

# Come cambia il sonno dalle prime fasi di vita all'adolescenza

**Lino Nobili**

IRCCS Istituto G. Gaslini

Dipartimento di Neuroscienze, riabilitazione, oftalmologia,  
genetica e scienze materno-infantili

Università di Genova



## Outlines

**Struttura e regolazione del Sonno**

Maturazione del sonno

Sonno, sviluppo e plasticità neuronale

Sonno e adolescenza

# Sonno NREM e sonno REM

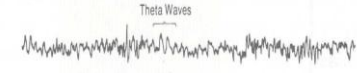
Awake — Low Voltage — Random, Fast



Drowsy — 8 to 12 cps — Alpha Waves



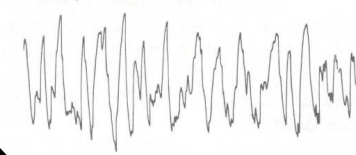
Stage 1 — 3 to 7 cps — Theta Waves



Stage 2 — 12 to 14 cps — Sleep Spindles and K Complexes



Delta Sleep (S Sleep) — 1/2 to 2 cps — Delta Waves

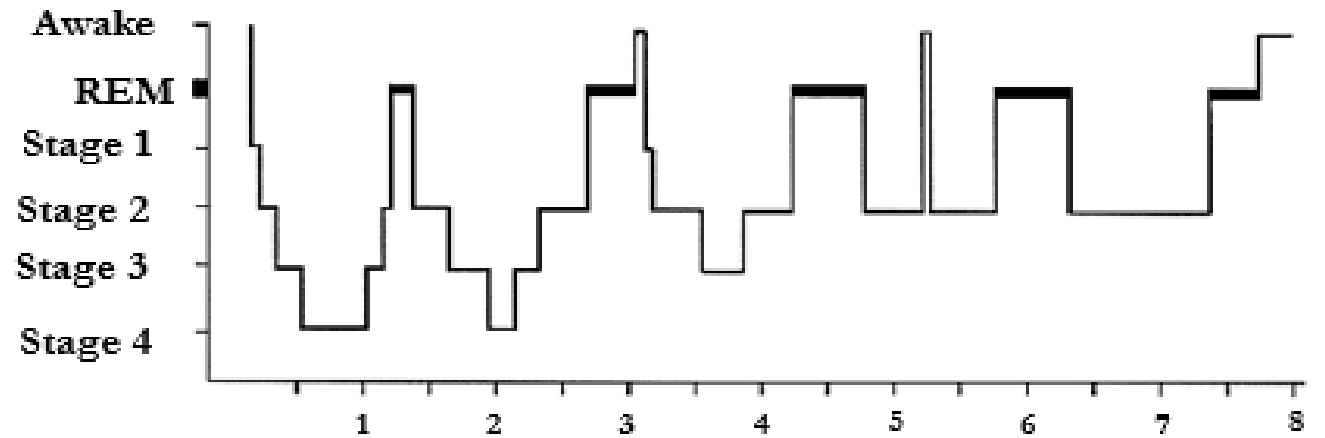


Sonno NREM

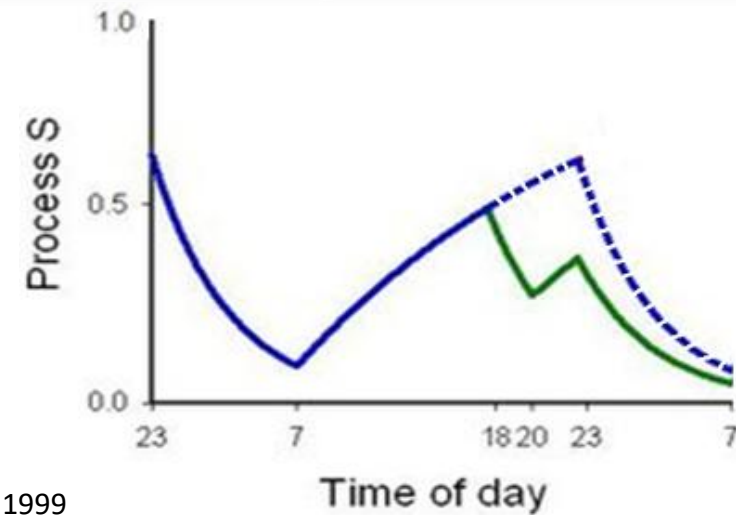
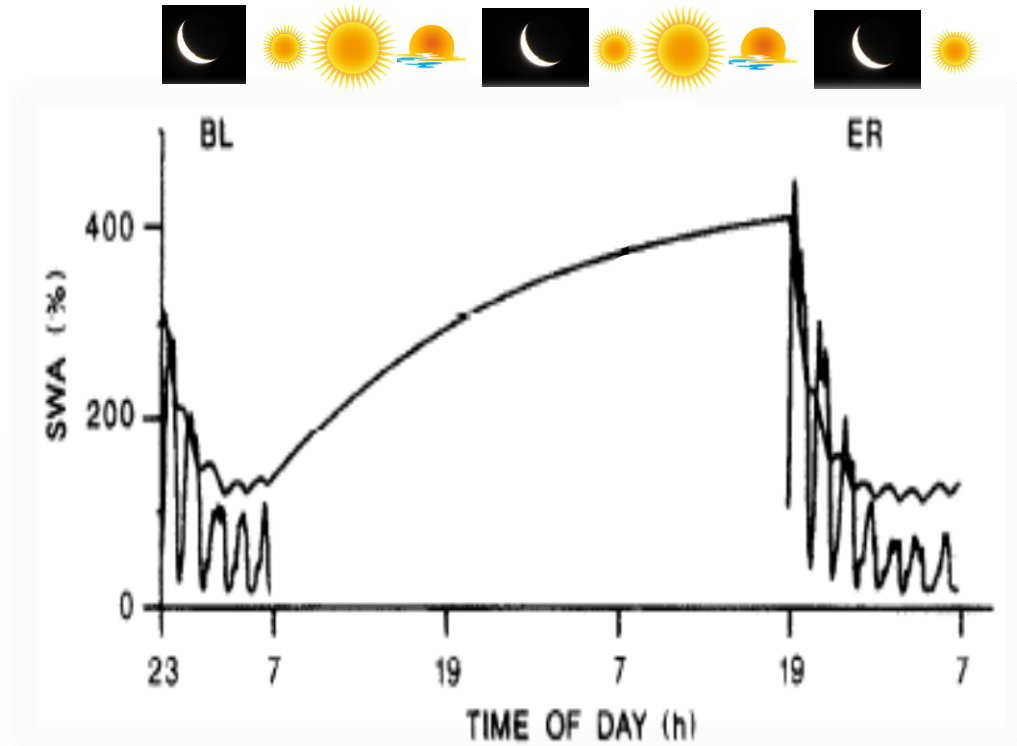
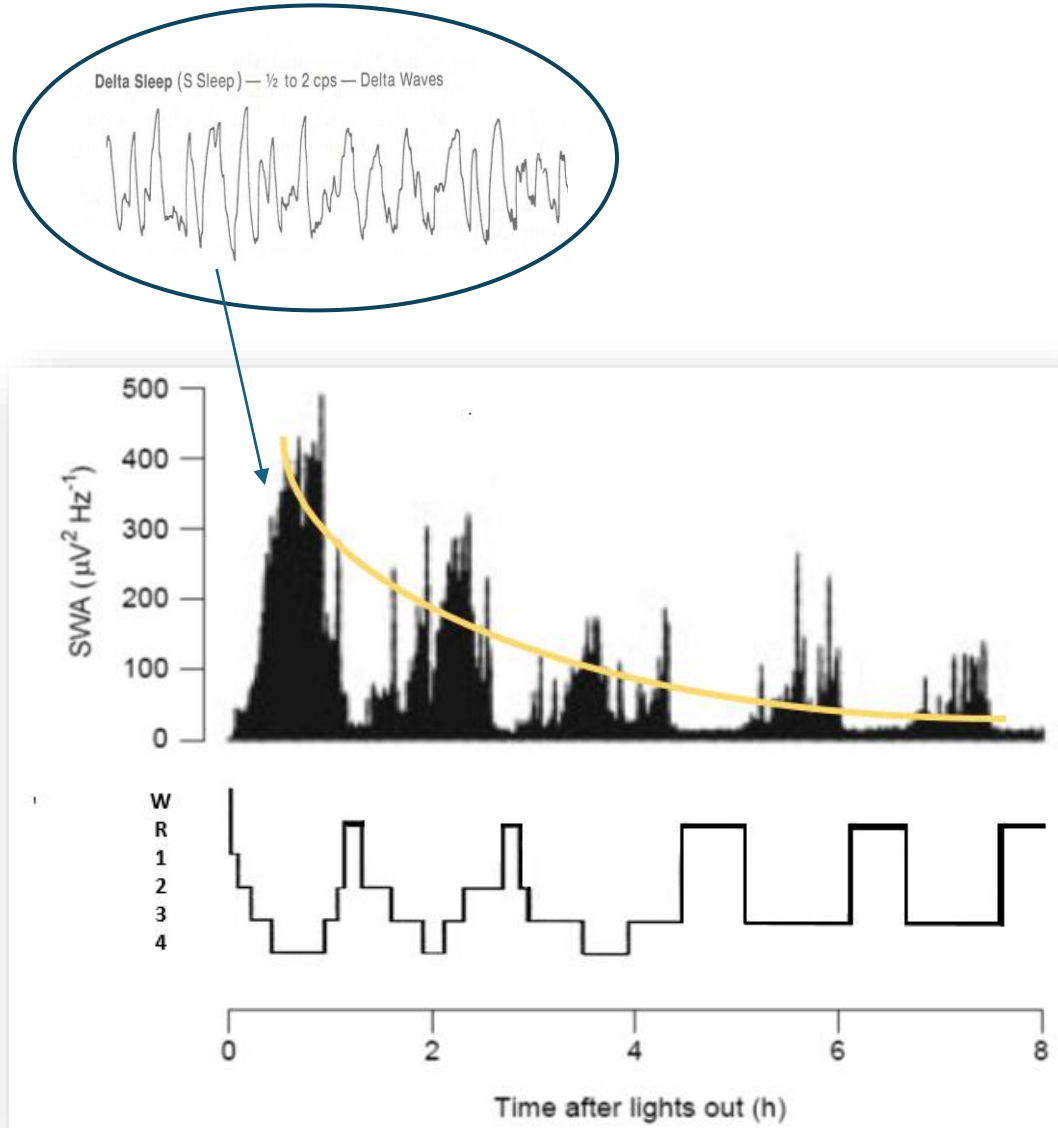
Sonno REM



