Schlaf und Autismus

W. Cassel

Klinikum der Philipps-Universität,
Schlafmedizinisches Zentrum, Marburg

Warum schlafen wir eigentlich?

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Konzentrationsfähigkeit

Warum schlafen wir eigentlich?

Zellreparatur

Vergessen

Erholung

Lernen

Wachsen

Demenzprophylaxe

Stimmung

Wundheilung

Gelassenheit

Immunfunktion stärken

Konfliktverarbeitung

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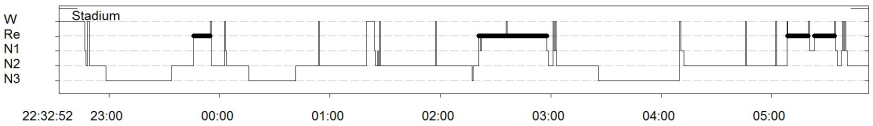
Schlafprofil normaler Schlaf



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Schlafstörungen

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Schlafstörungen

ICSD-3:

- Insomnien
- Schlafbezogene Atmungsstörungen
- Hypersomnien
- Zirkadiane Schlaf-Wach-Rhythmusstörungen
- Parasomnien
- Schlafbezogene Bewegungsstörungen
- Andere Schlafstörungen

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Schlafbezogene Bewegungsstörungen – Restless Legs Syndrom

Gesamtbevölkerung: 5 %

♀ Postmenopause: 10 %

Symptome des Restless Legs Syndroms

https://www.medpertise.de/restless-legs-syndrom/

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Schlafstörungen bei Kindern mit Autismus

Table 1. Prevalence and Mean Age of Sleep Disorder Diagnoses and Sleep-Related Procedures in Children with Autism as Compared with Matched Controls

	ASD (n = 48,762)		Controls (n = 243,810)		Comparison of Mean Ages
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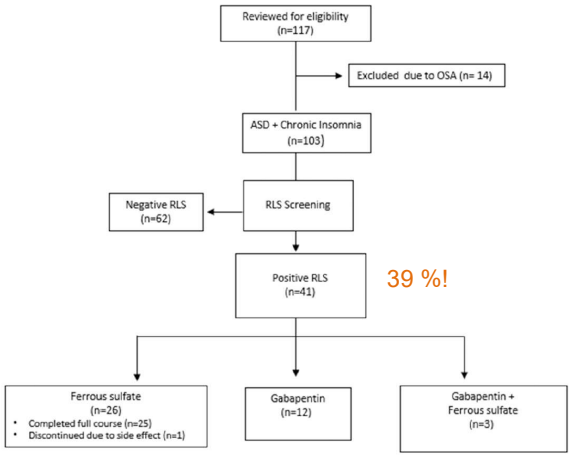
RLS wird bei ASD häufig unterschätzt

Figure 1—Flow diagram of study patients through treatment approach.



ASD = autism spectrum disorder, OSA = obstructive sleep apnea, RLS = restless legs syndrome.

Kanney ML, Durmer JS, Trotti LM, Leu R. Rethinking bedtime resistance in children with autism: is restless legs syndrome to blame? J Clin Sleep Med. 2020 Dec 15;16(12):2029-2035. doi: 10.5664/jcsm.8756. PMID: 32804073; PMCID: PMC7848937.

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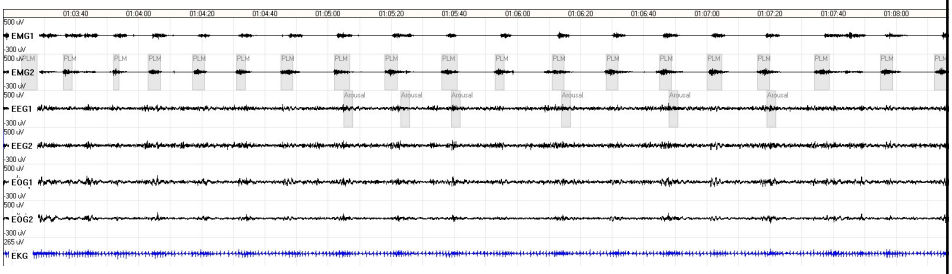
RLS in der Polysomnographie: PLM



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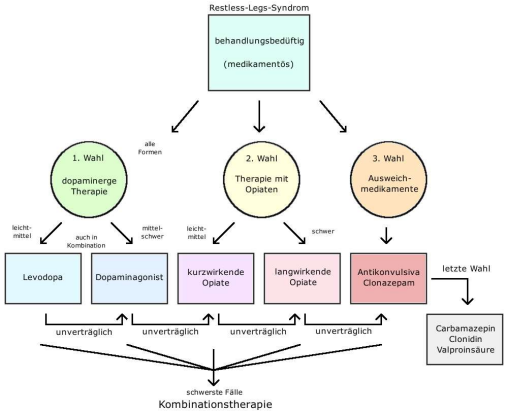
Restless Legs – was kann ich tun?

- Ausreichende Eisenversorgung: Ferritin > 75 µg/l, Transferrinsättigung > 20 %
- Ausreichende Vitamin D (40-70 µg/l) und Vitamin B12 Versorgung

- Ggf. medikamentöse Therapie mit Dopaminergika



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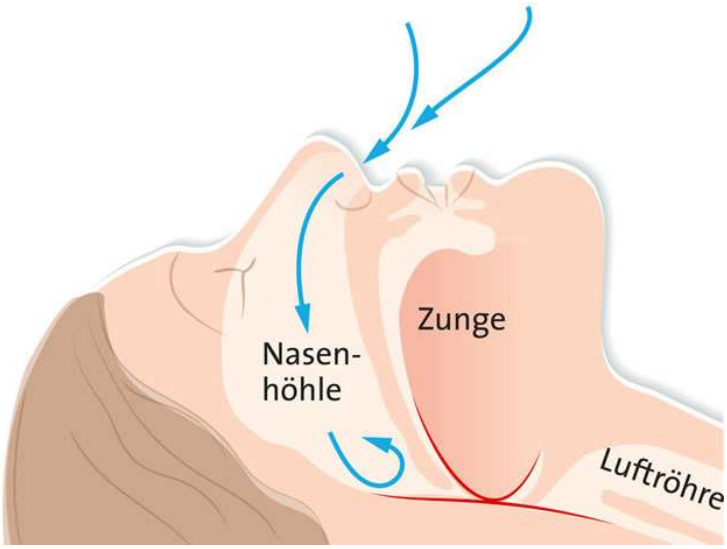
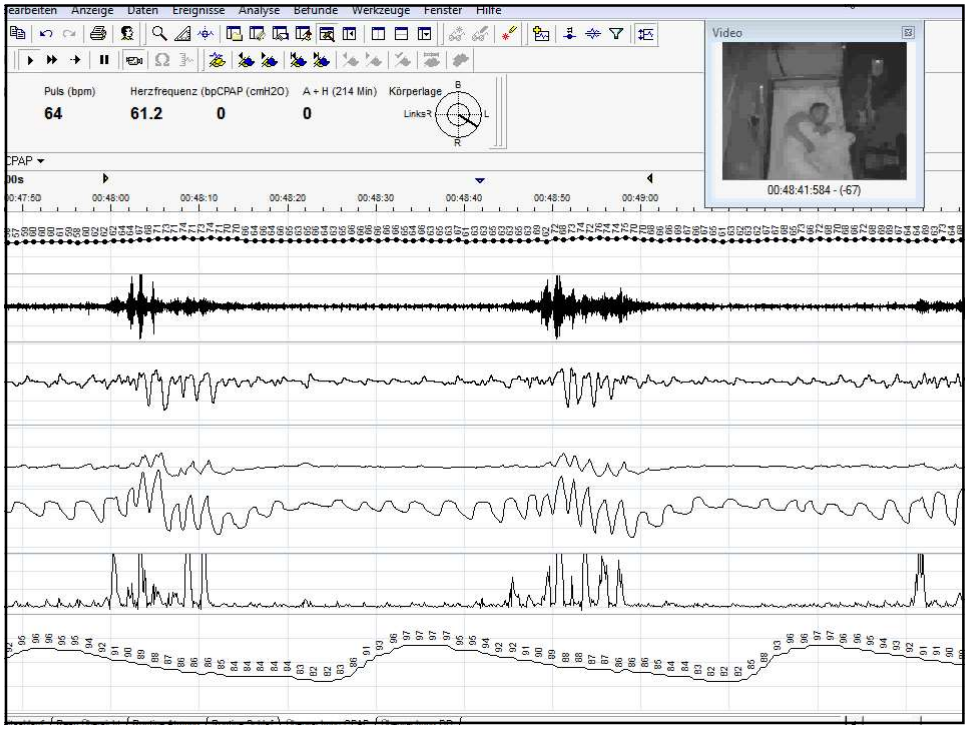
Schlafbezogene Atmungsstörungen





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Schlafstörungen bei Kindern mit Autismus

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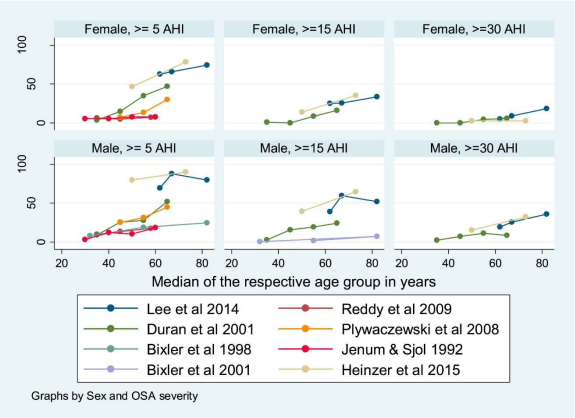
Schlafbezogene Atmungsstörungen – Schlafapnoe

♂ 13-33 %
♀ 6-19 %

Progesteron:
- Atemantrieb ⬆
- Tonus Pharynx ⬆

Östrogen:
- Schleimhaut ⬆
- Interm. Hypoxie ⬇



Chamara V. Senaratna, Jennifer L. Perret, Caroline J. Lodge, Adrian J. Lowe, Brittany E. Campbell, Melanie C. Matheson, Garun S. Hamilton, Shyamali C. Dharmage, Prevalence of obstructive sleep apnea in the general population: A systematic review, Sleep Medicine Reviews, Volume 34, 2017, Pages 70-81, ISSN 1087-0792, https://doi.org/10.1016/j.smrv.2016.07.002.

