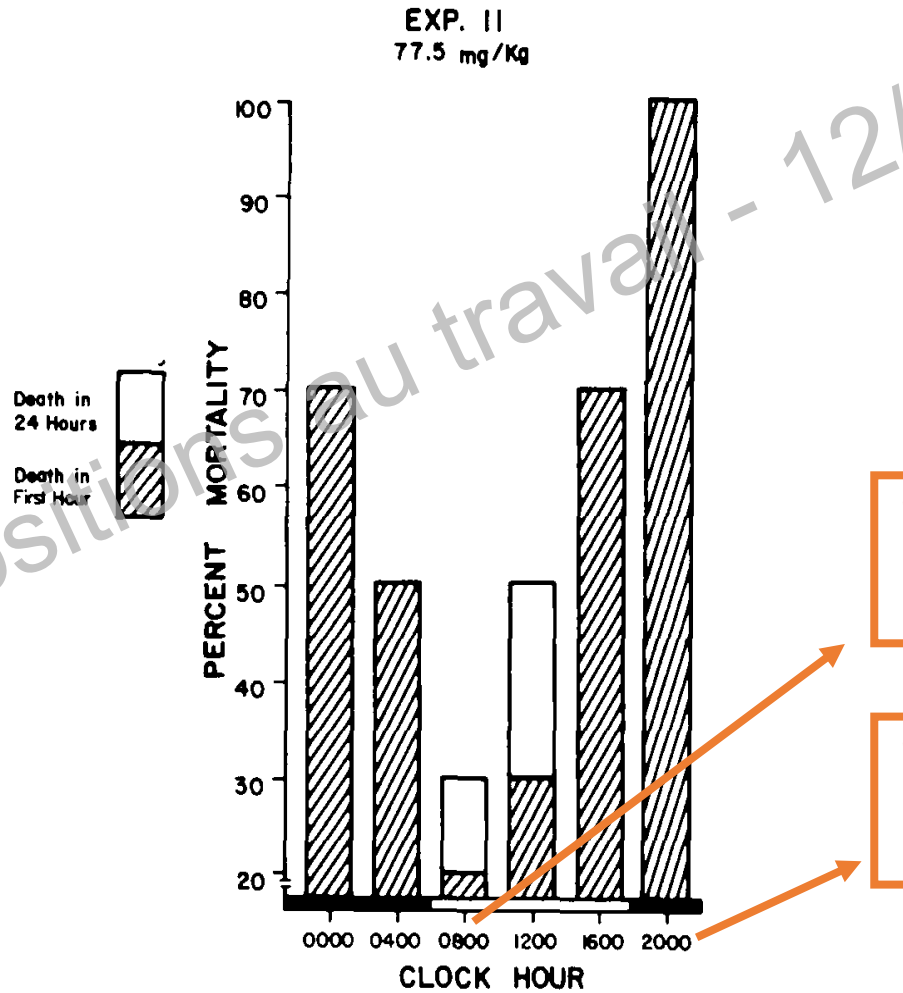


Silva et al. 2021

Adapté de Martins Caetano

Même effet en fonction du moment de l'exposition ?