## Ipnogramma

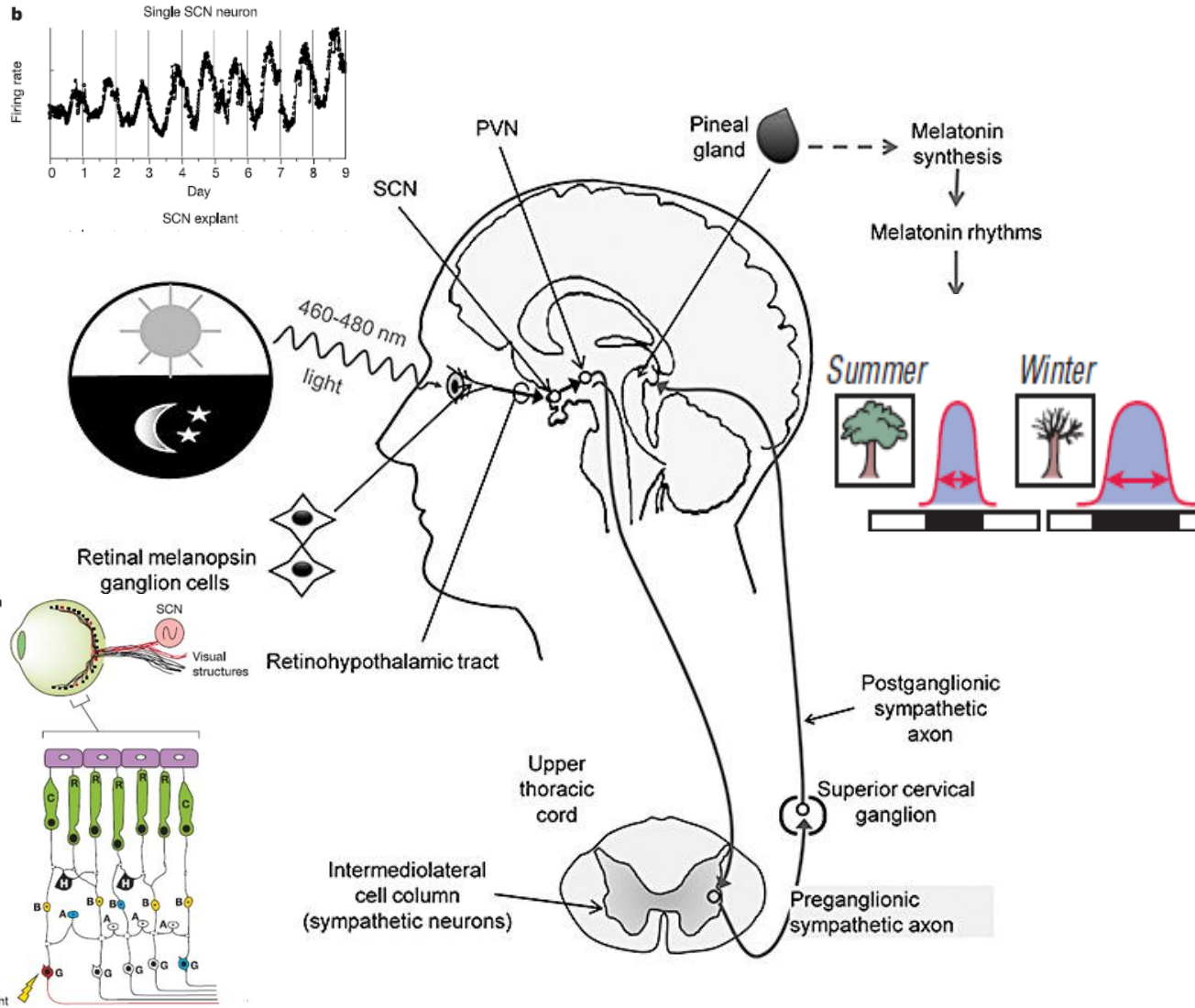


# Regolazione omeostatica del sonno



# Regolazione Circadiana del sonno: fattori sincronizzanti

## Orologio principale

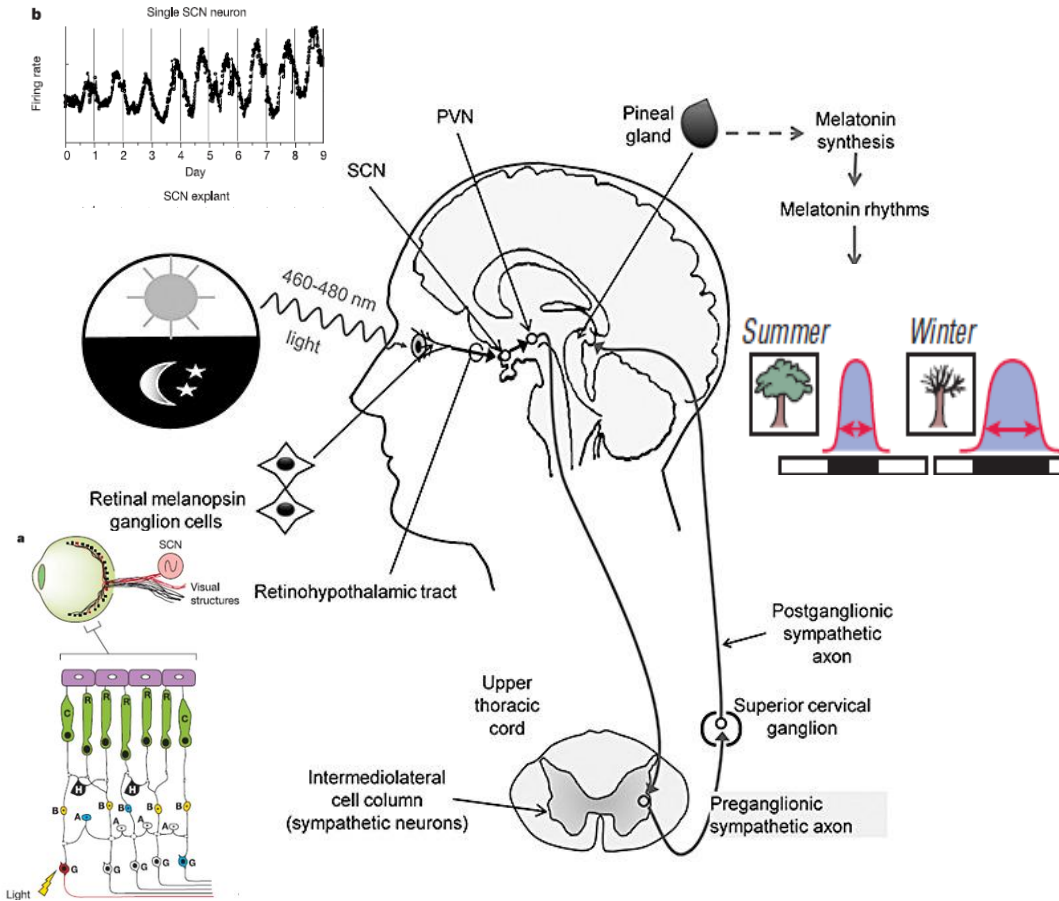


attività fisica,  
assunzione di cibo,  
contatto sociale,...

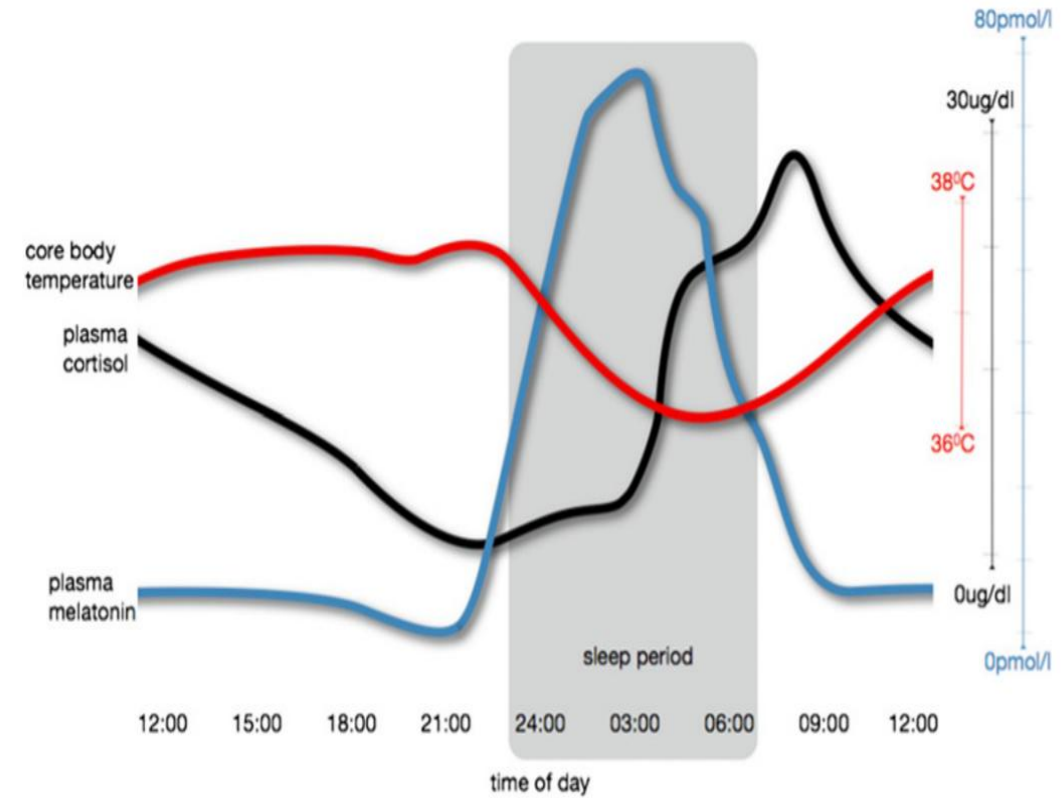


# Regolazione Circadiana del sonno: fattori sincronizzanti

## Orologio principale



attività fisica,  
assunzione di cibo,  
contatto sociale,...



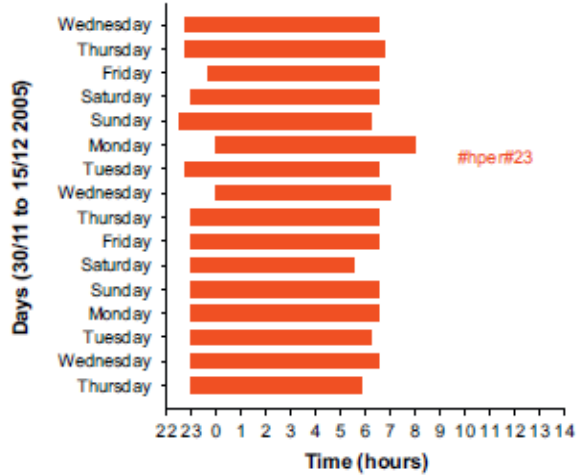
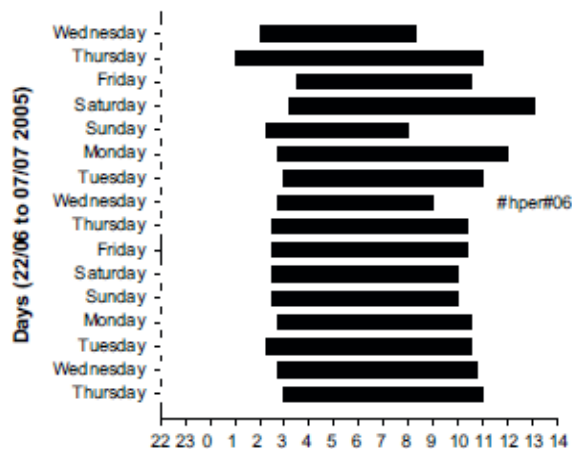
Hickie et al. BMC Medicine 2013

Modified from Tan et al 2011

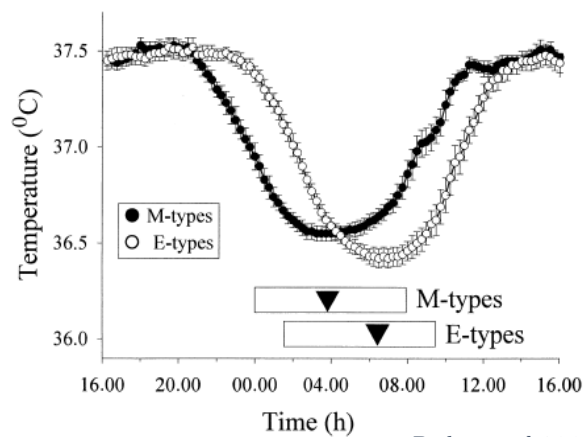
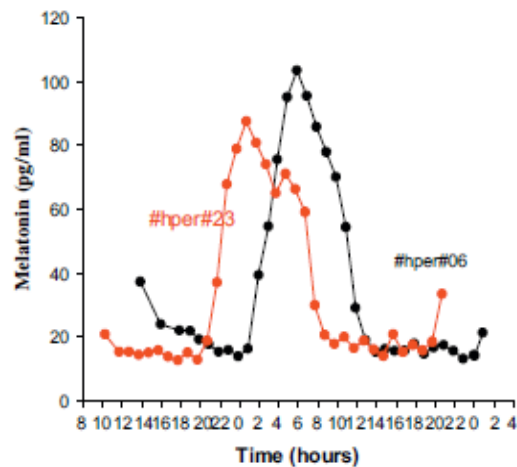
# I “clock genes”