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Herz-Kreislauf-Erkrankungen in Folge von OSA

- Arterielle Hypertonie
- Schlaganfall
- Herzinfarkt
- Koronare Herzerkrankung
- Herzrhythmusstörungen, akuter Herztod
- Chronische Herzinsuffizienz

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CPAP = Continuous Positive Airway Pressure
kontinuierlicher positiver Atemwegdruck

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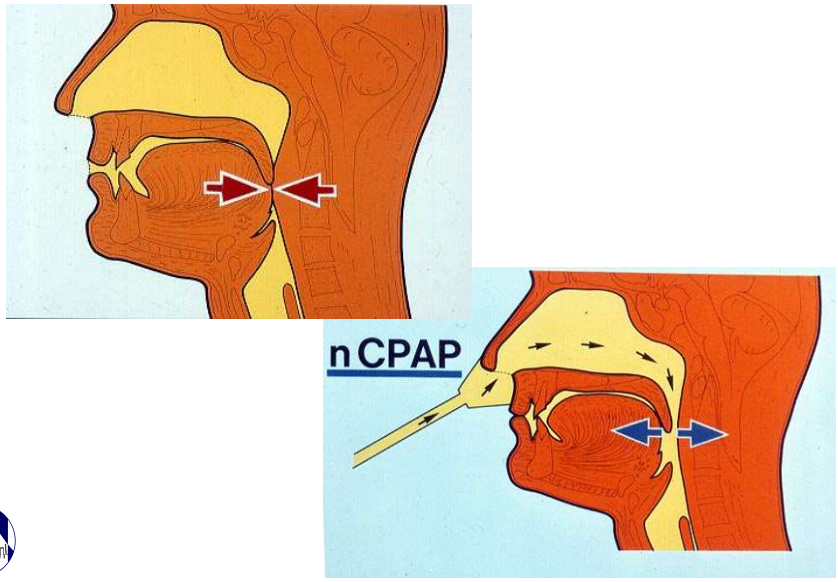

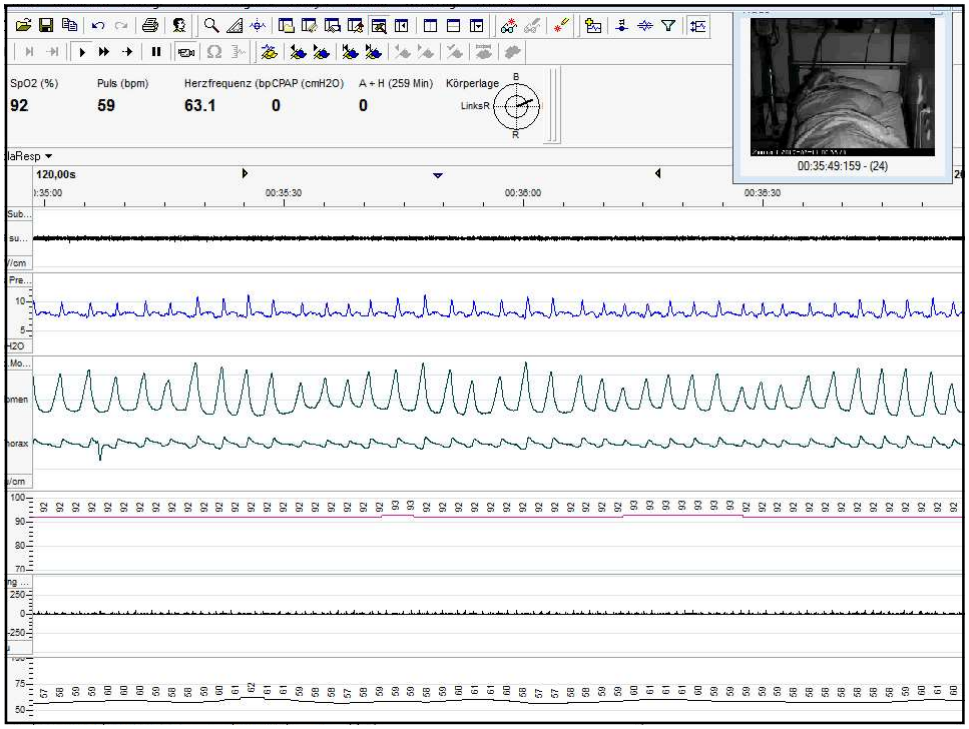

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Insomnien – Ein- und Wiedereinschlafstörungen

Das mit Abstand häufigste Schlafproblem!

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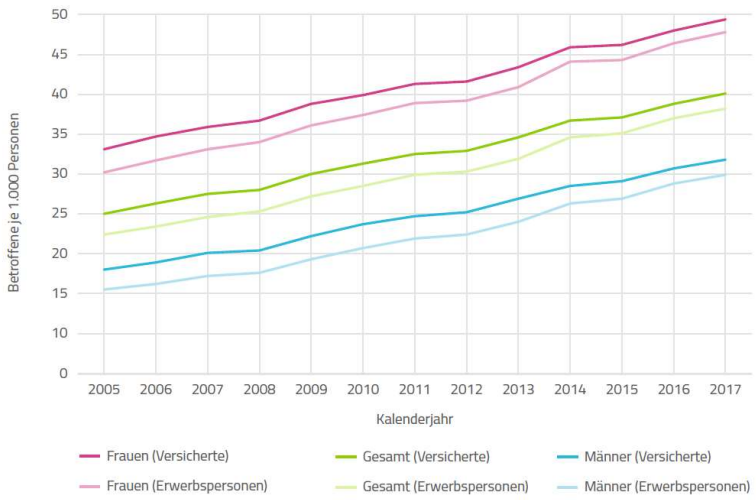
Schlafprobleme nehmen zu!



Thomas G. Grobe, Susanne Steinmann, Julia Gerr

Schriftenreihe zur Gesundheitsanalyse – Band 17

Gesundheitsreport 2019

Schlafstörungen

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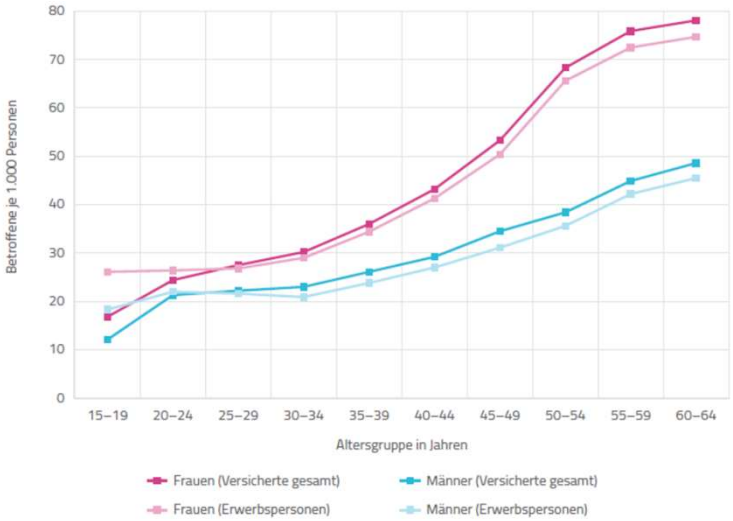
Schlafprobleme nehmen mit dem Alter zu!



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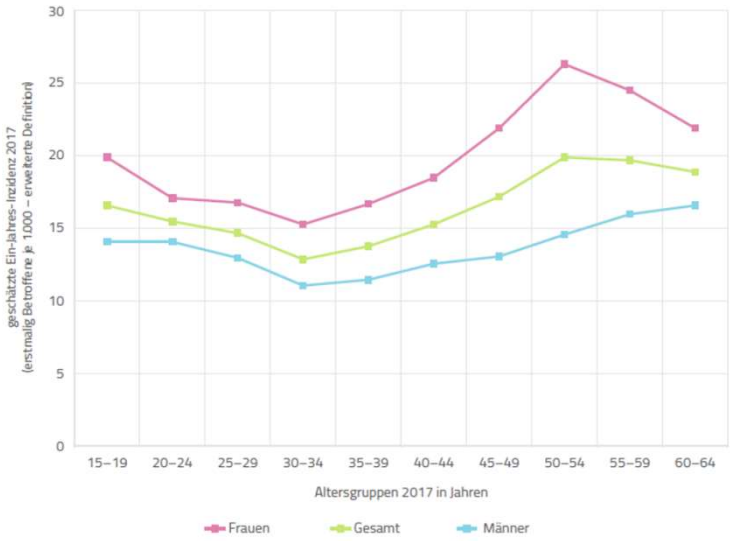
Wann treten Schlafprobleme neu auf?



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Schriftenreihe zur Gesundheitsanalyse – Band 12

Gesundheitsreport 2019

Schlafstörungen

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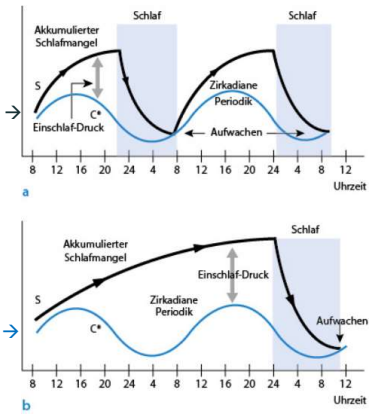
Wie wird Schlaf reguliert?

Wie wird Schlaf geregelt: Funktionelles Modell
Das 2-Komponenten Modell der Schlafregulation nach Borbély

Prozess S →



Prozess S → Schlafdruck

Prozess C →

Prozess C → circadian, Chronobiologie

Becker-Carus, C. (2021, 22. April). Schlafregulation, Schlafsteuerung. In M. A. Wirtz (Hrsg.): Dorsch Lexikon der Psychologie. Bern: Hogrefe. Verfügbar unter: https://dorsch.hogrefe.com/stichwort/schlafregulation-schlafsteuerung

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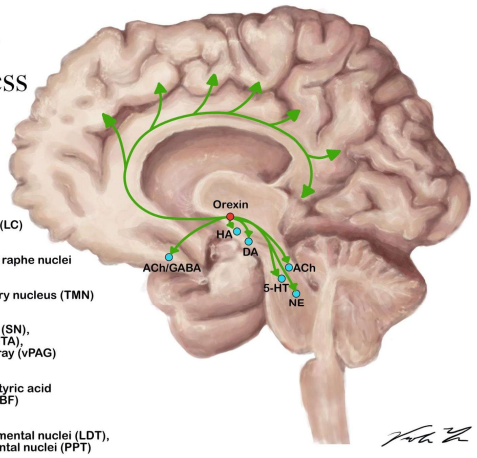
System for Sustaining Wakefulness



Key

NE = norepinephrine
located: locus coeruleus (LC)

5-HT = serotonin
located: dorsal & median raphe nuclei

HA = histamine
located: tuberomammillary nucleus (TMN)

DA = dopamine
located: substantia nigra (SN),
ventral tegmental area (VTA),
ventral periaqueductal gray (vPAG)

ACh = acetylcholine
GABA = gamma-aminobutyric acid
located: basal forebrain (BF)

ACh = acetylcholine
located: laterodorsal tegmental nuclei (LDT),
pedunculopontine tegmental nuclei (PPT)

https://cpb-us-w2.wpmucdn.com/wordpress.lehigh.edu/dist/b/1881/files/2020/09/IMG_0826-copy-2.jpg
https://wordpress.lehigh.edu/portraits-of-the-brain/textbook-chapter-images/

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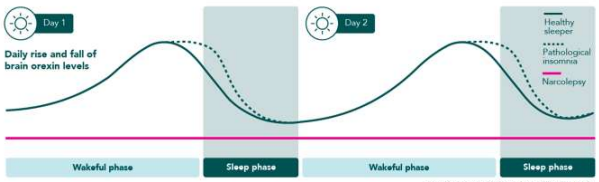
Orexin regelt unsere Wachbereitschaft



From Sun Y, et al. 2021[1] (CC-BY-NC-ND 4.0)

- **Hyperarousal** at night can lead to disrupted sleep and daytime functioning impairment[2]

1. Sun Y, et al. Front Neurol Neurosci. 2021;45:22-37; 2. Levenson JC, et al. *Chest*. 2015;147:1179–1192

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Wie wird Schlaf geregelt: Funktionelles Modell
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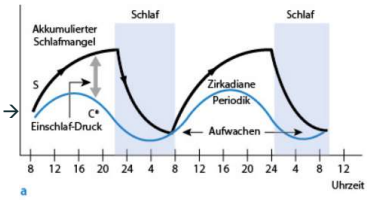
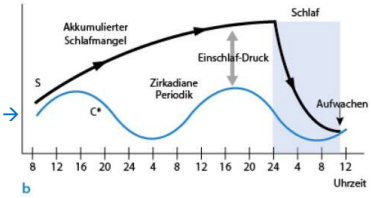


Prozess S → Schlafdruck

Prozess C →



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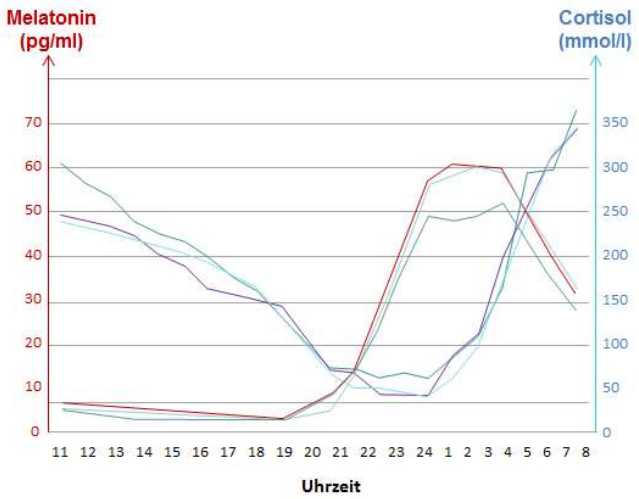
Melatonin-Spiegel
Maximum 1-4 Uhr



https://www.computerbase.de/forum/attachments/csm_hormonspiegel_12dbf14dde-png.693252/, 29.04.21.