Variabilité 24h prononcée

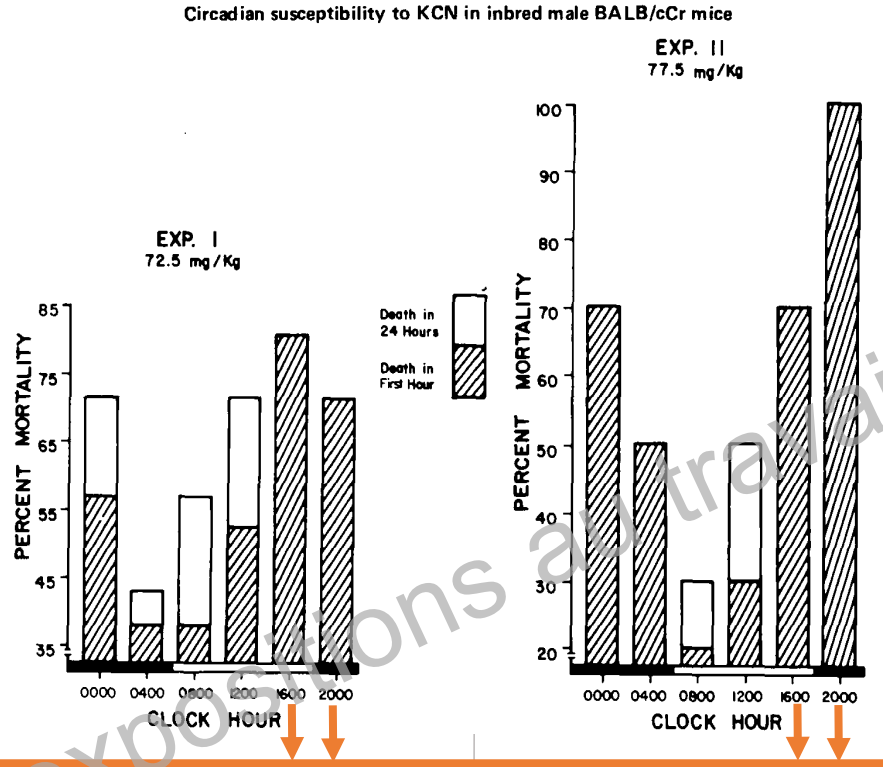


Bafitis *et al.*, 1978

Taux de mortalité H1: 20 %

Taux de mortalité H1: 100 %

Même effet en fonction du moment de l'exposition ?



Susceptibilité

=

Transition entre les périodes d'inactivité diurne et l'activité nocturne

Bafitis *et al.*, 1978

Main Results of a Randomized Multicenter Trial Comparing Flat Versus Chronomodulated Chemotherapy in 186 Patients With Metastatic Colorectal Carcinoma

Effect	Flat	Chrono	*P* value
Hospitalization for toxicities	31[a]	10	0.001
Severe mucositis	76	14	0.0001
Functional impairment (periph sensory neuro)	31	16	0.01
Tumor response > 50%	29	51	0.003

Très peu d'études chez l'homme

TABLE 1 Characteristics of studies focusing on the chronotoxicity of xenobiotics in humans

	n	Study design	Treatment	Chrono intervals considered	Circadian disruption	Xenobiotics involved	Outcome(s)
study 1[52]	193	4 studies: prospective twin cohort, nested case-control and community/ hospital case-control	Perinatal period	−89 to 300 days since birth	Fetal and postnatal cyclic metal patterns	Zinc and copper	Average duration of zinc-copper cycles; regularity with which the cycles recur; and number of complex features within a cycle in relation with autism spectrum disorder (ASD) distinguishing ASD cases from controls
study 2[51]	18	3 panel studies	Disinfection (chlorine) use	24 hr	Diurnal (24 h) variation	Trihalomethanes (THM) – chlorine	Time of exposure within the day dictated the magnitude of urinary THM levels and concomitant toxicity (oxidative damage with 4-hydroxynonenal lipid peroxidation marker) measurements
study 3[53]	14840	1 cohort study	Self-poisoning	4-hr intervals from 00.00-23.59 daily	Circadian fluctuations in transporters and CYP450s	Pesticides (organophosphorus)	Probability of survival/death after self-poisoning

Makris KC, 2021

Diurnal variation in probability of death following self-poisoning in Sri Lanka—evidence for chronotoxicity in humans

Robert Carroll,[1] Chris Metcalfe,[1] David Gunnell,[1,2] Fahim Mohamed[2,3] and Michael Eddleston[2,4,5]*

2012

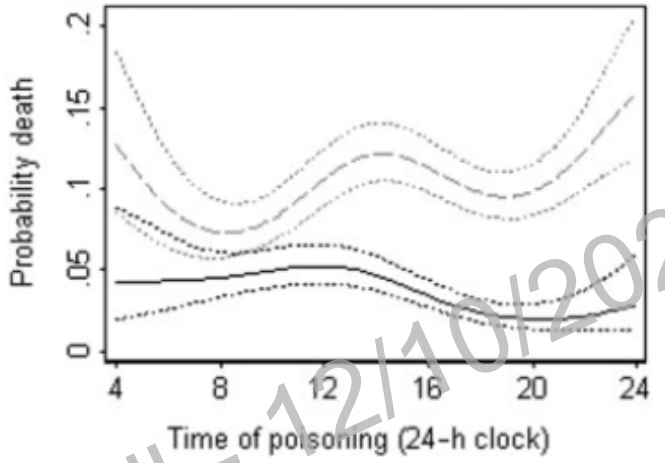


Figure 2 Diurnal variation (95% CIs) in the probability of death following oleander (solid black line) and OP insecticide (dashed grey line) ingestion

