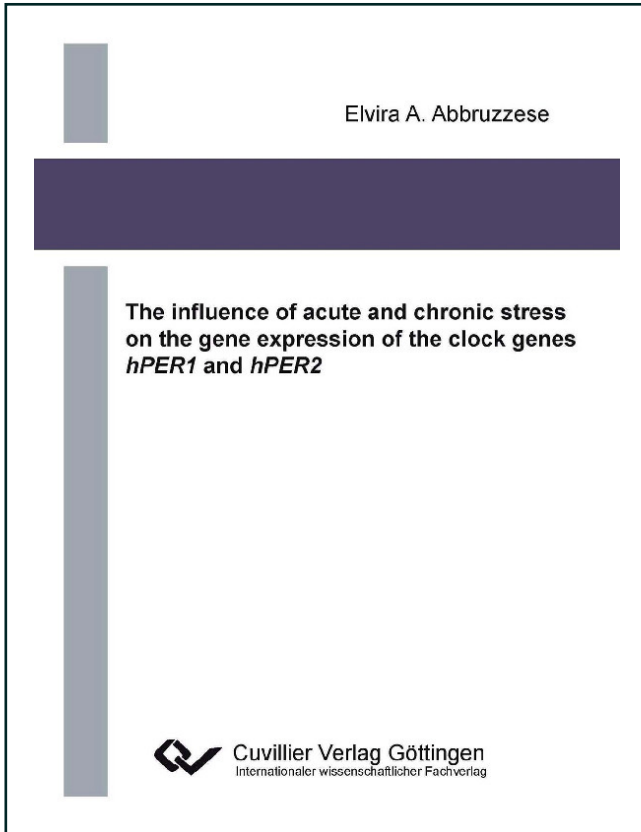




Elvira Abbruzese (Autor)

## **The influence of acute and chronic stress on the gene expression of the clock genes *hPER1* and *hPER2***



<https://cuvillier.de/de/shop/publications/230>

Copyright:

Cuvillier Verlag, Inhaberin Annette Jentsch-Cuvillier, Nonnenstieg 8, 37075 Göttingen,  
Germany

Telefon: +49 (0)551 54724-0, E-Mail: [info@cuvillier.de](mailto:info@cuvillier.de), Website: <https://cuvillier.de>

## ABSTRACT

1. Introduction .....	1
-----------------------	---

## PART I: THEORETICAL BACKGROUND

2. Stress .....	3
2.1. Biological and psychological stress concepts .....	3
2.2. The hypothalamic-pituitary-adrenal axis .....	8
2.2.1. Cortisol – a well measurable parameter of the HPA axis .....	10
3. Gene expression .....	13
3.1. Nucleic acids .....	14
3.2. Transcription .....	15
3.2.1. The initiation phase of transcription .....	15
3.2.2. The elongation phase of transcription .....	17
3.2.3. The termination phase of transcription .....	18
3.3. Post-transcriptional processing .....	18
3.3.1. Special cases: Editing mRNA and alternative splicing .....	19
3.4. Translation .....	20
3.4.1. The initiation phase of translation .....	20
3.4.2. The elongation phase of translation .....	22
3.4.3. The termination phase of translation .....	23
3.5. Post-translational modification .....	23
3.6. The regulation of gene expression .....	24
3.6.1. Transcriptional regulation .....	24
3.6.2. Post-transcriptional regulation .....	26
3.6.3. Translational regulation .....	27
3.6.4. Post-translational regulation .....	27
4. The Circadian Clock .....	29
4.1. Photosensitive Receptors of the Retina .....	31
4.2. The Suprachiasmatic Nuclei .....	32
4.3. Clock Genes and their transcriptional/translational feedback loops .....	32
4.4. Timekeepers .....	33
4.5. The Circadian Clock and Health .....	35
4.5.1. Circadian Rhythms and Cancer .....	36
4.5.1.1. Chronotherapy .....	37
4.5.2. Affective disorders .....	38
4.5.2.1. Therapy approaches in affective disorders .....	39
4.6. The Circadian Clock and Stress .....	39
4.7. Possible pathways of interaction between the circadian clock and glucocorticoids .....	40
4.8. Findings of associations between stress and the circadian clock .....	41
5. Study idea, questions and hypotheses .....	43
6. Methods .....	44
6.1. Subjects and Recruitment Criteria: .....	44
6.2. Procedure and Measurements: .....	44
6.2.1. Sampling Methods and Analysis of mRNA and Cortisol .....	45
6.2.2. Collection of Psychometric Data .....	45
6.2.3. Control and Stress Condition .....	46
6.3. Ethics .....	46

## PART II: EMPIRICAL STUDIES

7.	Data analysis 1: The impact of age, chronic stress and increase of cortisol after awakening .....	47
7.1.	Introduction.....	47
7.2.	Methods and Material.....	49
7.2.1.	Subjects and Recruitment Criteria .....	49
7.2.2.	Procedure and Measurements .....	50
7.2.3.	Psychometric Data.....	51
7.2.4.	Statistics .....	51
7.3.	Ethics.....	51
7.4.	Results .....	52
7.4.1.	Higher gene expression of <i>hPER1</i> and <i>hPER2</i> in older subjects .....	52
7.4.2.	Chronic stress is associated with higher expression of <i>hPER2</i> .....	53
7.4.3.	Levels of cortisol after awakening are significantly associated with gene expression levels of <i>hPER1</i> and <i>hPER2</i> .....	54
7.5.	Discussion .....	56
8.	Data analysis 2: Acute and chronic psychosocial stress affects the gene expression of <i>hPER1</i> .....	59
8.1.	Introduction.....	59
8.2.	Methods.....	60
8.2.1.	Subjects and Recruitment Criteria .....	61
8.2.2.	Control/stress condition and sampling intervals .....	61
8.2.3.	Procedure and Measurements .....	61
8.2.4.	Psychosocial stress test .....	62
8.2.5.	Psychometric Data.....	62
8.2.6.	Statistics .....	62
8.2.7.	Ethics .....	63
8.3.	Results .....	63
8.3.1.	Significant increase of cortisol after psychosocial stress task “resets” <i>hPER1</i> .....	64
8.3.2.	Strong mutual interactions between <i>hPER1</i> and Cortisol – the communication between two systems .....	66
8.3.3.	<i>hPER1</i> expression differs significantly in subjects with high vs. subjects with low chronic stress levels – particularly after psychosocial stress .....	71
8.4.	Discussion .....	72

## PART III: GENERAL DISCUSSION

9.	General considerations and summary of the results of the empirical studies .....	75
9.1.	Data analysis 1: The impact of age, chronic stress and increase of cortisol after awakening .....	76
9.2.	Data analysis 2: Acute and chronic psychosocial stress affects the gene expression of <i>hPER1</i> .....	77
10.	Methodological considerations and limitations .....	78
11.	Discussion of the results .....	82
12.	Clinical implications and directions for future research .....	84
13.	Literature.....	86
14.	Figures and tables .....	106