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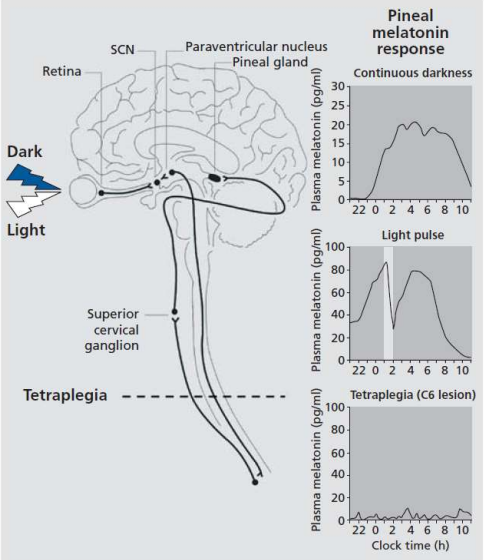

Lockley, Steven W.; Arendt, Josephine; Skene, Debra J. (2007): Visual impairment and circadian rhythm disorders. In: *Dialogues in clinical neuroscience* 9 (3), S. 301–314.

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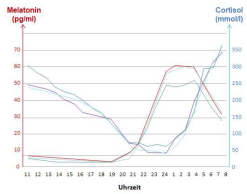


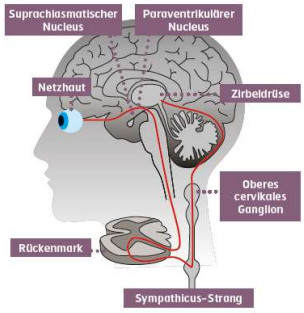
Licht → SCN

SCN → Zirbeldrüse

Zirbeldrüse → Melatonin

Melatonin → SCN

MT-1 Rezeptor MT-2 Rezeptor



Dibner C et al. The mammalian circadian timing system: organization and coordination of central and peripheral clocks. Annu Rev Physiol. 2010;72:517–49
Partch CL et al. Molecular architecture of the mammalian circadian clock. Trends Cell Biol. 2014;24(2):90–9

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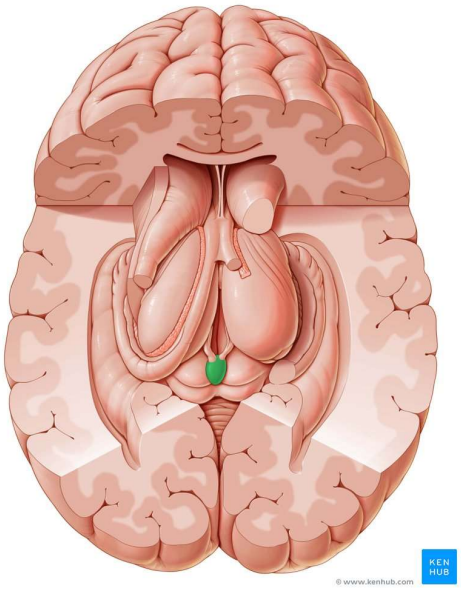

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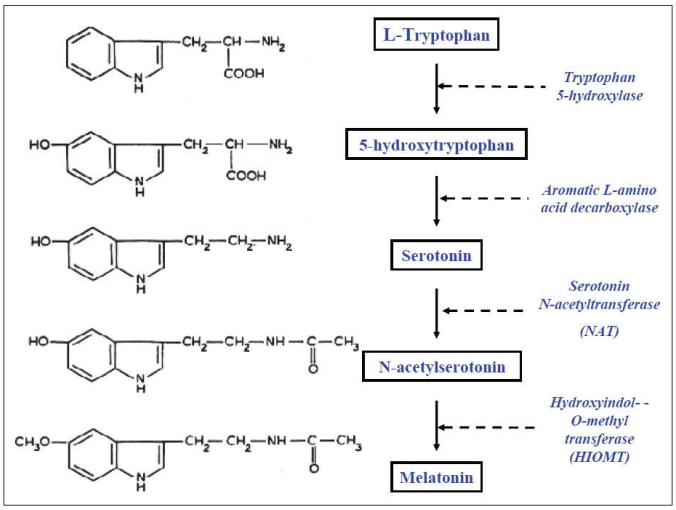
Melatoninsynthese



J Physiol Pharmacol. 2011 Feb;62(1):13-9.
Melatonin and aging: prospects for human treatment.
Bubenik GA[1], Konturek SJ.

Niedriges Melatonin der Mutter prädestiniert für ASD

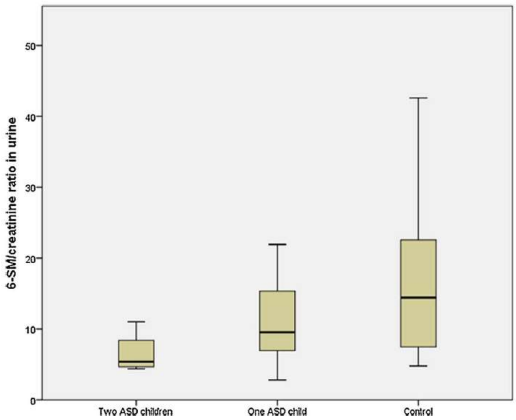


Fig. 4. 6-SM/creatinine ratio in urine of mothers. The values have been recalculated to the age of the mother at child birth.

Wiebe Braam, Friederike Ehrhart, Anneke P.H.M. Maas, Marcel G. Smits, Leopold Curfs, Low maternal melatonin level increases autism spectrum disorder risk in children, Research in Developmental Disabilities, Volume 82, 2018, Pages 79-89, ISSN 0891-4222, https://doi.org/10.1016/j.ridd.2018.02.017.

Melatoninausschüttung bei ASD ist in vielen Fällen reduziert

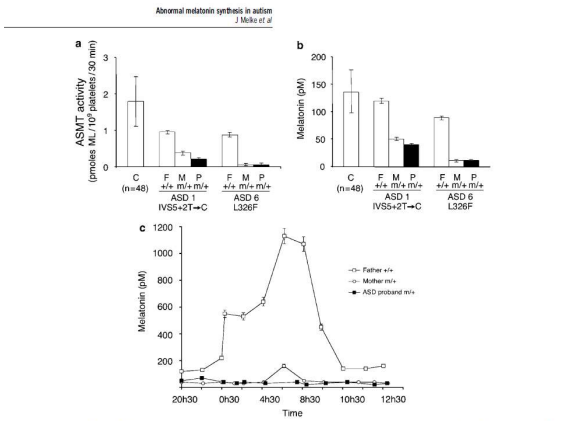


Figure 2 Impact of the ASMT mutations on enzyme activity and melatonin concentration. (**a**) ASMT activity, measured in platelets of the members of families autism spectrum disorder (ASD) 1 and ASD 6 carrying the splice–site IVS5 + 2T > C and the L326F *ASMT* mutations, respectively. (**b**) Blood melatonin concentration in the same individuals. (**c**) Nocturnal melatonin profile of family ASD 1. The proband (male, 24 years old) and his mother (53 years old) are heterozygous (m/ +) for the splice–site mutation IVS5 + 2T > C. The proband's father (55 years old) has no *ASMT* mutation (+ / +). Error bars represent s.d. C: controls; F: father; M: mother; P: proband.

Melke, J., Goubran Botros, H., Chaste, P. *et al.* Abnormal melatonin synthesis in autism spectrum disorders. *Mol Psychiatry* **13**, 90–98 (2008). https://doi.org/10.1038/sj.mp.4002016

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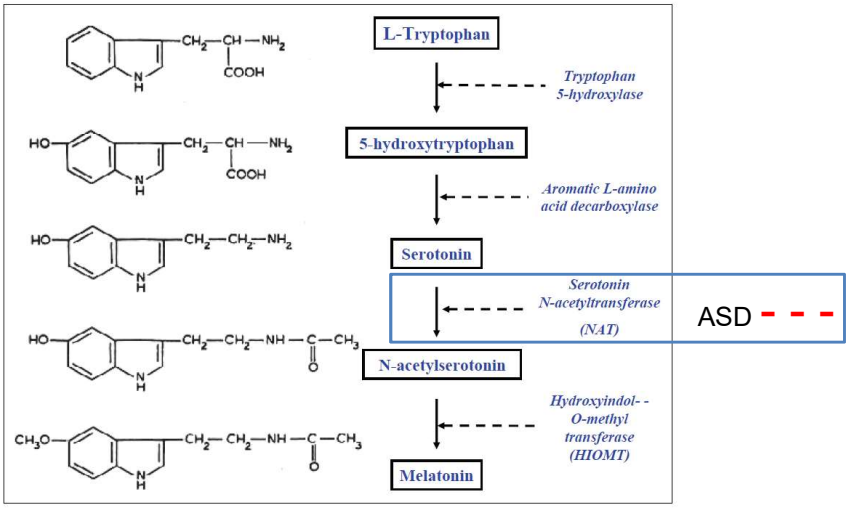
Melatoninsynthese bei ASD oft beeinträchtigt



J Physiol Pharmacol. 2011 Feb;62(1):13-9.
Melatonin and aging: prospects for human treatment.
Bubenik GA[1], Konturek SJ.