KEY MESSAGES

- Medicines and poisons are metabolized by enzymes and transporters with circadian rhythms. The importance of these rhythms to clinical outcome in therapeutic use or after poisoning is unclear.
- In a large Sri Lankan cohort of self-poisoned patients, patients who had ingested oleander seeds in the late morning were three times more likely to die than those who had ingested seeds in the late afternoon and evening.
- A weaker but contrasting effect was seen in patients ingesting OP insecticides, with a greater risk of death in those self-poisoning in the afternoon and evening. No evidence was found of diurnal variation in case fatality in the other pesticides investigated.
- This evidence of chronotoxicity suggests that optimization of administration times during therapeutic drug development may improve the balance of benefit and side effects for some pharmaceuticals.

Environment International 112 (2018) 33–40

Contents lists available at ScienceDirect

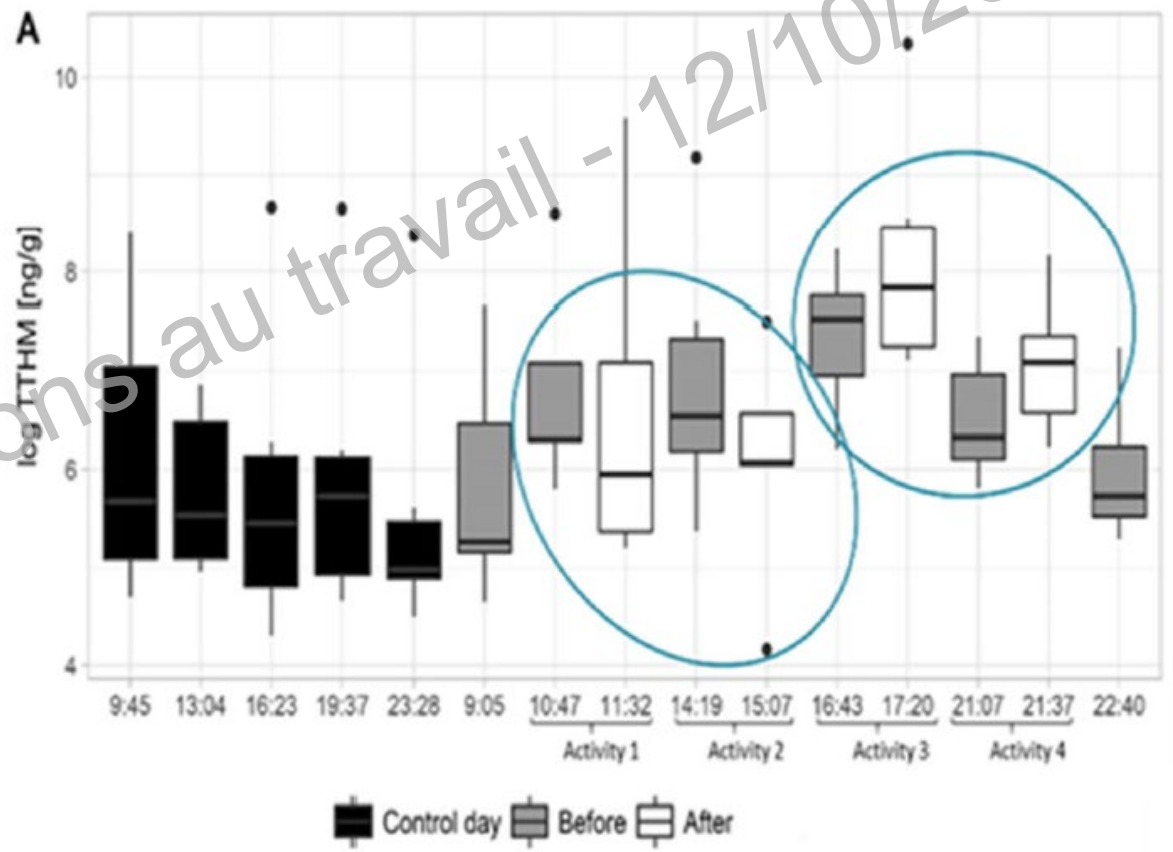
Environment International

journal homepage: www.elsevier.com/locate/envint

Time of the day dictates the variability of biomarkers of exposure to disinfection byproducts

Stephanie Gängler[a], Pantelis Charisiadis[a], Ratanesh Seth[b], Saurabh Chatterjee[b], Konstantinos C. Makris[a,*]