D.-J. Dijk, S.N. Archer / *Sleep Medicine Reviews* 14 (2010) 151–160

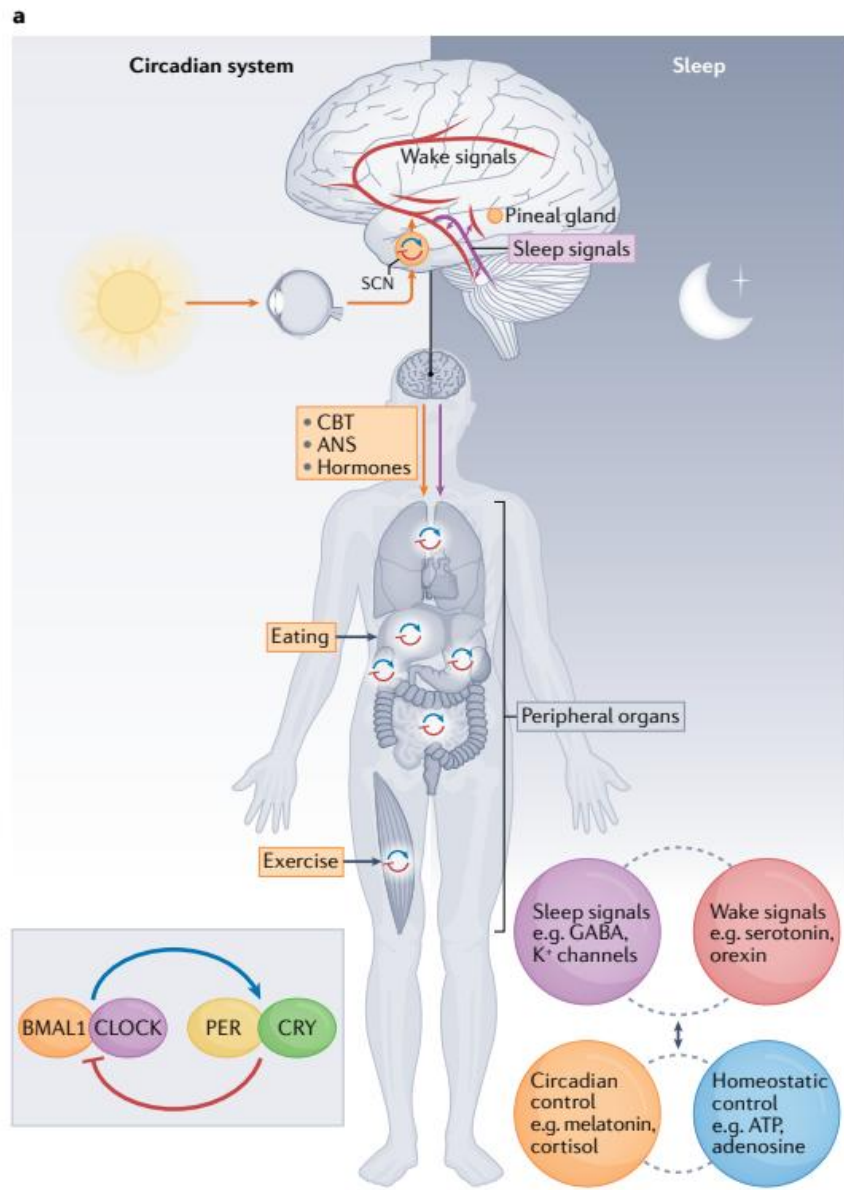
**Sleep Timing (Field Data)**



**Plasma Melatonin and PER3RNA (Constant Routine Data)**

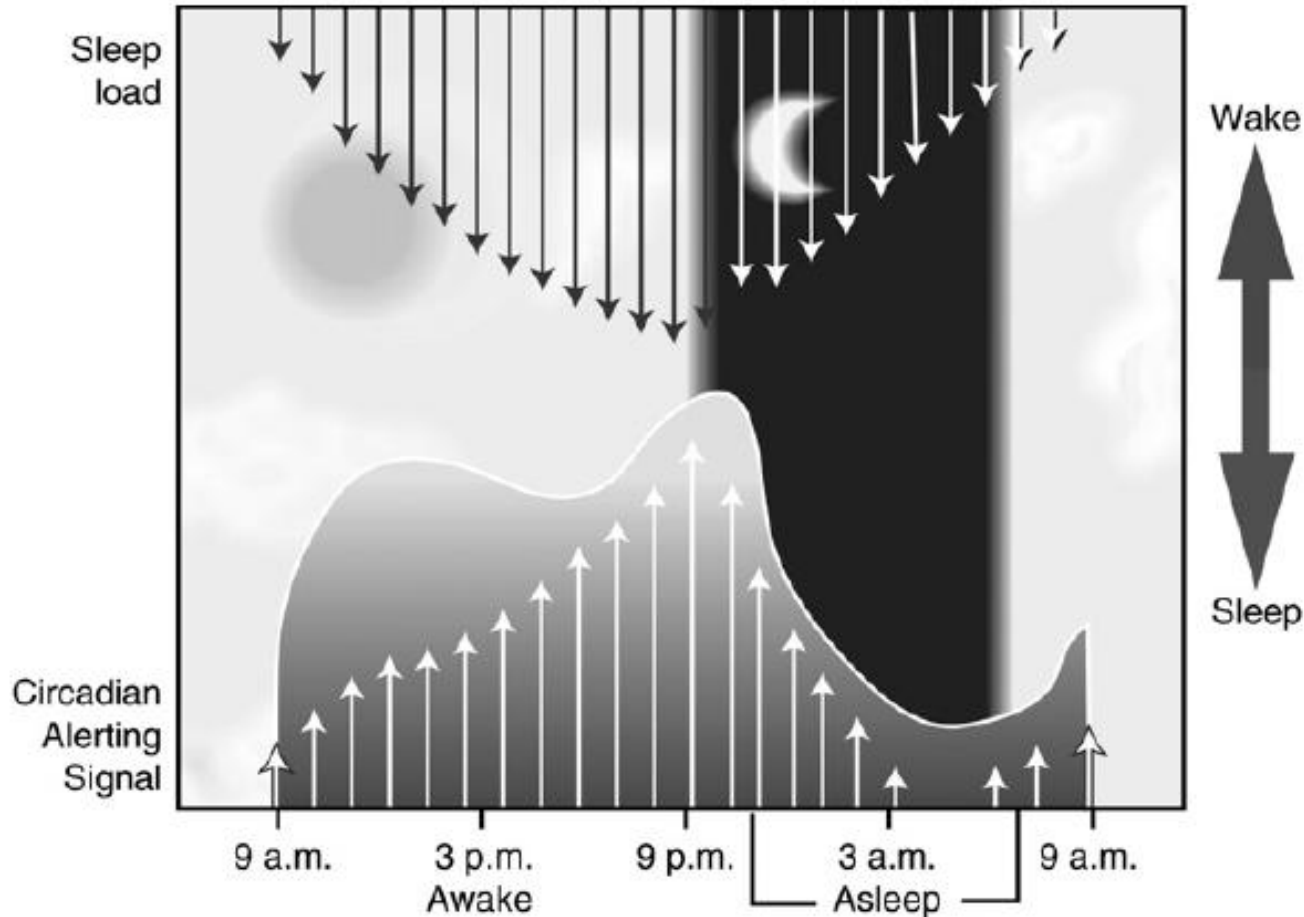


*Baber et al 1998*



Lane et al., *Nature Reviews Genetics* (2022)

# Accoppiamento del ritmo circadiano con il processo omeostatico



Il completo sviluppo del processo omeostatico e del ritmo circadiano, così come il loro accoppiamento con il ciclo luce-buio è essenziale per mantenere una buona struttura del sonno e livelli normali di vigilanza durante il giorno.

## Outlines

Struttura e regolazione del Sonno

**Maturazione del sonno**

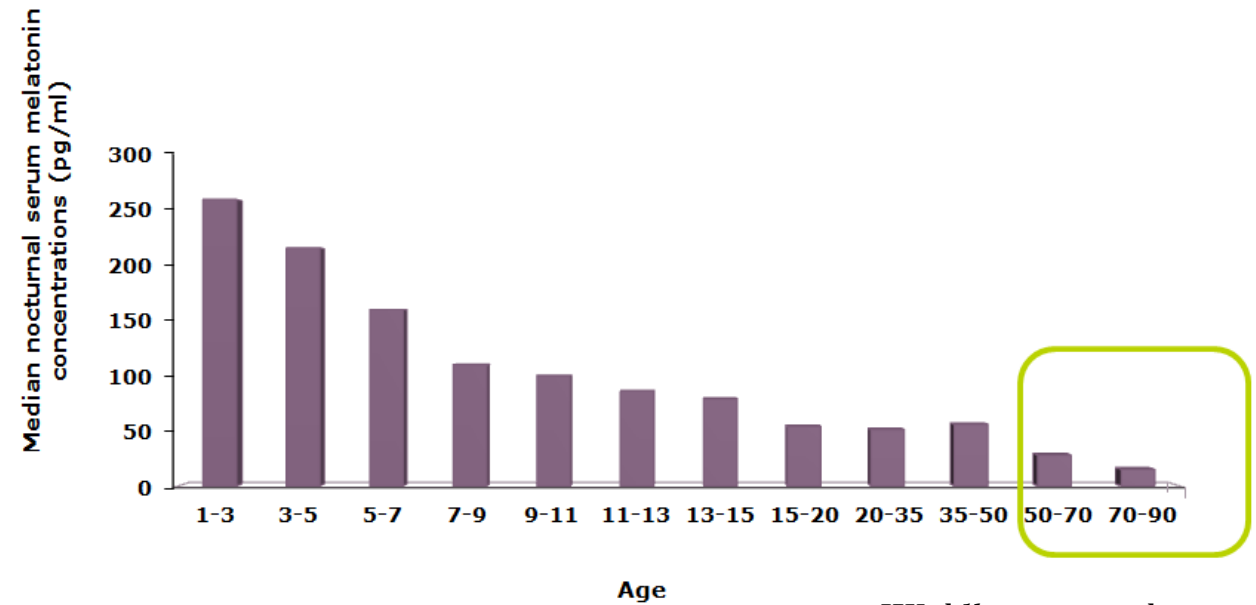
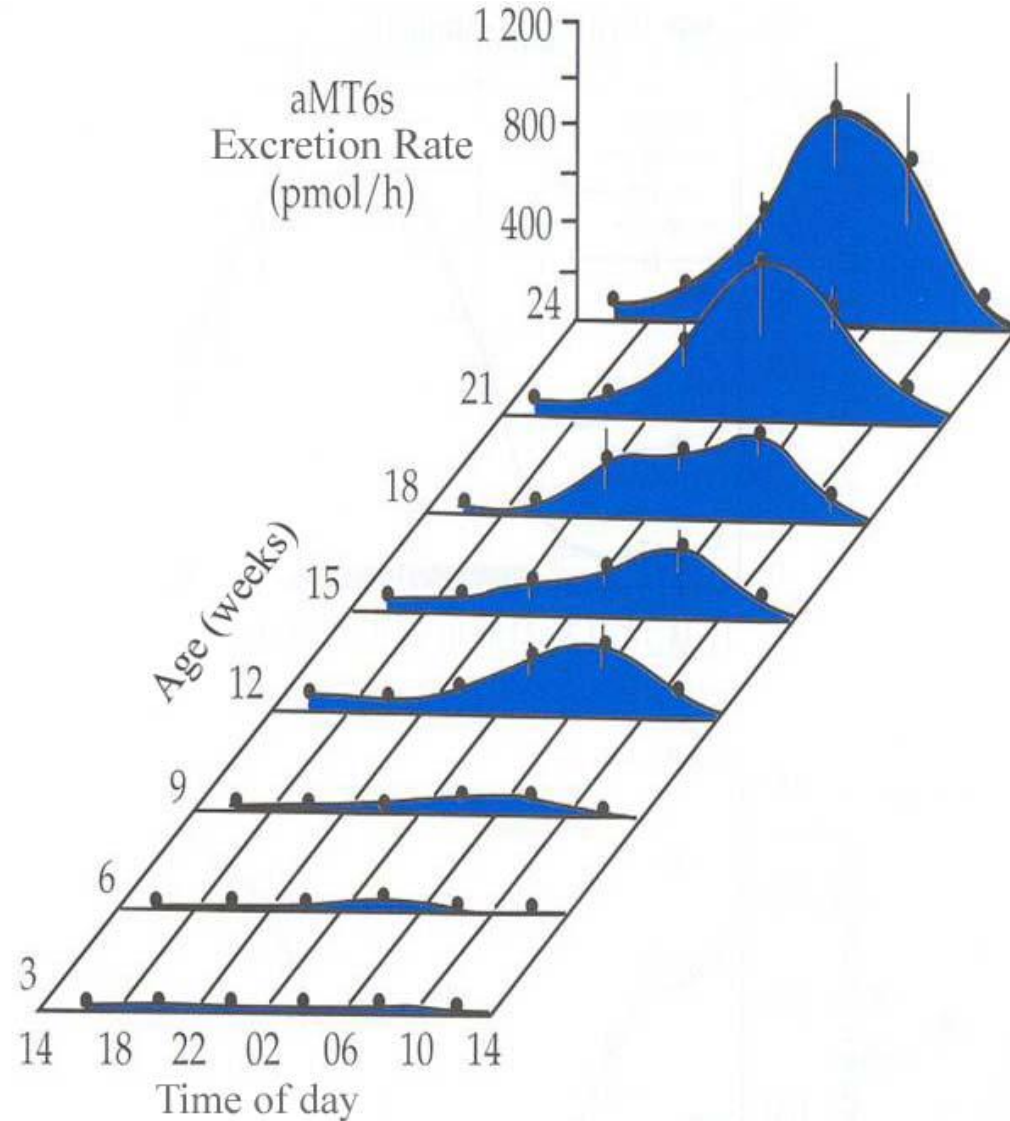
Sonno, sviluppo e plasticità neuronale