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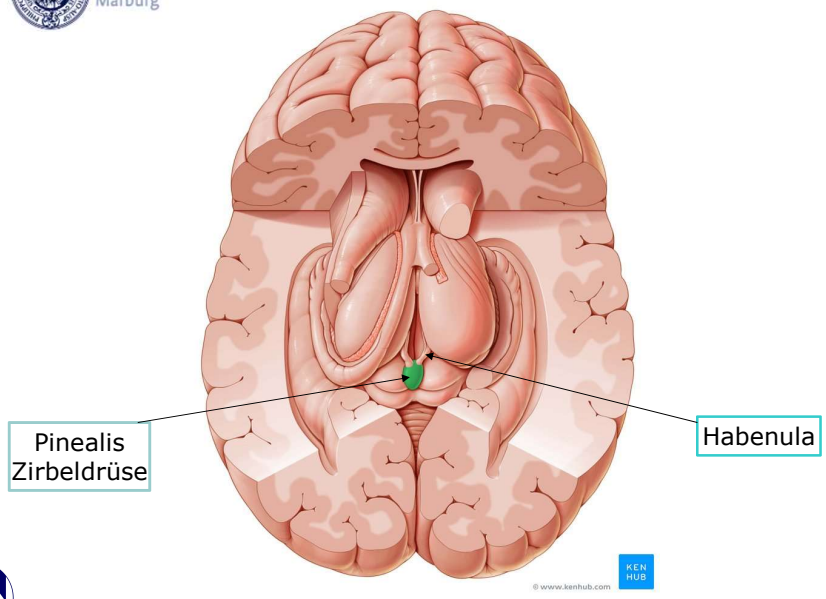

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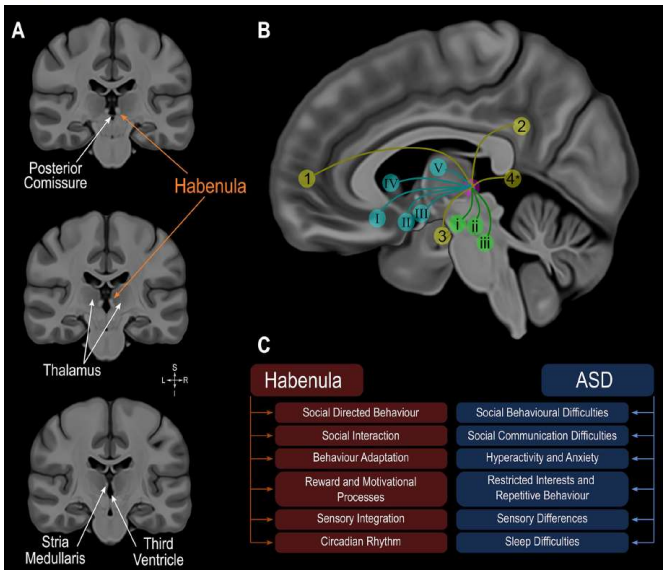
Habenula → ASD?



Germann J, Gouveia FV, Brentani H, Bedford SA, Tullo S, Chakravarty MM, Devenyi GA. Involvement of the habenula in the pathophysiology of autism spectrum disorder. Sci Rep. 2021 Oct 27;11(1):21168. doi: 10.1038/s41598-021-00603-0. PMID: 34707133; PMCID: PMC8551275.

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- Niedriges Melatonin bei Menschen mit Autismus
- Niedriges Melatonin der Mutter erhöht das Risiko für Autismus
- Wie kann man Melatonin erhöhen?

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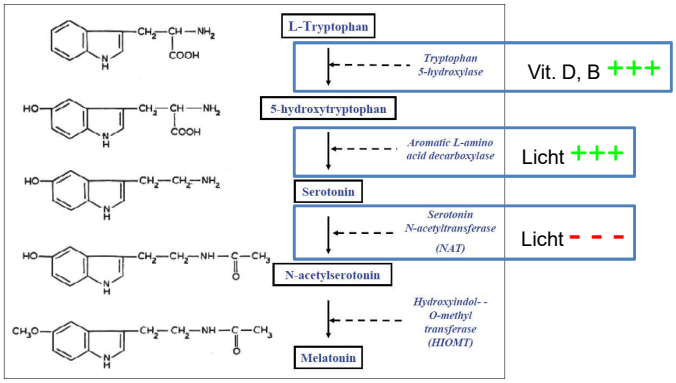
Melatoninsynthese



J Physiol Pharmacol. 2011 Feb;62(1):13-9.
Melatonin and aging: prospects for human treatment.
Bubenik GA[1], Konturek SJ.

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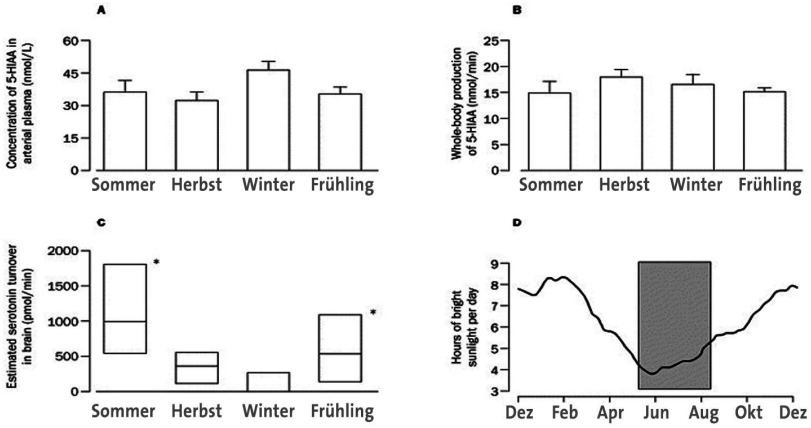
Serotonin und Licht



Effect of sunlight and season on serotonin turnover in the brain
G W Lambert, C Reid, D M Kaye, G L Jennings, M D Esler
Lancet 2002; 360: 1840–42

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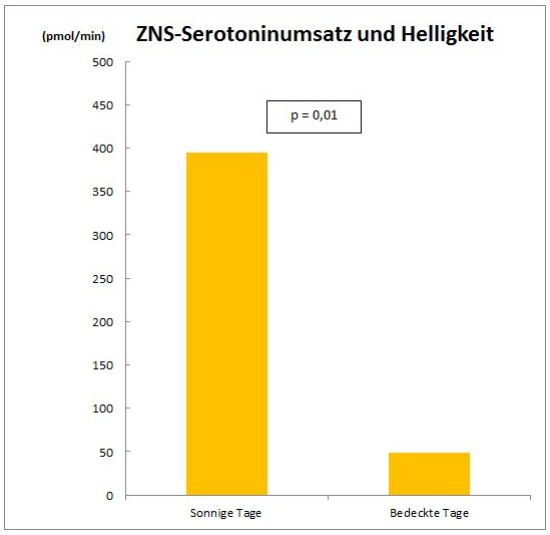
Serotonin und Licht



Nach: Effect of sunlight and season on serotonin turnover in the brain
G W Lambert, C Reid, D M Kaye, G L Jennings, M D Esler
Lancet 2002; 360: 1840–42

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Der Melatoninspiegel sinkt

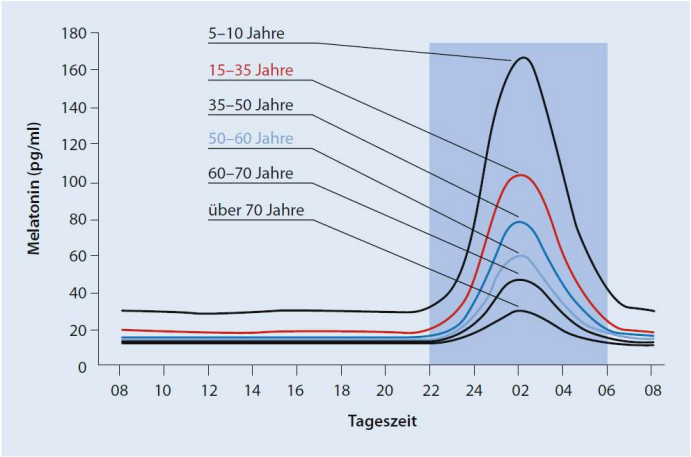

Abb. 1 ▲ Melatonin-Tagesrhythmus. (Mod. nach [16])

Gynäkologische Endokrinologie https://doi.org/10.1007/s10304-018-0221-z
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W. Cassel · P. Cassel
Guter Schlaf im besten Alter

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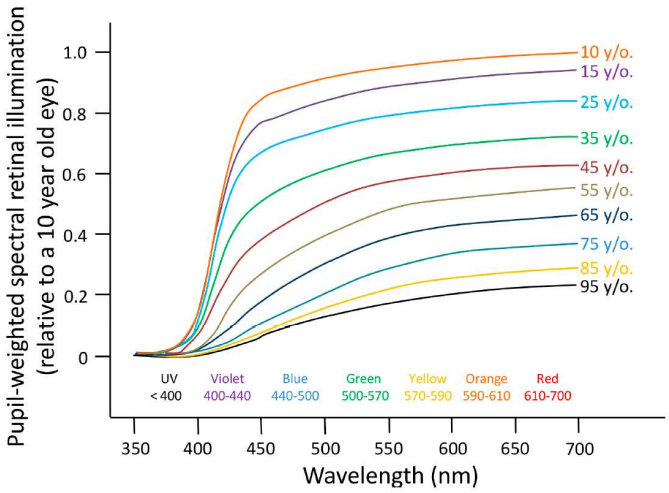
Das Auge wird weniger lichtempfindlich



Turner, P.L.; Mainster, M.A. Circadian photoreception: Ageing and the eye's important role in systemic health. *Br. J. Ophthalmol.* **2008**, *92*, 1439–1444.

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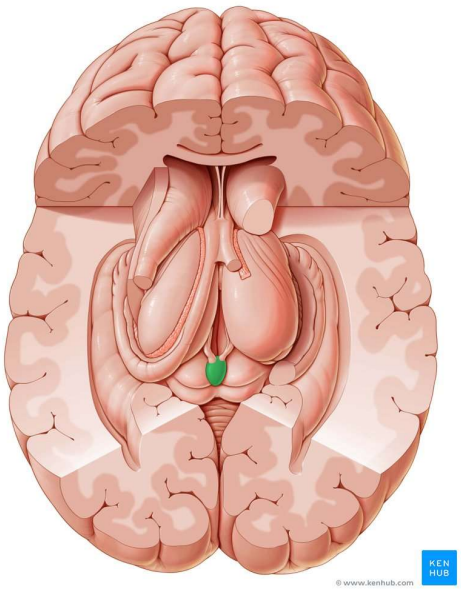

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Die Zirbeldrüse verkalkt

Age group	N	TPV	NPV	CPV	POC (%)
0–9	20	55.1 ± 18.69	55.04 ± 18.69	0.06 ± 0.22	0.1
10–19	22	86.15 ± 29.94	80.93 ± 28.14	5.22 ± 11.86	6.05
20–29	24	78.68 ± 19.3	69.56 ± 22.66	9.12 ± 17.6	11.59
30–39	20	93.24 ± 23.68	77.42 ± 23.04	15.81 ± 18.64	16.95
40–49	22	116.7 ± 44.51	83.68 ± 30.86	33.02 ± 42.41	28.29
50–59	18	104.69 ± 31.13	79.64 ± 31.87	25.05 ± 27.93	23.92
60–69	21	131.04 ± 88.55	94.15 ± 71.44	36.89 ± 33.47	28.15
≥70	20	101.73 ± 30.6	81.46 ± 32.11	20.27 ± 26.29	19.92
Total	167				
p value		<0.001	0.03	<0.001	<0.001

Table 1: Distribution of the pineal volume parameters according to age groups.
N: Number, **TPV:** Total pineal volume, **NPV:** Non-calcified pineal volume, **CPV:** Calcified pineal volume, **POC:** Proportion of calcification.

