



Universiteit
Leiden
The Netherlands

The circadian system throughout the seasons of life

Buijink, M.R.

Citation

Buijink, M. R. (2024, June 27). *The circadian system throughout the seasons of life*. Retrieved from <https://hdl.handle.net/1887/3765852>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3765852>

Note: To cite this publication please use the final published version (if applicable).

The circadian system throughout the seasons of life

M. Renate Buijink

Colofon

The circadian system throughout the seasons of life, 2024, Monica Renate Buijink

ISBN: 9789464699791

Cover by: Anne Simon

Layout by: Bregje Jaspers | ProefschriftOntwerp

Printed by: ProefschriftMaken | www.proefschriftmaken

All rights are reserved. No part of this publication may be reproduced, stored, or transmitted in any form or by any means, without the permission of the copyright owners.

The circadian system throughout the seasons of life

Proefschrift

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof.dr.ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op donderdag 27 juni 2024
klokke 11:15 uur

door
Monica Renate Buijink
Geboren te Amersfoort
in 1985

Promotoren

Prof. dr. J. H. Meijer

Prof. dr. T. Hankemeier

Copromotor

Dr. S. Michel

Promotiecommissie

Prof. dr. P. E. Slagboom, LUMC

Prof. dr. A. Sumova, Czech Academy of Sciences

Prof. dr. S. E. la Fleur, AMC

Prof. dr. ir. Peter ten Dijke, LUMC

Voor mijn moeder

Table of contents

List of abbreviations	8
Chapter 1. General introduction	11
Chapter 2. A multi-level assessment of the bidirectional relationship between aging and the circadian clock	27
Chapter 3. Uncovering functional signature in neural systems via random matrix theory	73
Chapter 4. Evidence for weakened intercellular coupling in the mammalian circadian clock under long photoperiod	101
Chapter 5. Aging affects the capacity of photoperiodic adaptation downstream from the central molecular clock	129
Chapter 6. The influence of neuronal electrical activity on the mammalian central clock metabolome	163
Chapter 7. Aging selectively dampens oscillation of lipid abundance in white and brown adipose tissue	191
Chapter 8. Loss of temporal coherence in the aging circadian system: A metabolomics approach	219
Chapter 9. General discussion	249
Nederlandse samenvatting	265
Dankwoord	271
Curriculum vitae	275
List of publications	277

List of abbreviations

AABA	alpha-aminobutyric acid
ACSF	artificial cerebrospinal fluid
AD	Alzheimer's disease
AVP	arginine vasopressin
BAIBA	beta-aminoisobutyric acid
BAT	brown adipose tissue
BDNF	brain-derived neurotrophic factor
Bmal1	brain and muscle ARNT-like 1
Ca	calcium
cAMP	cyclic adenosine monophosphate
clock	circadian locomotor output cycles Kaput
cry	cryptochrome
Cry1	cryptochrome 1
Cry2	cryptochrome 2
DAG	diacylglycerols
DD	constant darkness
DL	dorsolateral
E/I balance	balance between excitatory and inhibitory activity
EEG	electroencephalography
ExT	external time
fMRI	functional magnetic resonance imaging
GABA	γ -aminobutyric acid
ICA	independent component analysis
ipRGCs	intrinsically photosensitive retinal ganglion cells
L	lateral
L5	lowest 5-hour bin of activity
LC-MS	liquid chromatography–mass spectrometry
LD	light-dark
LP	long photoperiod
LPS	lipopolysaccharide challenge
M	medial
M10	highest 10-hour bin of activity
MEG	magnetoencephalography
MRI	magnetic resonance imaging
MS	mass spectrometry
mTOR	mammalian target of rapamycin
NAD ⁺	nicotinamide adenine dinucleotide
NAD ⁺ /NADH	nicotinamide adenine dinucleotide, oxidized/reduced

NF-kB	nuclear factor kappa-light-chain-enhancer of activated B cells
PACAP	pituitary adenylate cyclase activating peptide
PCA	principal component analysis
per	period
Per1	period 1
Per2	period 2
PER2::LUC	PERIOD2::LUCIFERASE
PGC-1 α	peroxisome proliferator-activated receptor gamma coactivator 1-alpha
PI	phosphoinositide
PIR	passive infrared
PP1	photoperiod 1
PP2	photoperiod 2
PRX	peroxiredoxin
PVN	paraventricular nucleus of the hypothalamus
RHT	retinohypothalamic tract
RMT	random matrix theory
ROIs	regions of interest
ROS	reactive oxygen species
SCN	suprachiasmatic nucleus
SD	standard deviation
SIRT1	sirtuin 1; silent mating type information regulation 2 homolog 1
SP	short photoperiod
sPVZ	subparaventricular zone
TAG	triacylglycerol
TG[O]	alkyldiacylglycerols
TTFL	transcription-translation feedback loop
VIP	vasoactive intestinal protein
VIP-KO	VIP knock-out
VM	ventromedial
WAT	white adipose tissue
ZIC-CHILIC-MS	zwitterionic hydrophilic interaction liquid chromatography mass spectrometry
ZT	zeitgeber time