Sonno e adolescenza

## Maturazione del ritmo circadiano

- Il sistema circadiano, l'orologio biologico principale, inizia a svilupparsi nell'utero e riceve indicazioni biologiche dalla madre attraverso la placenta.
- L'«orologio principale» continua a svilupparsi per i primi due anni di vita. Durante questo periodo sensibile, l'orologio riceve input dai segnali temporali ambientali attraverso la luce e dai segnali temporali materni attraverso gli ormoni presenti nel latte materno.
- Il ritmo circadiano della temperatura corporea emerge tra le 6 e le 12 settimane di età e la sua ampiezza aumenta nei primi mesi di vita.
- La secrezione di melatonina inizia a manifestare un'alternanza di secrezione in parallelo con il ritmo luce buio (giorno/notte) all'età di 12 settimane.
- I ritmi circadiani del cortisolo compaiono tra le 8 e le 12 settimane.

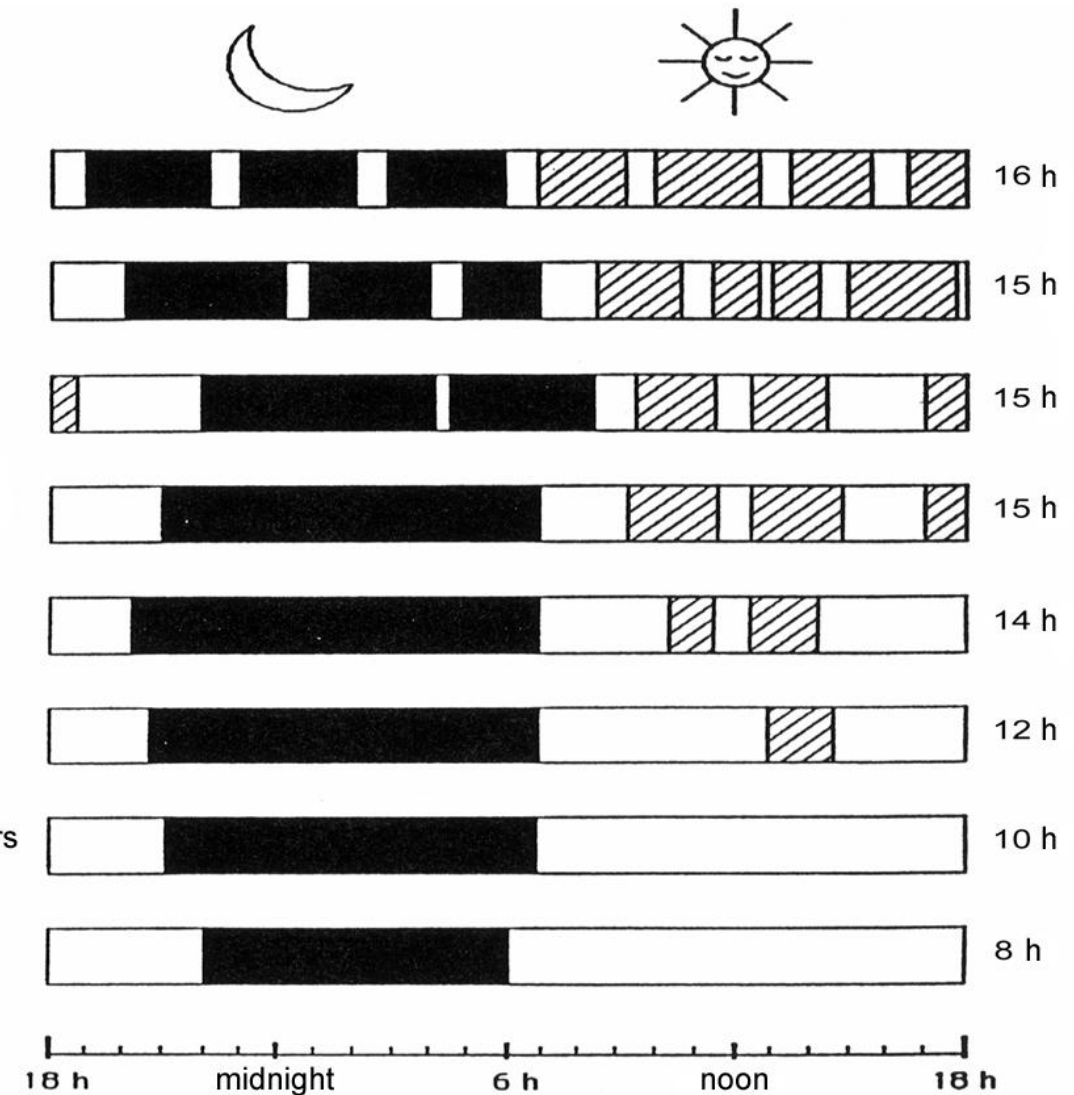
# Secrezione di melatonina nel corso della vita



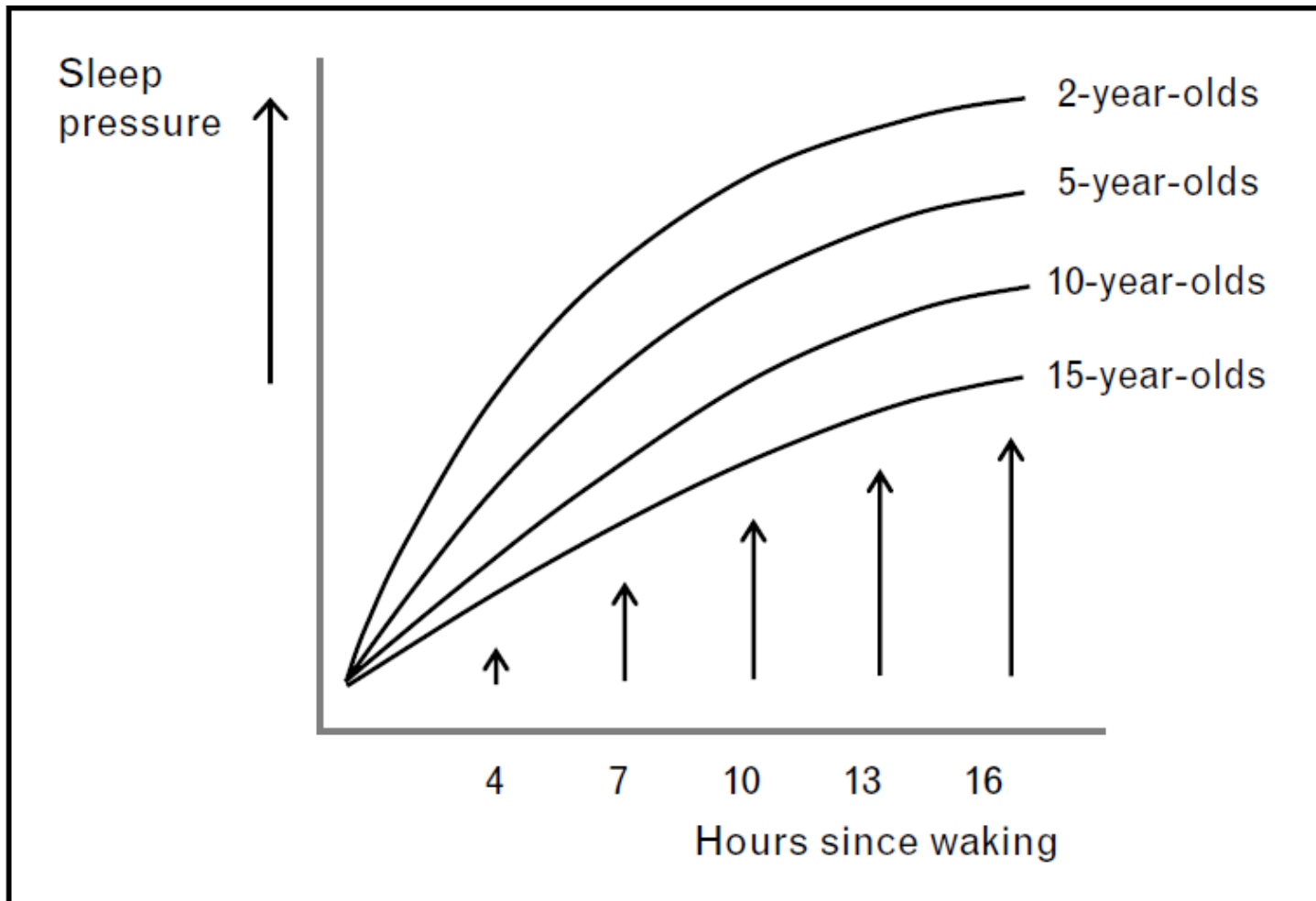
*Waldhauser et al. 1988;*

# Consolidamento dei periodi di sonno

- Pattern ultradiano polifasico fino a 44 settimane gestazionali.
- A 5-6 settimane il sonno è più concentrato di notte e la veglia più presente di giorno.
- A 12-14 settimane si stabilisce un pattern diurno con un lungo periodo di sonno notturno.
- A 6 mesi i lattanti mostrano un pattern circadiano con periodo, ampiezza e fase simili a quelli dell'adulto.



# La pressione omeostatica cambia nel corso dello sviluppo



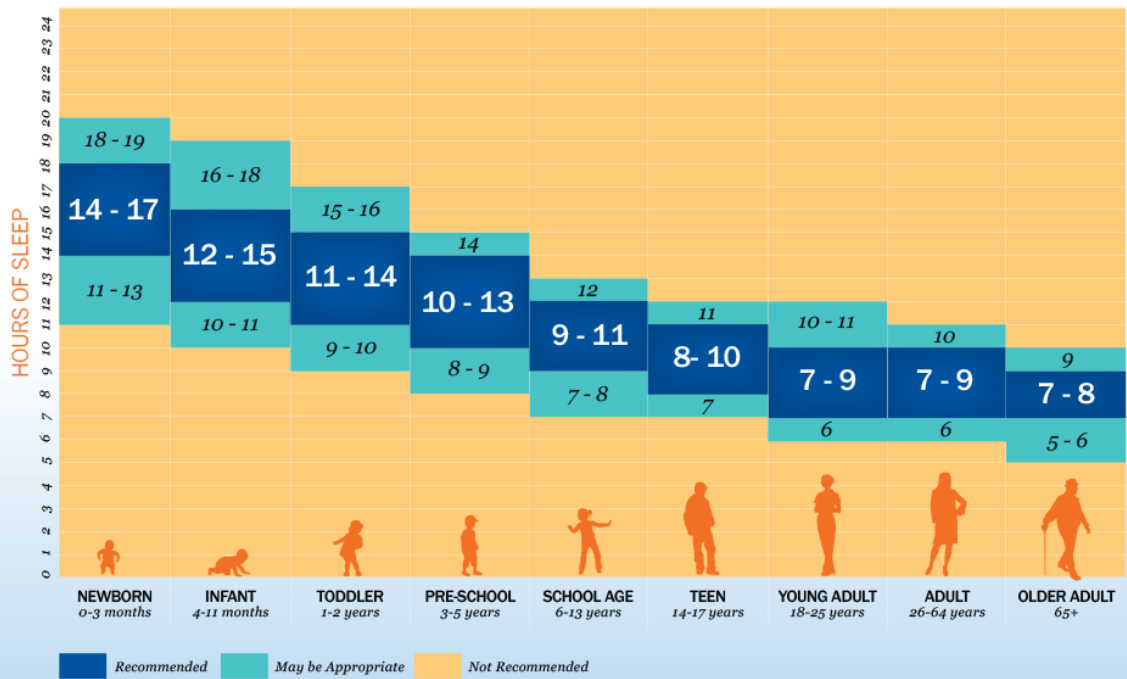
L'omeostasi del sonno emerge nel secondo mese di vita

Proposed developmental changes in accumulation of sleep pressure as a function of time since waking depicted for different ages. Sleep pressure accumulates more slowly during the day with increasing age.