Beker-Acay, M et al 2016 Assessment of Pineal Gland Volume and Calcification in Healthy Subjects: Is it Related to Aging? *Journal of the Belgian Society of Radiology*, 100(1): 13, pp. 1–7, DOI: http://dx.doi.org/10.5334/jbr-btr.892

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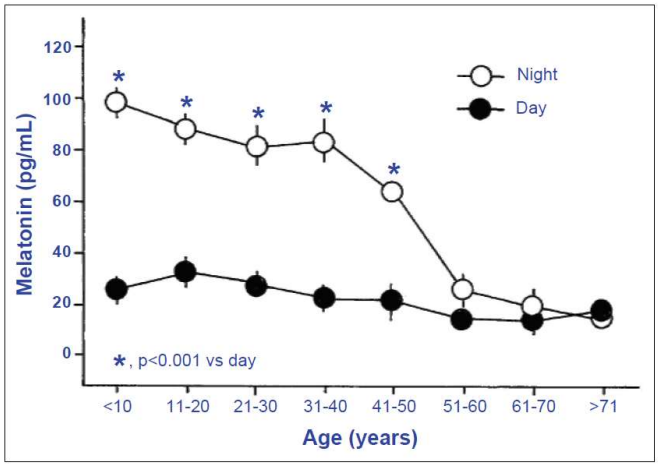
Nacht-Tag Differenz Melatonin



Karasek M, Winczyk K (2006) Melatonin in humans. J Physiol Pharmacol 57 Suppl 5:19–39

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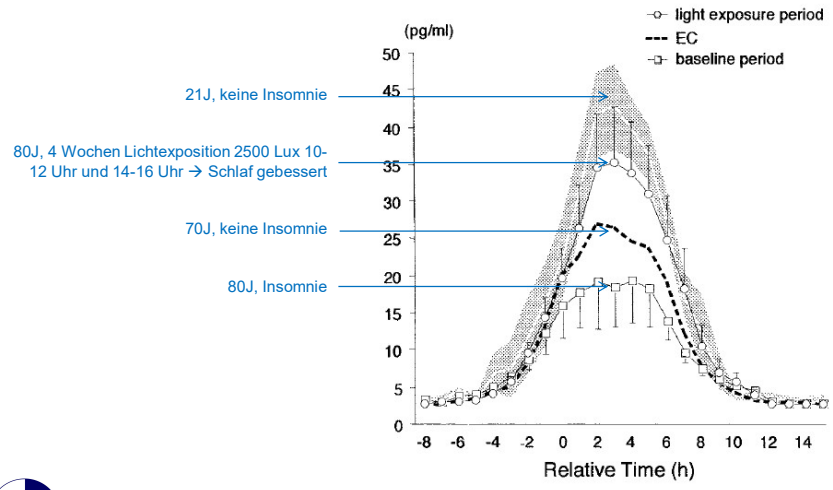
Vierstündige Lichtexposition Altersheim



Mishima K, Okawa M, Shimizu T, Hishikawa Y. Diminished melatonin secretion in the elderly caused by insufficient environmental illumination. *J Clin Endocrinol Metab.* 2001;86(1):129-134. doi:10.1210/jcem.86.1.7097

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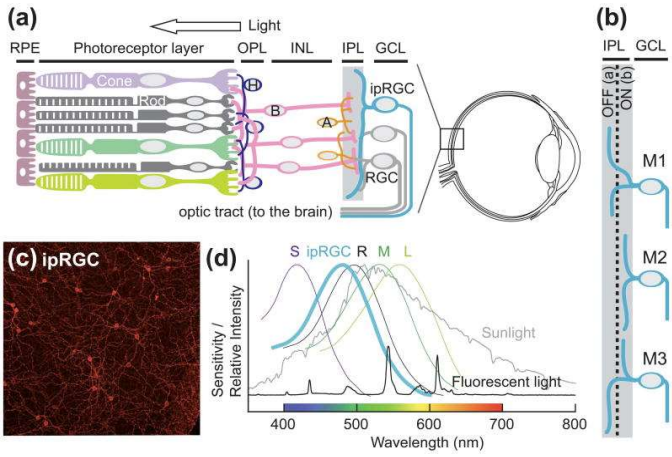
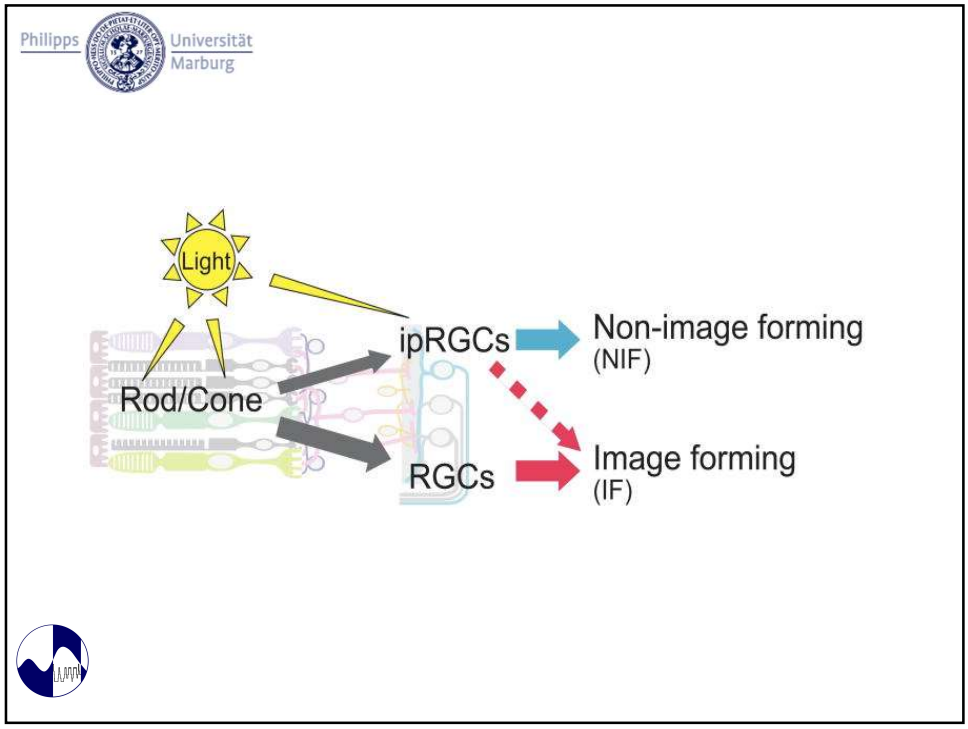
Die inner Uhr wird durch eher helles, „blaues“ Licht gesteuert

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Marburg
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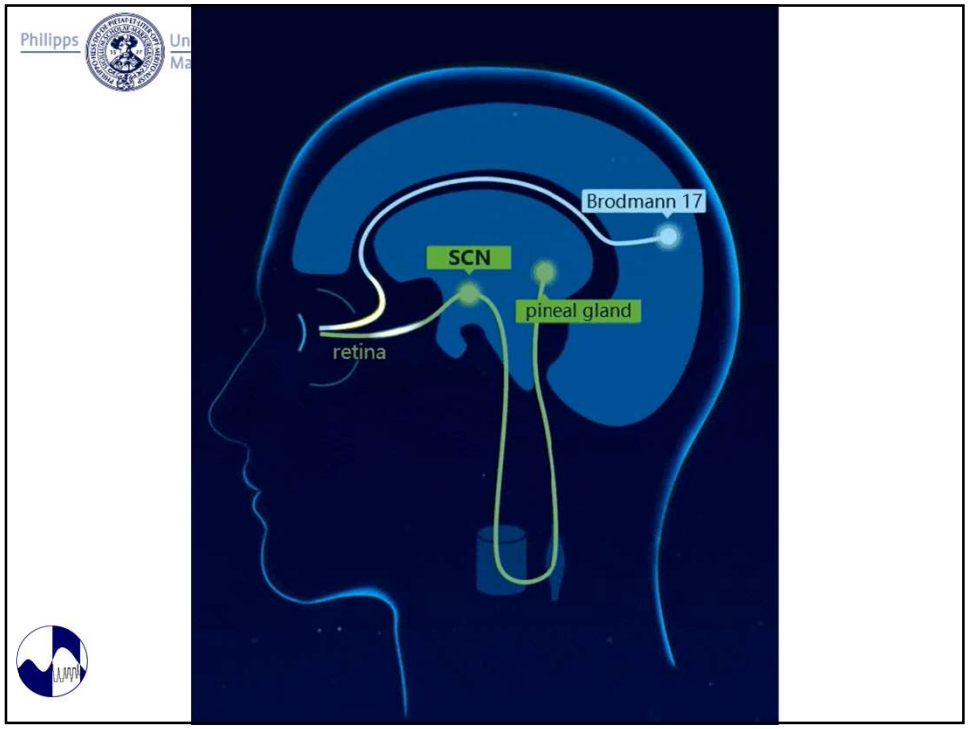
(IF)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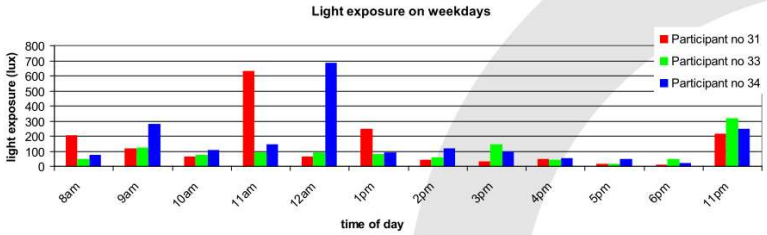
Brodmann 17
SCN
pineal gland
retina

Philipps Universität Marburg



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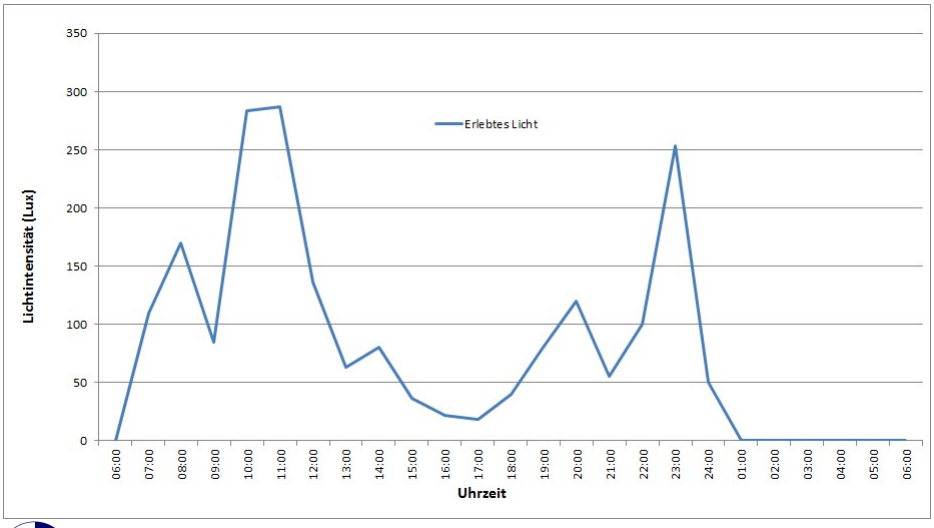

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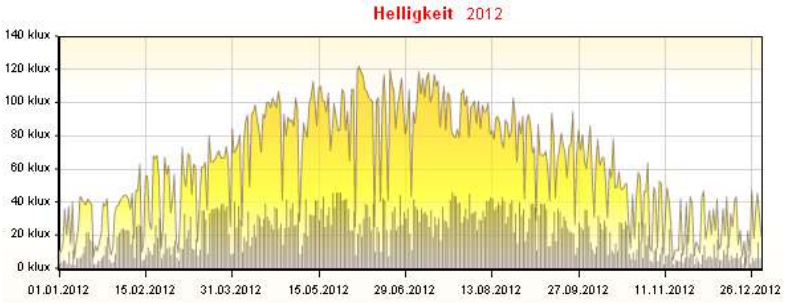