2018



Occupational exposure to chemicals and unusual working hours

A literature review

Jenny-Anne S. Lie [1], Magne Bråtveit [2], Shanbeh Zienolddiny [1]

1) National Institute of Occupational health, Oslo, Norway. Department of Occupational Medicine and Epidemiology (JASL), Department of Chemical and Biological Work Environment (SZ), 2) University of Bergen, Norway. Department of Global Public Health and Primary Care

SWEDISH WORK ENVIRONMENT AUTHORITY

The Nordic Expert Group

The Nordic Expert Group - a Nordic collaboration for production of criteria documents on chemicals for occupational exposure limits.

What is the scientific knowledge regarding the combined effect of unusual working hours and chemical exposure?

Photo: Eirik Linder Aspelund

Occupational exposure limits (OELs) usually assume an 8-hour workday, 5 days a week and a 40 hour work week. A significant proportion of the work force is employed in other work schedules

Circadian rhythms and the time of exposure (day-night) may affect the biotransformation of chemicals, which may in turn affect the toxicity.

Is it necessary to adjust OELs with regard to working hours?

A literature search in 6 databases:

Embase
Medline OSH Reference Collection
ProQuest Health and Safety Science
ProQuest Toxline
SCOPUS
Web of Science

Inclusion criteria:

Peer-reviewed articles in English language

Clearly defined metrics of exposure to both *chemicals* and *unusual working hours*

Clearly defined outcomes (health or safety)

Estimates of associations between exposure and outcome presented

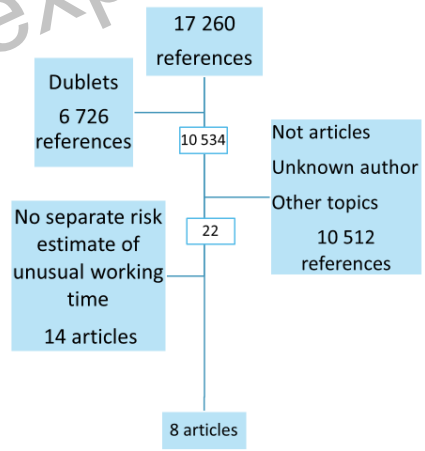


Photo: Eirik Linder Aspelund

Results:

More reduced pulmonary function during night shift for workers exposed to dust in steel plants and to endotoxins in potato processing.

A synergistic effect between exposure to unusual working hours and organic solvents on spontaneous abortion among laboratory personnel.

Increased coronary artery disease mortality among workers exposed to carbon disulphide (CS_2) and unusual working hours (1 of 2 studies).

Reduced sleep quality among acetone-exposed shift workers.

Potential mechanisms :

Disruption of circadian rhythms has been hypothesized as a plausible common biological mechanism for the combined effects of unusual working hours and chemical exposure.

The circadian rhythmicity is also important for maintaining metabolism and detoxification of chemicals and xenobiotics.

The liver is the major metabolizing organ in the body. Disruption of circadian rhythmicity and the metabolic oscillations in the liver may occur due to change of sleep patterns or intake of meals at unusual times, which may lead to disruption of the metabolism of chemicals, and to sleep disorders.

Conclusion :

The reviewed data were insufficient to identify specific chemicals for OEL adjustment related to shift work, and to provide new information of relevance for adjustment of OELs for extended working hours.

Several models exist, to adjust OELs in order to compensate for exposure during extended work hours, and the decreased recovery between shifts.

Overall, a modified Quebec model, which is partly based on Haber's rule is suggested for determining the adjustment method for different categories of chemicals for extended working hours.

Photo: Eirik Linder Aspelund

This research was made for the Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals (NEG), whose main task is to produce criteria documents to be used by the regulatory authorities as the scientific basis for setting occupational exposure limits for chemical substances. (www.nordicexpertgroup.org).

STAMI NATIONAL INSTITUTE OF OCCUPATIONAL HEALTH

UNIVERSITAS BERGENSIS

24th International Symposium on Shiftwork and Working Time, Idaho 2019

En synthèse

- Il existe des rythmes circadiens de susceptibilité à des agents chimiques chez les animaux et chez l'homme

- Quels effets de la polyexposition « horaires atypiques » x « substances chimiques » ? très peu de données en milieu de travail

- Beaucoup de questions soulevées, assez peu de réponses

- En pratique : besoin d'études de recherche