# La durata del sonno



## SLEEP DURATION RECOMMENDATIONS



SLEEPFOUNDATION.ORG | SLEEP.ORG

Hirshkowitz M, The National Sleep Foundation's sleep time duration recommendations: methodology and results summary, Sleep Health (2015), <http://dx.doi.org/10.1016/j.sleh.2014.12.010>

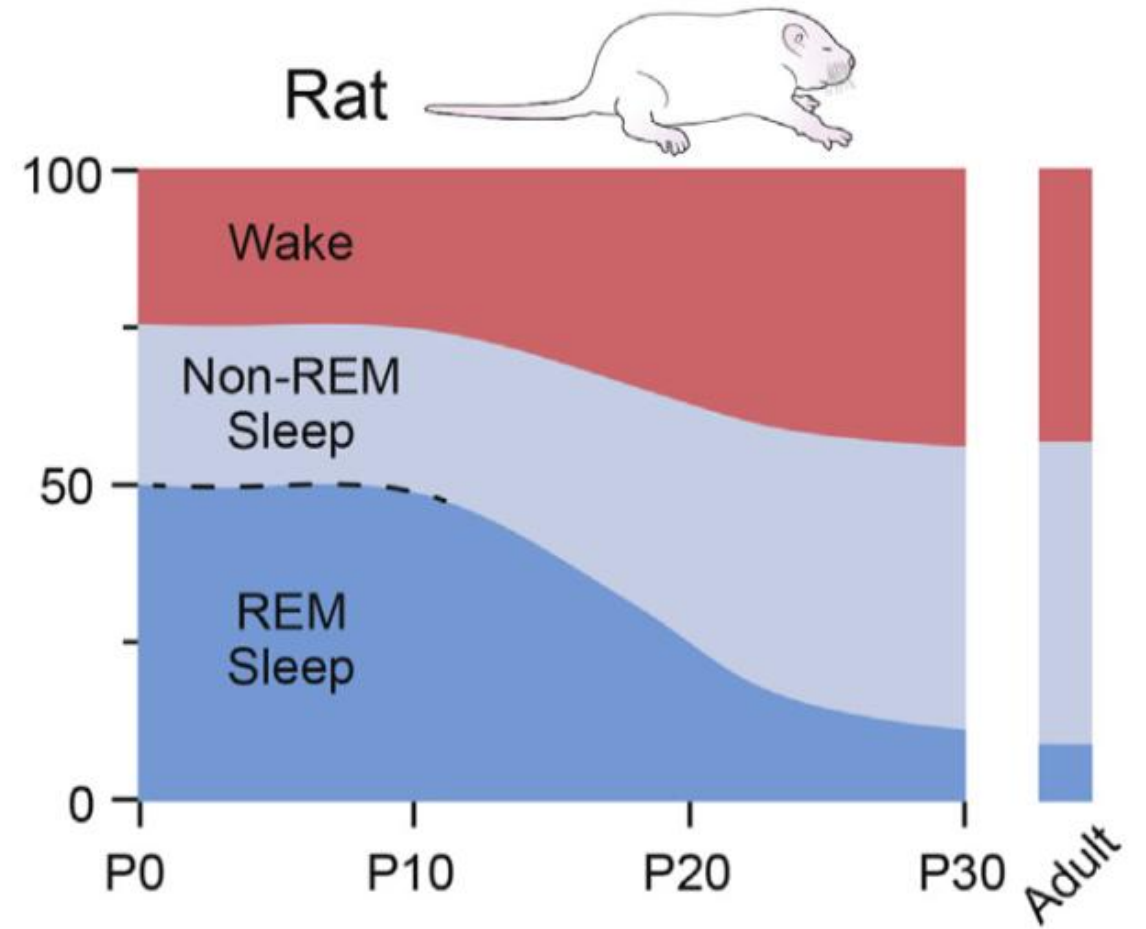
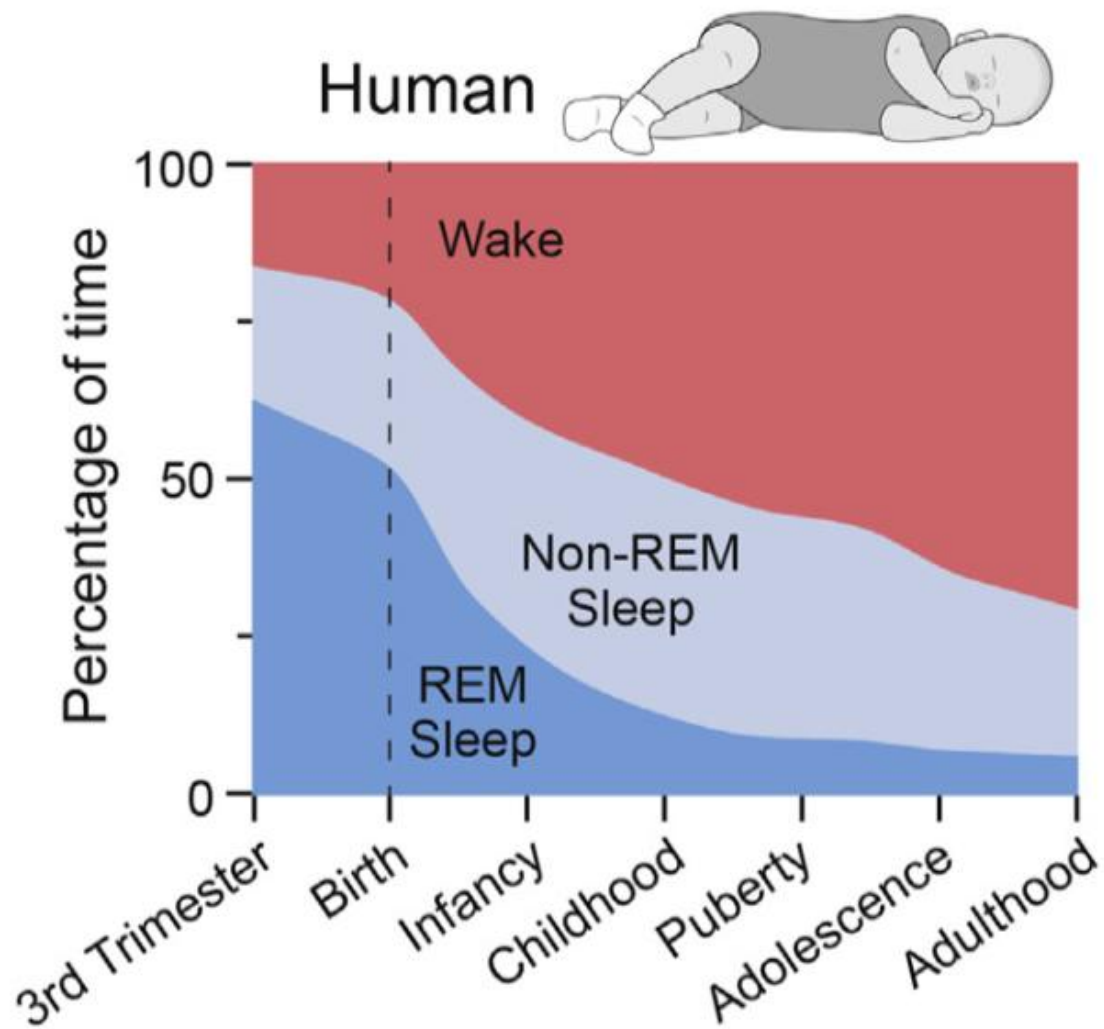
### CONSENSUS STATEMENT

Recommended Amount of Sleep for Pediatric Populations:  
A Consensus Statement of the American Academy of Sleep Medicine

### CONSENSUS RECOMMENDATIONS

- **Infants\* 4 months to 12 months should sleep 12 to 16 hours per 24 hours (including naps) on a regular basis to promote optimal health.**
- **Children 1 to 2 years of age should sleep 11 to 14 hours per 24 hours (including naps) on a regular basis to promote optimal health.**
- **Children 3 to 5 years of age should sleep 10 to 13 hours per 24 hours (including naps) on a regular basis to promote optimal health.**
- **Children 6 to 12 years of age should sleep 9 to 12 hours per 24 hours on a regular basis to promote optimal health.**
- **Teenagers 13 to 18 years of age should sleep 8 to 10 hours per 24 hours on a regular basis to promote optimal health.**