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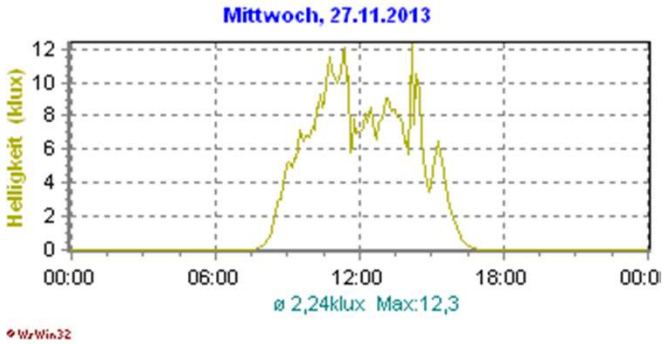

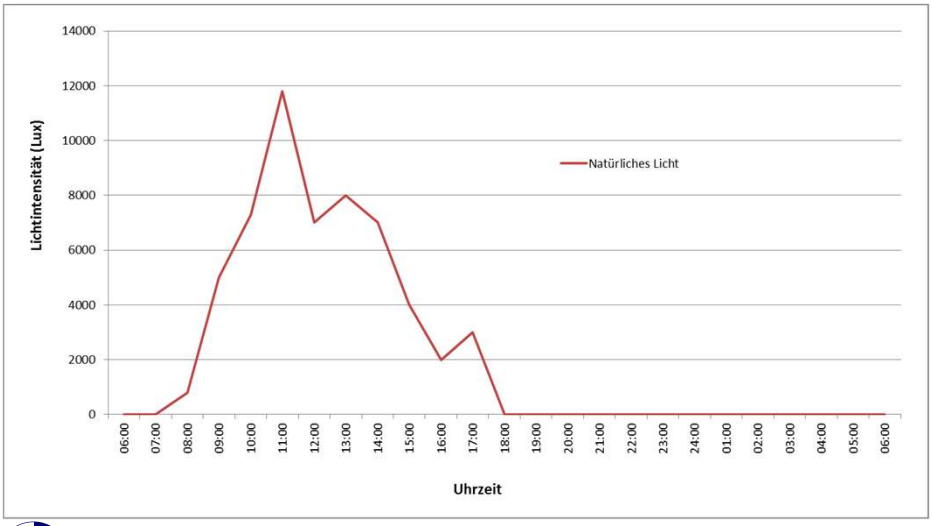
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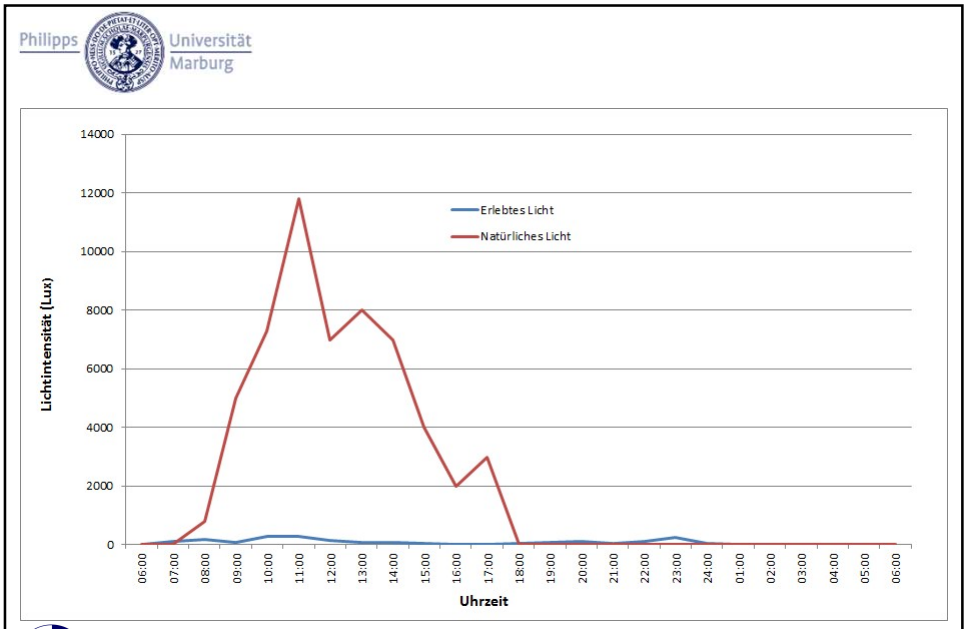
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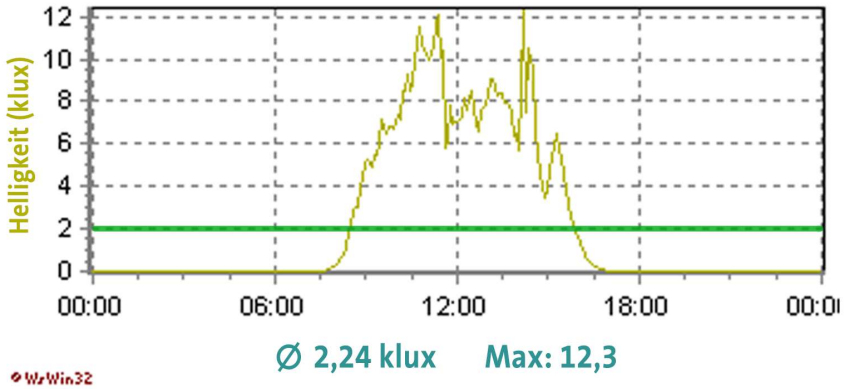
Mittwoch, 27.11.2013



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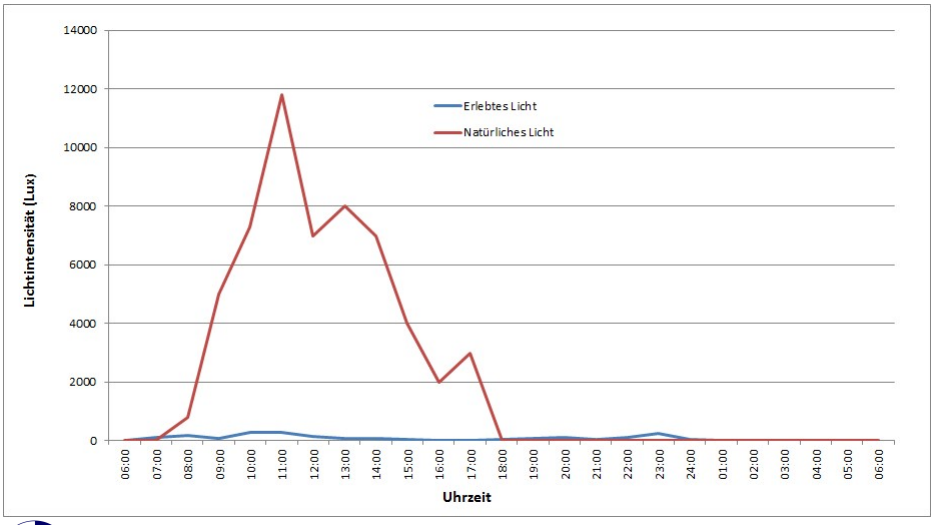

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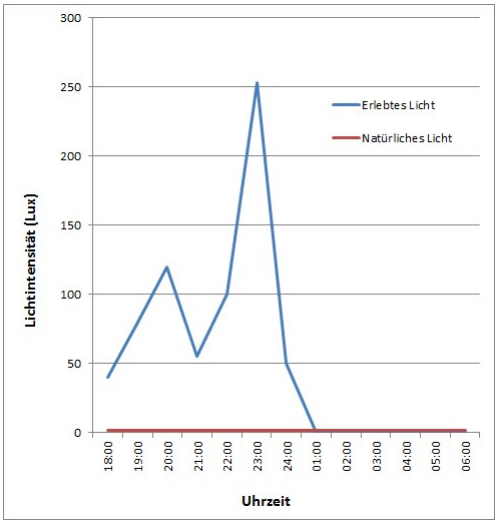

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https://www.glasshop-wiesner.de/spiegel-kristallspiegel.html

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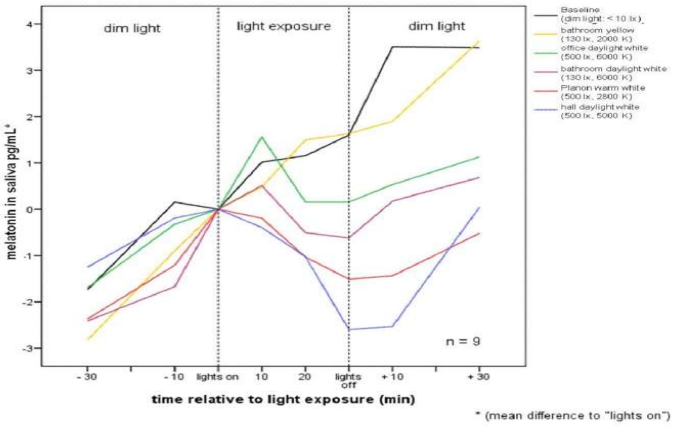

Figure 2. Group means of saliva melatonin concentrations; lines represent the different lighting conditions. Data are given relative to the zero point that represents melatonin concentrations at "lights on". Values on *X*-axis represent mean differences of melatonin concentrations to "lights on".

Wahnschaffe A, Haedel S, Rodenbeck A, Stoll C, Rudolph H, Kozakov R, Schoepp H, Kunz D. Out of the lab and into the bathroom: evening short-term exposure to conventional light suppresses melatonin and increases alertness perception. Int J Mol Sci. 2013 Jan 28;14(2):2573-89. doi: 10.3390/ijms14022573. PMID: 23358248; PMCID: PMC3588603.

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- Lichtmangel am Tag beeinträchtigt die Melatoninproduktion.
- Lichtüberschuss in der Nacht beeinträchtigt die Melatoninsekretion.
- Lichtmangel am Tag und Lichtüberschuss in der Nacht verschlechtern den Schlaf.

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Wie kann man schlechten Schlaf verbessern?