# Variazioni quantitative e qualitative



## Outlines

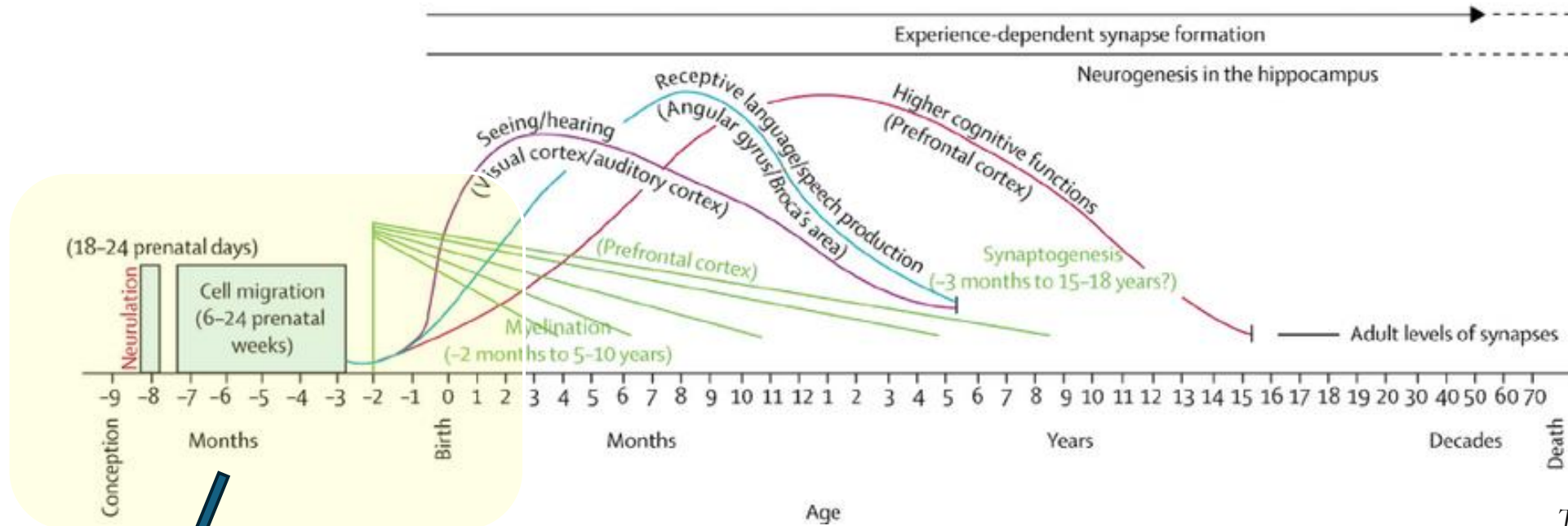
Struttura e regolazione del Sonno

Maturazione del sonno

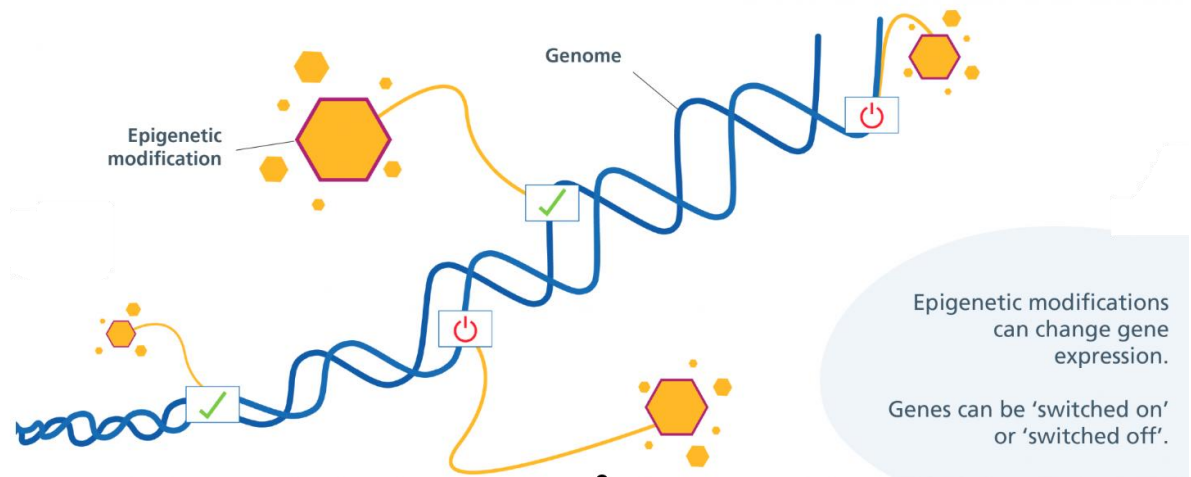
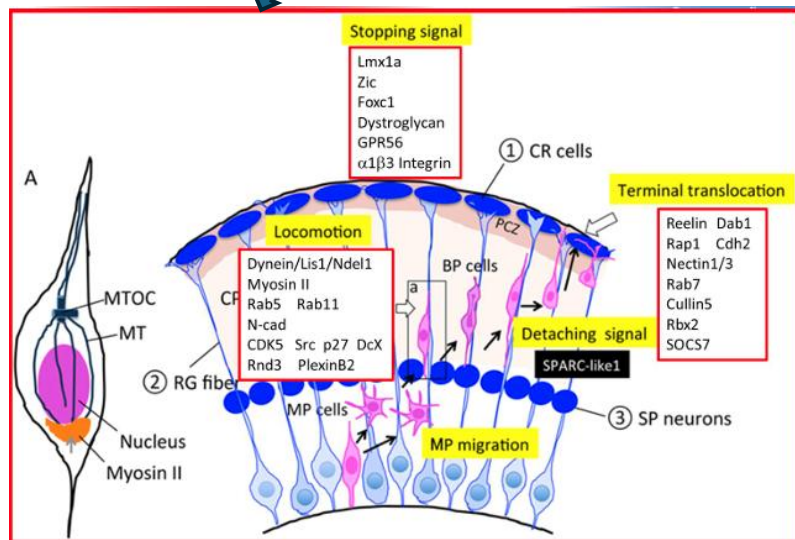
**Sonno, sviluppo e plasticità neuronale**

Sonno e adolescenza

# Sviluppo cerebrale



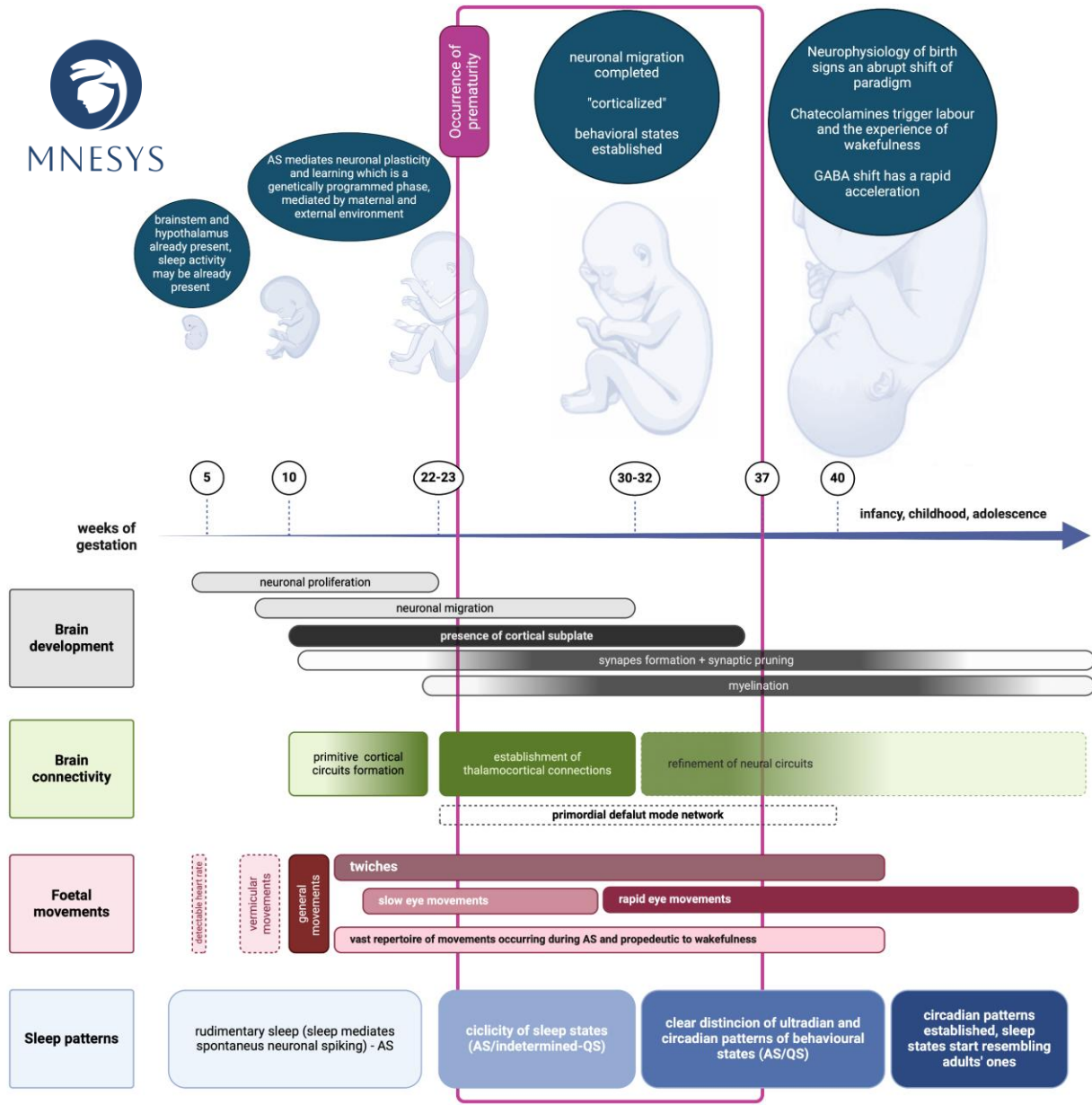
Thompson and Nelson (2001)



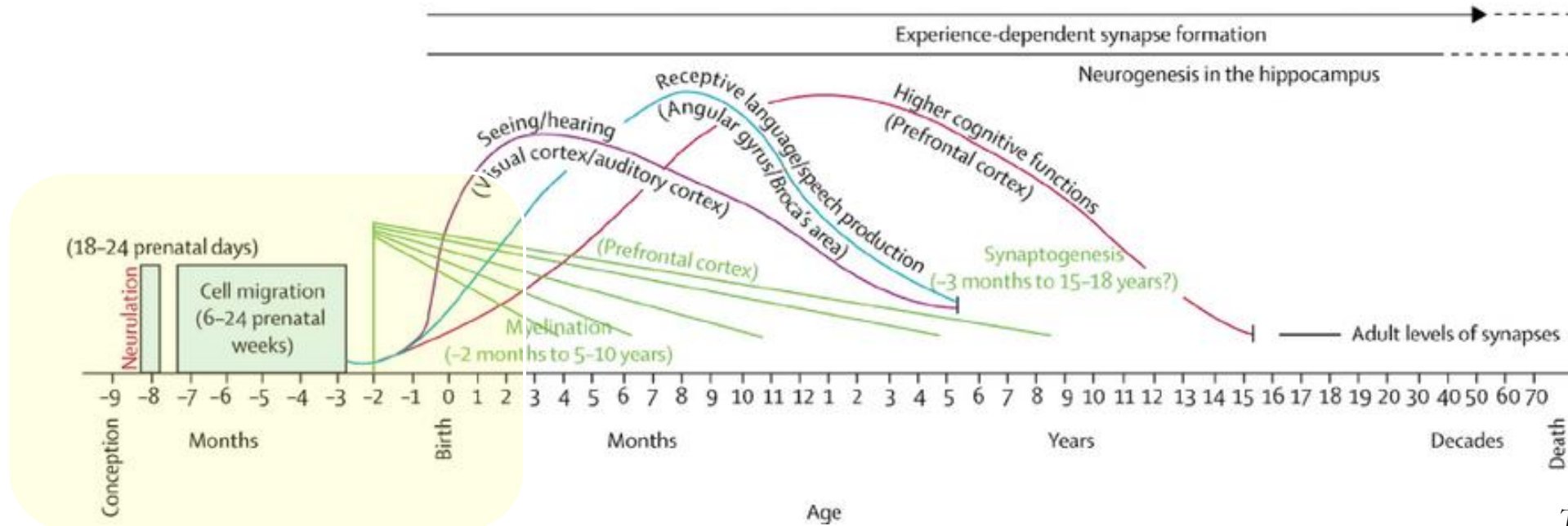
# Sonno fetale



MNESYS



# Sviluppo cerebrale: il sonno come “motore dei processi di sviluppo”



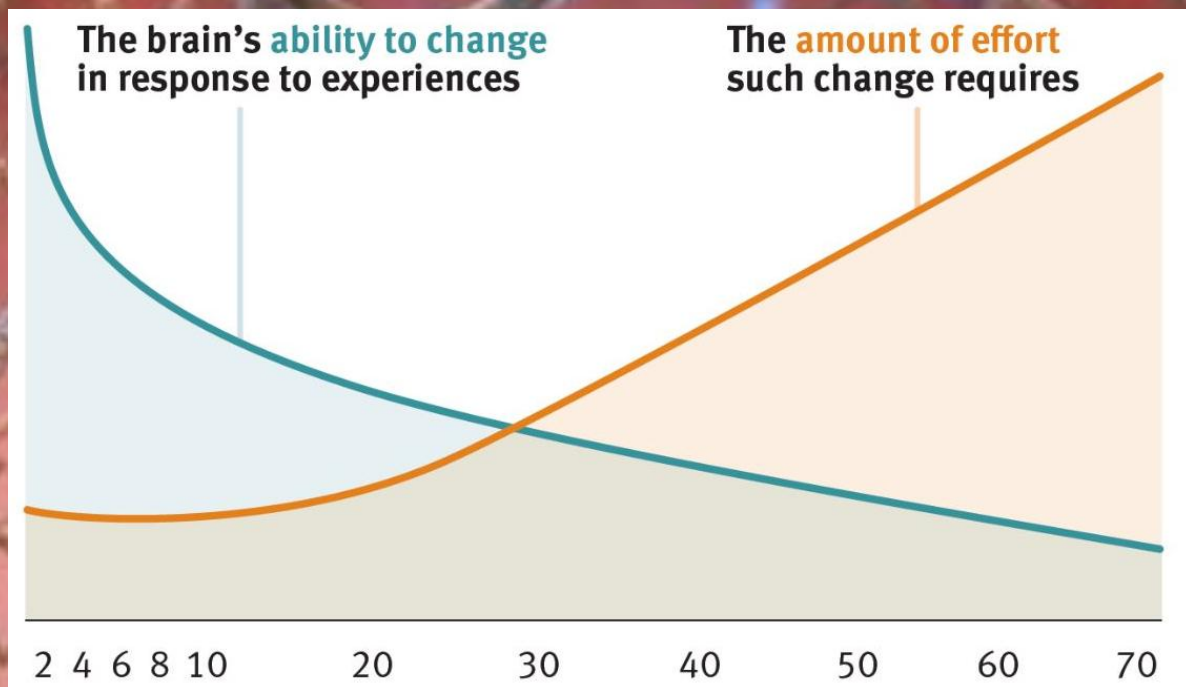
*Thompson and Nelson (2001)*

Le oscillazioni del sonno sono insieme un indicatore e un motore di questi processi.

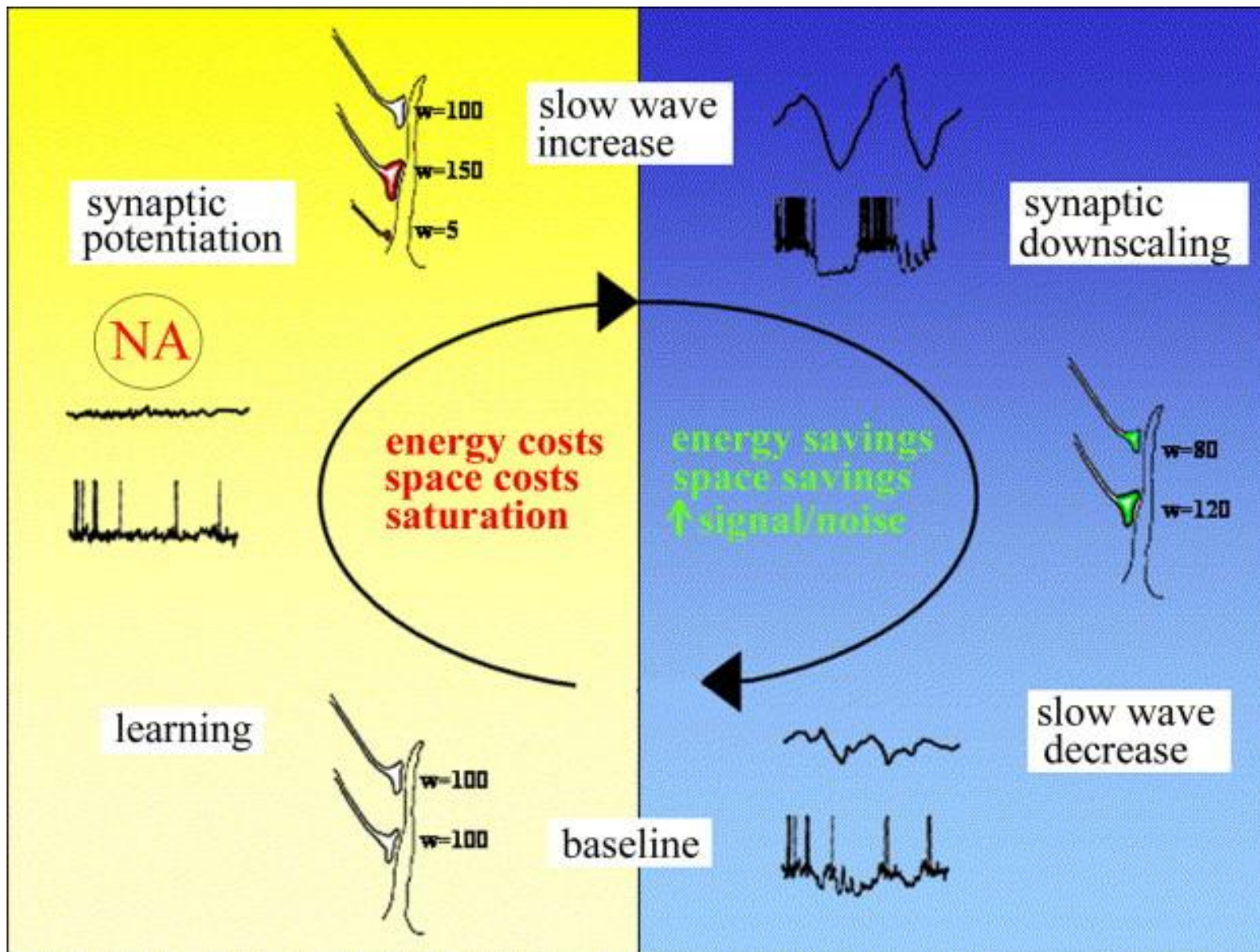


# Neuroplasticità

- La capacità del cervello di cambiare nel corso della vita in risposta all'esperienza.
- Il cervello umano ha la capacità di riorganizzarsi formando nuove connessioni tra i neuroni. Oltre a fattori genetici, l'ambiente in cui una persona vive così come le sue azioni, giocano un ruolo significativo nella plasticità.



# Sonno e plasticità cerebrale



Cirelli and Tononi

Science

2017

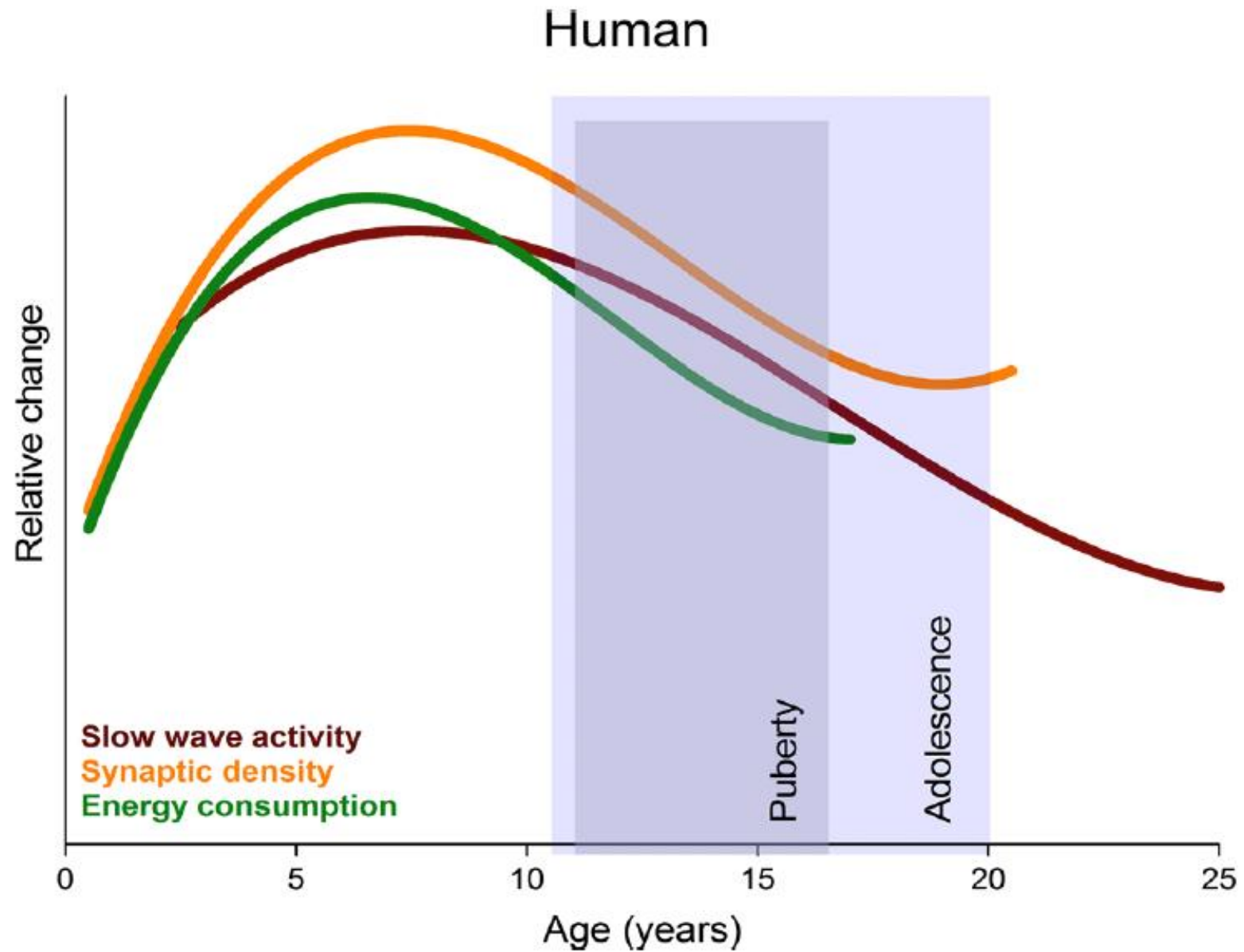
REPORT

SLEEP RESEARCH

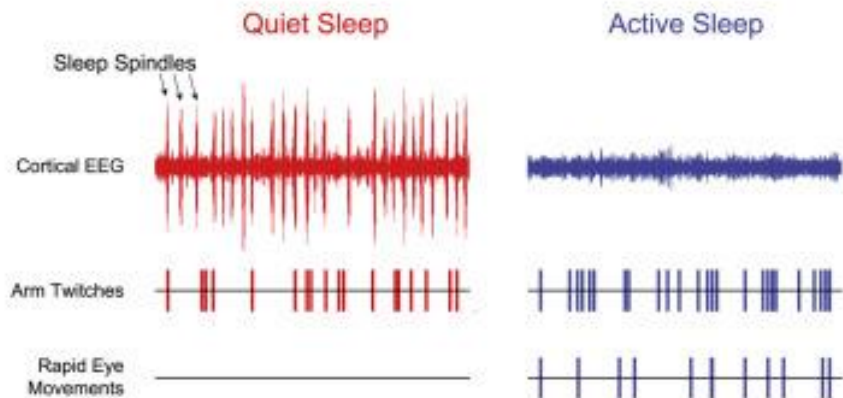
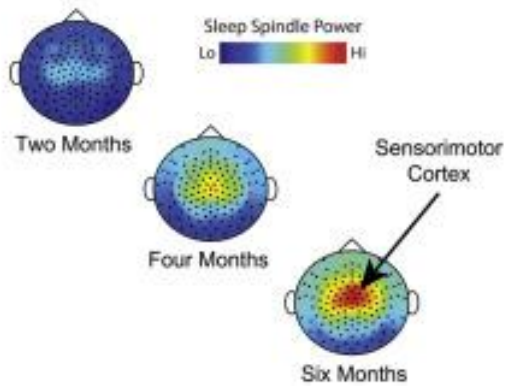
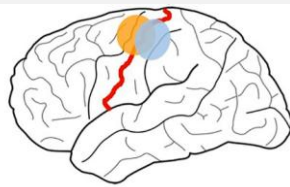
## Ultrastructural evidence for synaptic scaling across the wake/sleep cycle

Luisa de Vivo,<sup>1</sup> Michele Bellesi,<sup>1,2</sup> William Marshall,<sup>1</sup> Eric A. Bushong,<sup>3</sup> Mark H. Ellisman,<sup>3,4</sup> Giulio Tononi,<sup>1\*</sup> Chiara Cirelli<sup>1\*</sup>

# Sonno e maturazione cerebrale: traiettorie coincidenti nel corso dello sviluppo



# I twitch nel sonno associati allo sviluppo sensorimotorio



Cerebral Cortex, April 2020;30: 2070–2082

doi: 10.1093/cercor/bhz223  
Advance Access Publication Date: 10 January 2020  
Original Article