Insomnie: Pharmakotherapie

Benzodiazepine und Z-Substanzen

Wirksamkeit und Wirkmechanismus	Nachteile
• Häufigste verordnete Hypnotika • Verstärkung der inhibitorischen Wirkung von GABA im ZNS • Verkürzung der Schlaflatenz und Erhöhung der Schlafeffizienz • Sedativ-hypnotisch, muskelrelaxierend, anxiolytisch und antikonvulsiv	• Abhängigkeitspotenzial • Toleranzentwicklung • Hangover-Effekte (Benommenheit) • Erhöhung des Sturzrisikos • Veränderung der Schlafarchitektur (Verkürzung der Tiefschlaf- und REM-Phasen) • Keine Langzeit-Anwendung möglich • Erhöhung des Demenz-Risikos

Block F. Praxisbuch neurologische Pharmakotherapie. Springer-Verlag, Heidelberg 2013
DGN-Leitlinie Nicht erholsamer Schlaf/Schlafstörungen. Somnologie 2009;13:4–160
KVB. Arzneimittel im Blickpunkt: Der Einsatz von Benzodiazepinen und Z-Substanzen bei Schlafstörungen. Nr. 34/2011

Der Melatoninspiegel sinkt

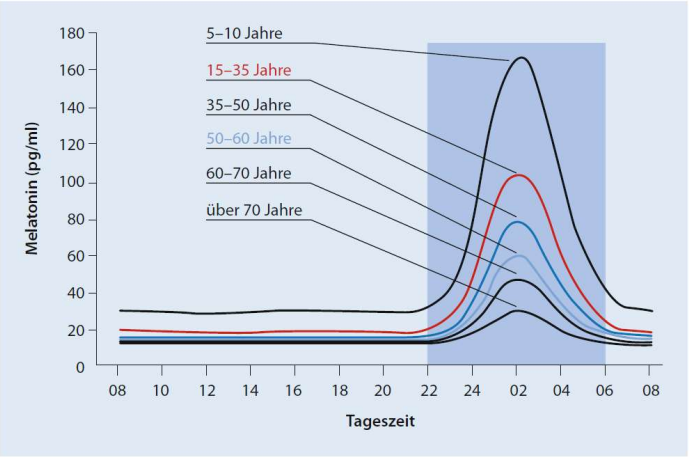

Abb. 1 ▲ Melatonin-Tagesrhythmus. (Mod. nach [16])

Gynäkologische Endokrinologie https://doi.org/10.1007/s10304-018-0221-z
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Guter Schlaf im besten Alter

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Schlaf über den Lebensablauf

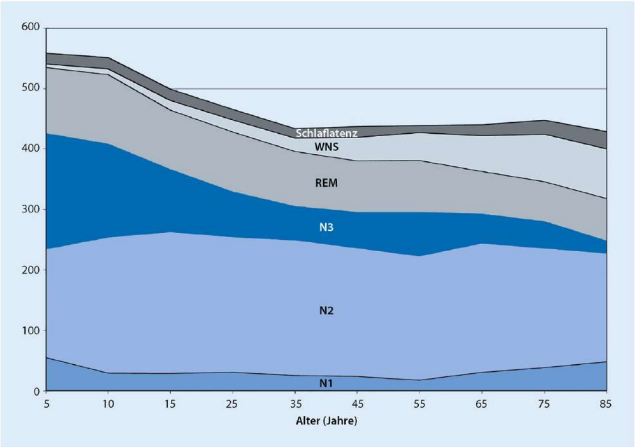

Abb. 3 ▲ Veränderungen des Schlafs über das Lebensalter für Einschlaflatenz (*Schlaflatenz*), Wachheit nach Schlafbeginn (*WNS*), REM-Schlaf (*REM*, „rapid eye movement"), Tiefschlaf (*N3*) und Leichtschlaf (*N2* und *N1*) in Minuten. (Mod. nach [22])

Gynäkologische Endokrinologie https://doi.org/10.1007/s10304-018-0221-z
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Guter Schlaf im besten Alter

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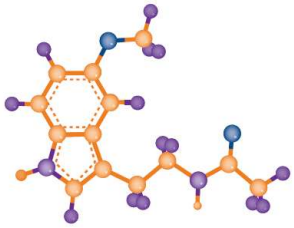
Insomnie: Pharmakotherapie - Melatonin

- Substitution des altersbedingten endogenen Melatonin-Mangels
- Erhöhung der Schlafneigung
- Regulation des Tag-Nacht-Wechsels
- Synchronisation des zirkadianen Rhythmus



Melatonin – ein Schlafmittel für Ältere. AMB 2008;42 http://www.der-arzneimittelbrief.de/de/Artikel.aspx?SN=6922 (Zugriff Juli 2016)

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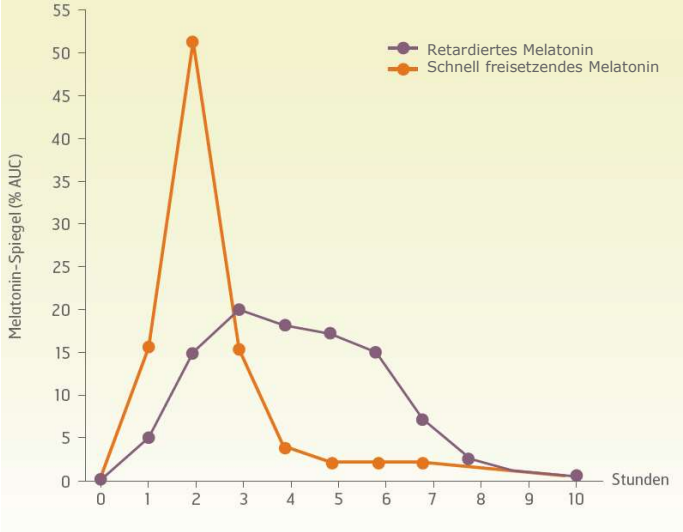
Melatonineinnahme



European Public Assessment Report (EPAR) for Circadin. Procedure No. EMEA/H/C/695. URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion/human/000695/WC500026808.pdf)

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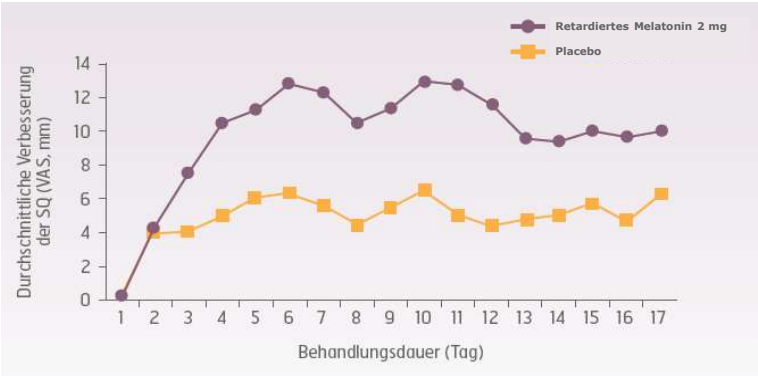
Retardiertes Melatonin verbessert die Schlafqualität



Luthringer R et al. The effect of prolonged-release melatonin on sleep measures and psychomotor performance in elderly patients with insomnia. Int Clin Psychopharmacol. 2009;24(5):239-49

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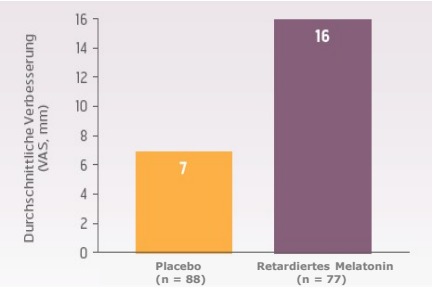
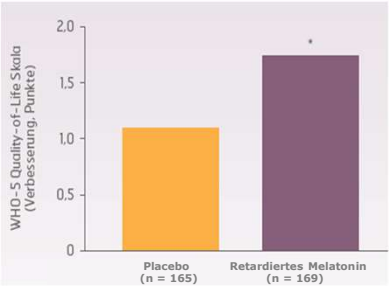
Retardiertes Melatonin verbessert Wachheit und Lebensqualität

Wachheit am Morgen[1]



Lebensqualität[2]



1. Lemoine P et al. Prolonged-release melatonin improves sleep quality and morning alertness in insomnia patients aged 55 years and older and has no withdrawal effects. J Sleep Res. 2007;16(4):372-80
2. Wade AG et al. Efficacy of prolonged release melatonin in insomnia patients aged 55-80 years: quality of sleep and next-day alertness outcomes. Curr Med Res Opin. 2007;23(10):2597-605

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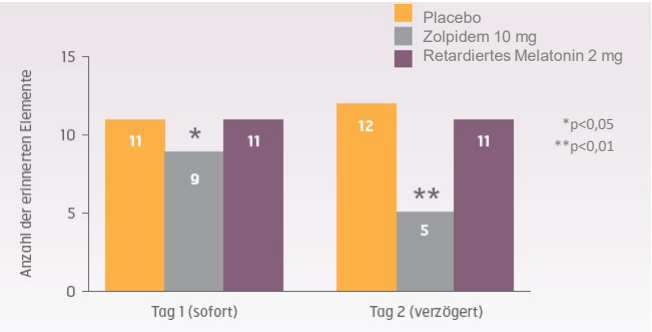
Retardiertes Melatonin: Keine Beeinträchtigung der Gedächtnisleistung



Otmani S et al. Effects of prolonged-release melatonin, zolpidem, and their combination on psychomotor functions, memory recall, and driving skills in healthy middle aged and elderly volunteers. Hum Psychopharmacol. 2008;23(8):693-705

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Verträglichkeit retardiertes Melatonin

- Die Rate der Nebenwirkungen lag auf Placebo-Niveau.[1,2]

	3 Wochen		6 Monate	
% der Patienten	Placebo	Melatonin	Placebo	Melatonin
Unerwünschte Wirkung	5,3%	6,1%	17,8%	12,9%
Therapieabbrüche	2%	2%	6,8%	5,6%

- Häufigste Nebenwirkungen waren:[2]
  - Kopfschmerzen
  - Nasopharyngitis
  - Rückenschmerzen
  - Arthralgie

1. Wade AG et al. Nightly treatment of primary insomnia with prolonged release melatonin for 6 months: a randomized placebo controlled trial on age and endogenous melatonin as predictors of efficacy and safety. BMC Med. 2010;8:51
2. Fachinformation Circadin® Stand Juli 2015

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Retardiertes Melatonin: Nutzen-Risiko-Profil

- Keine Änderung der Schlafarchitektur[1,2]
- Keine Hangover-Effekte[2,3]
- Keine erhöhte Sturzneigung[4]
- Kein Abhängigkeitspotenzial[5]
- Keine Toleranzentwicklung[5]
- Keine Rebound-Insomie[5]

1. Fachinformation Circadin® Stand Juli 2015
2. Luthringer R et al. The effect of prolonged-release melatonin on sleep measures and psychomotor performance in elderly patients with insomnia. Int Clin Psychopharmacol. 2009;24(5):239-49
3. Otmani S et al. Effects of prolonged-release melatonin, zolpidem, and their combination on psychomotor functions, memory recall, and driving skills in healthy middle aged and elderly volunteers. Hum Psychopharmacol. 2008;23(8):693-705
4. Otmani S et al. Effects of prolonged-release melatonin and zolpidem on postural stability in older adults. Hum Psychopharmacol. 2012;27(3):270-6
5. Lemoine P Prolonged-release melatonin for insomnia – an open-label long-term study of efficacy, safety, and withdrawal. Ther Clin Risk Manag. 2011;7:301–311

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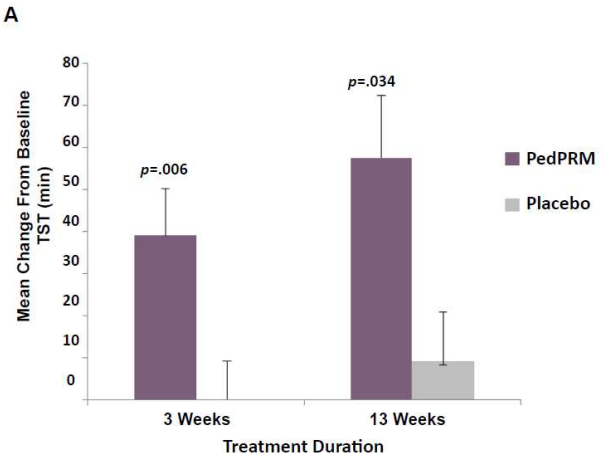
Retardiertes Melatonin bei ASD: verlängerte Schlafzeit



Paul Gringras, Tali Nir, John Breddy, Anat Frydman-Marom, Robert L. Findling: Efficacy and Safety of Pediatric Prolonged-Release Melatonin for Insomnia in Children With Autism Spectrum Disorder, . Journal of the American Academy of Child & Adolescent Psychiatry, Volume 56, Issue 11, 2017, Pages 948-957.e4, ISSN 0890-8567, https://doi.org/10.1016/j.jaac.2017.09.414.

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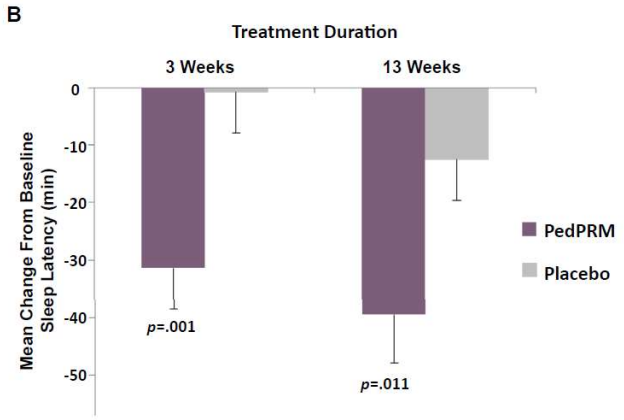
Retardiertes Melatonin bei ASD: schnelleres Einschlafen



Paul Gringras, Tali Nir, John Breddy, Anat Frydman-Marom, Robert L. Findling: Efficacy and Safety of Pediatric Prolonged-Release Melatonin for Insomnia in Children With Autism Spectrum Disorder, . Journal of the American Academy of Child & Adolescent Psychiatry, Volume 56, Issue 11, 2017, Pages 948-957.e4, ISSN 0890-8567, https://doi.org/10.1016/j.jaac.2017.09.414.

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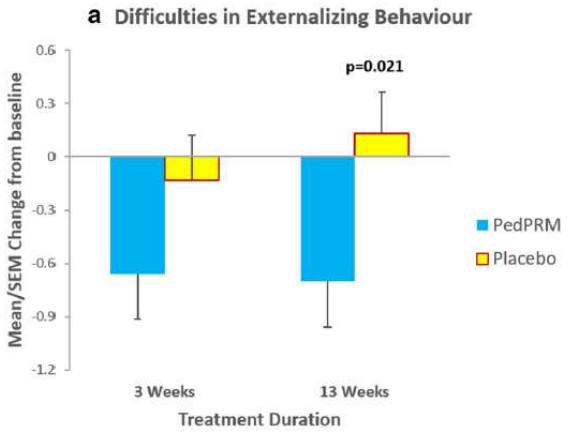
Retardiertes Melatonin bei ASD: weniger antisoziales Verhalten



Schroder, C.M., Malow, B.A., Maras, A. *et al.* Pediatric Prolonged-Release Melatonin for Sleep in Children with Autism Spectrum Disorder: Impact on Child Behavior and Caregiver's Quality of Life. *J Autism Dev Disord* **49**, 3218–3230 (2019). https://doi.org/10.1007/s10803-019-04046-5

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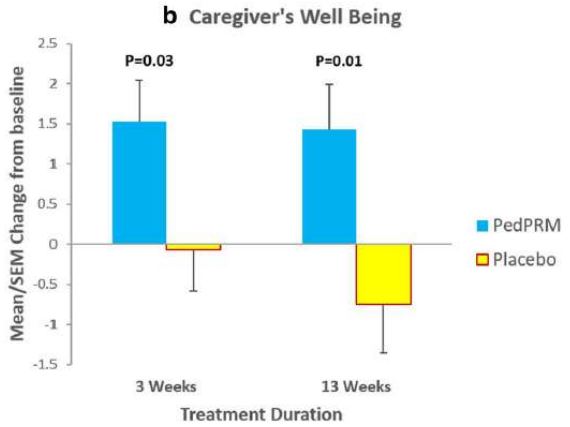
Retardiertes Melatonin bei ASD: bessere Lebensqualität der betreuenden Personen



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Zum Abschluss was zum Raten!

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- Entwicklung einer gelasseneren Einstellung zum Schlaf
  - ✓ Information zu Physiologie und Funktion des Schlaf
  - ✓ Korrektur falscher Erwartungen

Wie oft wacht ein gesunder Mensch nachts auf?

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- Entwicklung einer gelasseneren Einstellung zum Schlaf
  - ✓ Information zu Physiologie und Funktion des Schlaf
  - ✓ Korrektur falscher Erwartungen

Wie oft wacht ein gesunder Mensch nachts auf?

Insomniker: 0 – 1 mal

tatsächlich: Ø 25 mal (10 – 40), 4 – 6 mal länger (> 1 Minute)

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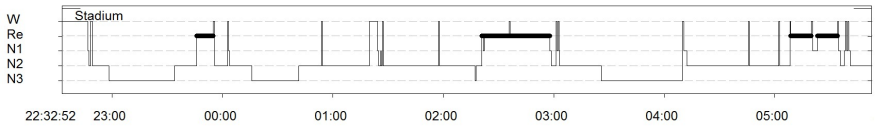
Schlafprofil normaler Schlaf



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Zusammenfassung

- Menschen mit Autismus haben häufiger Schlafprobleme als Kontrollen (Schlafapnoe, Restless Legs, Insomnie, Rhythmusstörungen).
- Das Dunkelheitshormon Melatonin ist bei Autismus oft erniedrigt, Melatoninmagel der Mutter erhöht das Risiko für Autismus.
- Die Einnahme von retardiertem Melatonin verbessert den Schlaf von Menschen mit Autismus.
- Chronobiologisch optimiertes Verhalten (viel Tageslicht, wenig nächtliches Kunstlicht) ist sinnvoll!

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Corkum et al. [3] concluded that sleep problems had been reported in about 25–50% of children with ADHD.

Pediatr Drugs (2017) 19:235–250
DOI 10.1007/s40272-017-0224-6

SYSTEMATIC REVIEW

Safety, Tolerability and Efficacy of Drugs for Treating Behavioural Insomnia in Children with Attention-Deficit/Hyperactivity Disorder: A Systematic Review with Methodological Quality Assessment

Shweta Anand[1] · Henry Tong[1,2] · Frank M. C. Besag[3,6] · Esther W. Chan[1] · Samuele Cortese[4,5] · Ian C. K. Wong[1,6]

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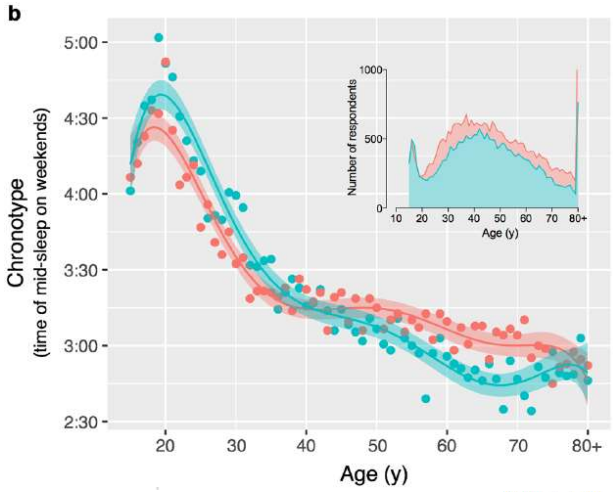
Chronotyp und Lebensalter



Citation: Fischer D, Lombardi DA, Marucci-Wellman H, Roenneberg T (2017) Chronotypes in the US – Influence of age and sex. PLoS ONE 12 (6): e0178782. https://doi.org/10.1371/journal.pone.0178782

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ADHS und Chronotyp

Table 1 Summary of studies included for review which examined chronotype/diurnal preference in ADHD

Authors and publication year	Study design	Participants	Paediatric, adolescent or adults	Circadian rhythms measures	Intervention	Summary of main results
Baird et al. (2012)	Case–control study	$N = 32$ (13 ADHD, 19 control)	Adult	Actigraphy, MEQ, salivary cortisol and melatonin, oral mucosa expression of PER2 and BMAL1	N/A	ADHD was associated with loss of the molecular rhythm of PER2 and BMAL1 in the oral mucosa. ADHD was also associated with greater eveningness and a delay of the cortisol rhythm referenced to wake time
Bijlenga et al. (2013b)	Cross-sectional	$N = 391$ (202 ADHD, 189 healthy control)	Adult (19–65)	Dutch Vragenlijst Ochtend/Avondmens questionnaire, based on MEQ and MCTQ; MCTQ	N/A	ADHD was associated with increased prevalence of delayed sleep phase disorder. ADHD was associated with later mid-sleep on free days
Caci et al. (2009)	Cross-sectional	Students ($N = 205$)	Adult	CSM	N/A	Eveningness related to inattentive symptoms of ADHD more so than hyperactivity/impulsivity
Gruber et al. (2012)	Case–control study	$N = 75$ (26 ADHD, 49 healthy control)	Childhood	Child morning–evening preference scale	N/A	ADHD was associated with greater eveningness. Evening orientation was associated with subjectively and objectively rated sleep-onset delay
Kooij and Bijlenga (2014)	Cross-sectional	$N = 543$	Adult	Likert-like self-rating of chronotype, self-reported presence of photophobia	N/A	More extreme evening types associated with ADHD; higher level of self-reported photophobia associated with ADHD
McGowan et al. (2016)	Cross-sectional	$N = 396$	Adults (mean age = 24)	MCTQ	N/A	Social jetlag is a significant predictor of ADHD symptoms and impulsivity, chronotype is not when social jetlag is included in the regression model
Rybak et al. (2007)	Cross-sectional	ADHD ($N = 29$)	Adult (20–60 yrs)	MEQ	N/A	Later circadian preference associated with increased self-reported symptoms of ADHD and increased commission errors on Conner's Continuous Performance Task
Vogel et al. (2015)	Case–control study	ADHD ($N = 202$), obesity ($N = 114$), healthy controls ($N = 154$)	Adult (18–65 yrs)	Dutch Vragenlijst Ochtend/Avondmens questionnaire, based on MEQ and MCTQ	N/A	ADHD group had shorter sleep on free days, later chronotype, more delayed sleep phase disorder indicators and more unstable eating patterns than the obese group
Voinescu et al. (2012)	Cross-sectional	$N = 301$	Adult	CSM	N/A	ADHD symptoms are associated with increased eveningness

Coogan AN, McGowan NM. A systematic review of circadian function, chronotype and chronotherapy in attention deficit hyperactivity disorder. *Atten Defic Hyperact Disord*. 2017;9(3):129-147. doi:10.1007/s12402-016-0214-5

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ADHD Atten Def Hyp Disord (2017) 9:129–147
DOI 10.1007/s12402-016-0214-5

REVIEW ARTICLE

A systematic review of circadian function, chronotype and chronotherapy in attention deficit hyperactivity disorder

Andrew N. Coogan[1] · Niall M. McGowan[1]

…. Melatonin verbessert Schlaf bei ADHS, aber nicht die eigentlichen Krankheitssymptome.
Melatonin wurde aber bisher fast nur als Schlafmittel und nicht zur Vorverlagerung des Chronotyps verwendet ….

…. There is stronger evidence of the use of melatonin in ADHD, with studies included in this review indicating beneficial effects on sleep but not on ADHD symptoms. It should be noted that most of the studies examined utilised melatonin as a somnolent, and not explicitly as a chronobiotic whose main effect would be to advance circadian phase….

…. Chronotyp "spät" ist eindeutig mit ADHS assoziiert.
Es gibt Forschungsbedarf!

…. Overall, results from this systematic review highlights a striking commonality of findings of circadian phase delays associated with ADHD, but also highlights the weakness of the literature surrounding chronotherapeutic interventions in ADHD and delineation of the aetiological significance of circadian dysfunction in ADHD.

Coogan AN, McGowan NM. A systematic review of circadian function, chronotype and chronotherapy in attention deficit hyperactivity disorder. *Atten Defic Hyperact Disord*. 2017;9(3):129-147. doi:10.1007/s12402-016-0214-5