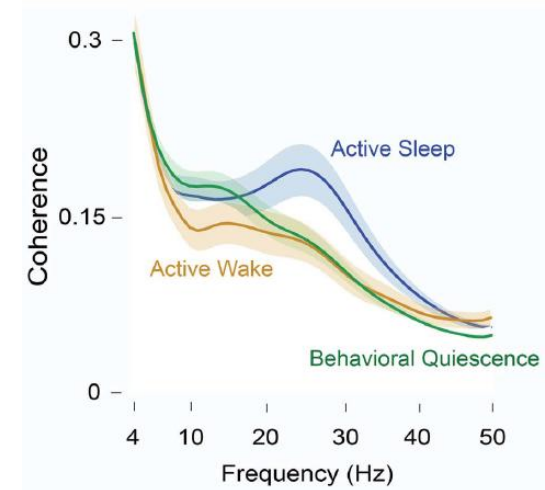
ORIGINAL ARTICLE

## Active Sleep Promotes Coherent Oscillatory Activity in the Cortico-Hippocampal System of Infant Rats

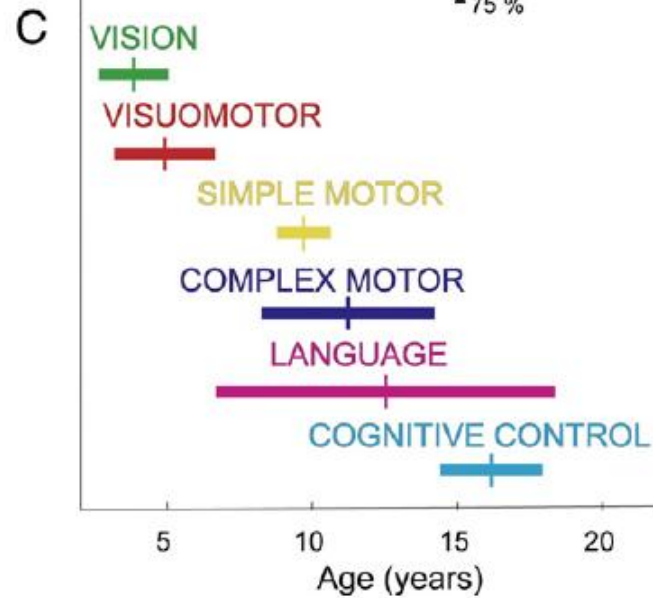
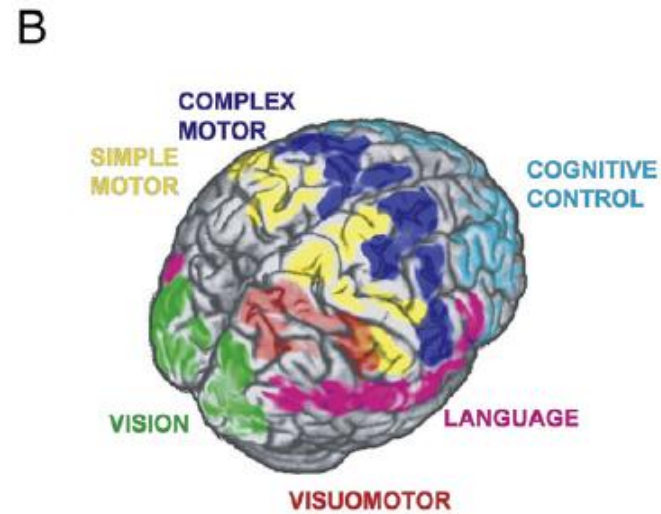
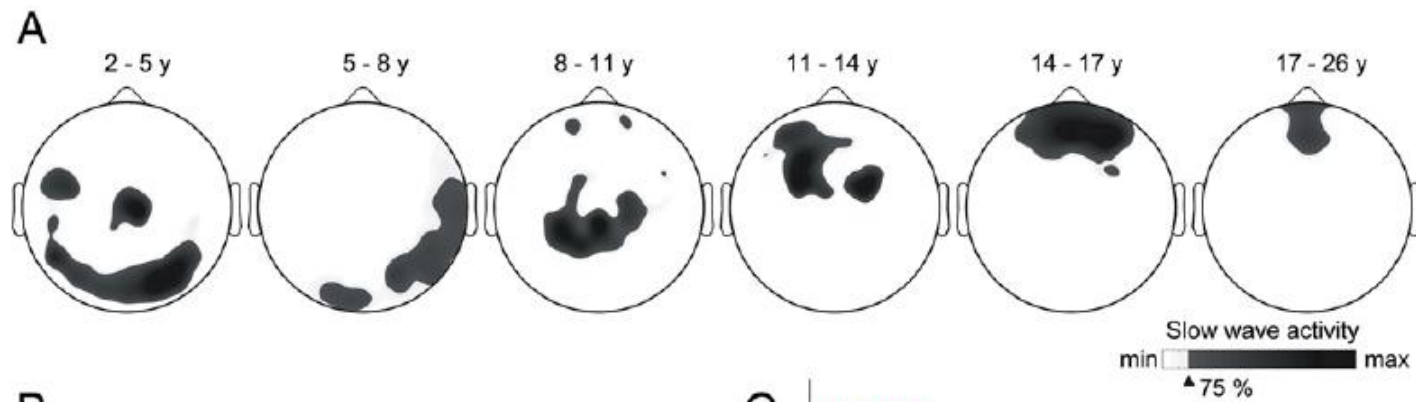
Carlos Del Rio-Bermudez<sup>1</sup>, Jangjin Kim<sup>1</sup>, Greta Sokoloff<sup>1,2</sup> and Mark S. Blumberg<sup>1,2,3,\*</sup>

<sup>1</sup>Department of Psychological and Brain Sciences, University of Iowa, Iowa City, IA 52242, USA, <sup>2</sup>Iowa Neuroscience Institute, University of Iowa, Iowa City, IA 52242, USA and <sup>3</sup>Interdisciplinary Graduate Program in Neuroscience, University of Iowa, Iowa City, IA 52245, USA

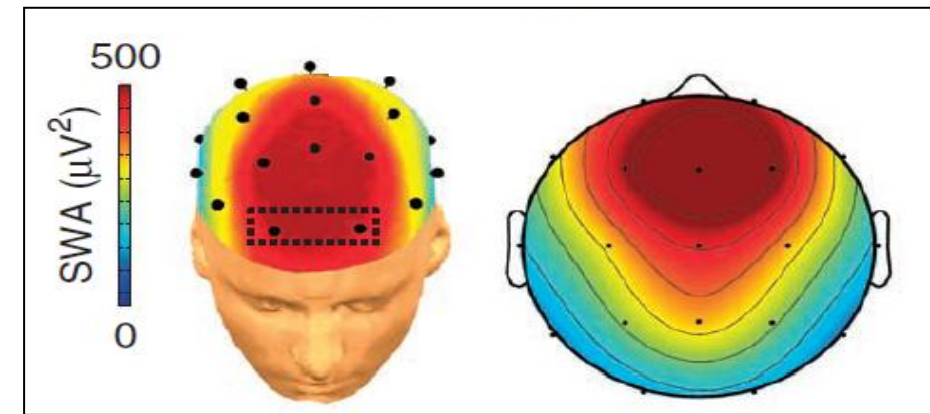
Address correspondence to Mark S. Blumberg. Email: mark-blumberg@uiowa.edu



# Sonno, plasticità cerebrale e neurosviluppo

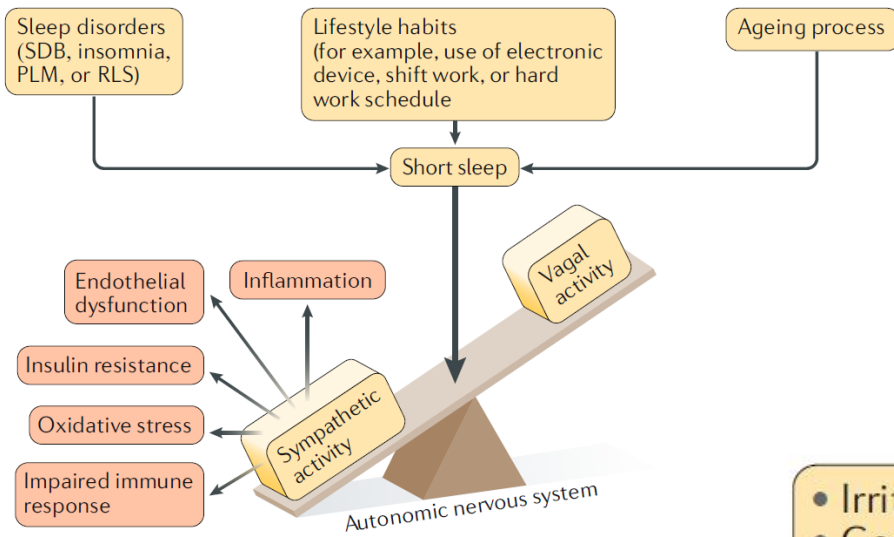


## Topografia del «sonno delta» nell'adolescenza



Mander et al Nature Neurosci 2016

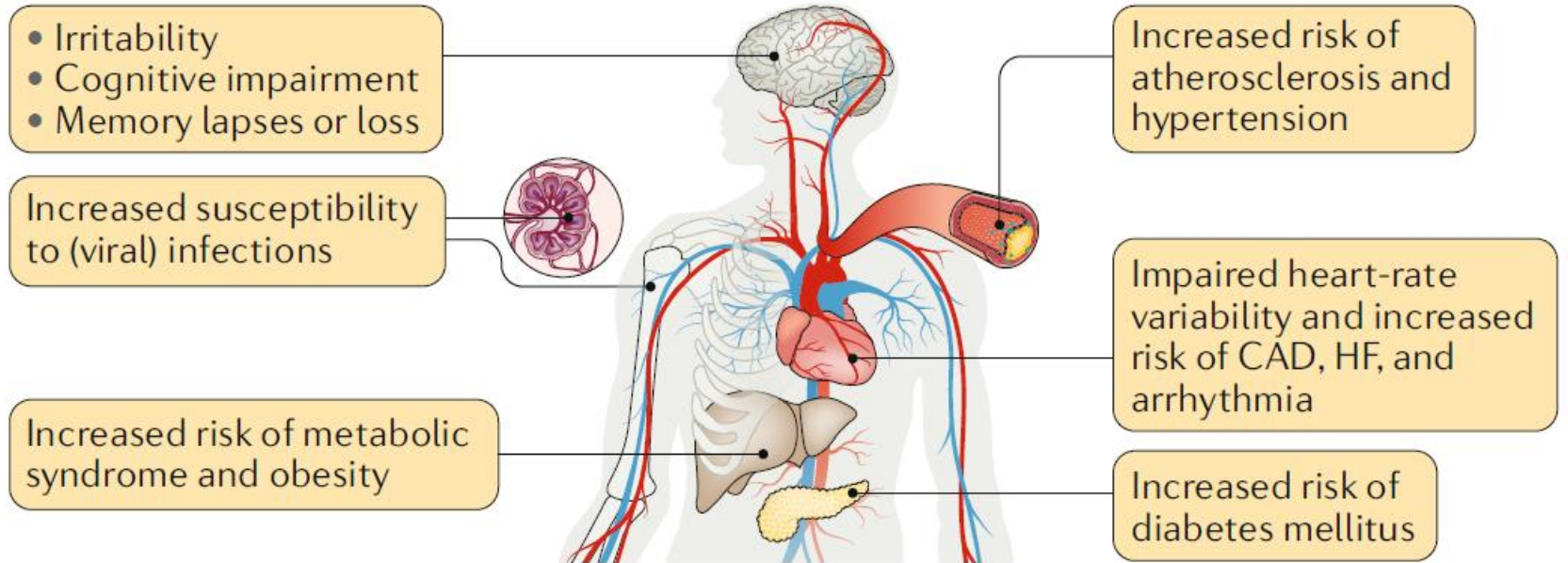
# Il sonno per il cervello, mente e corpo



PREVENTION OF CVD

## Short sleep duration and cardiometabolic risk: from pathophysiology to clinical evidence

Eleonora Tobaldini<sup>1</sup>, Elisa M. Fiorelli<sup>1</sup>, Monica Solbiati<sup>1</sup>, Giorgio Costantino<sup>1</sup>, Lino Nobili<sup>2</sup> and Nicola Montano<sup>1\*</sup>



# Sonno e sviluppo emotivo nei bambini in età prescolare

## Sleep Disturbances and Emotional and Behavioral Difficulties Among Preschool-Aged Children

Yujiao Deng, PhD; Zichen Zhang, BA; Yiding Gui, BA; Wen Li, PhD; Tingyu Rong, PhD; Yanrui Jiang, PhD; Qi Zhu, BA; Jin Zhao, PhD; Yunting Zhang, PhD; Guanghai Wang, PhD; Fan Jiang, MD, PhD

20.324 bambini di età compresa tra 3 e 4 anni  
(191 scuole dell'infanzia)  
17.233 (84,8%) follow-up a 2 anni

Children's Sleep Habits Questionnaire (CSHQ)  
Strengths and Difficulties Questionnaire

**EBD**: difficoltà emotivo-comportamentali

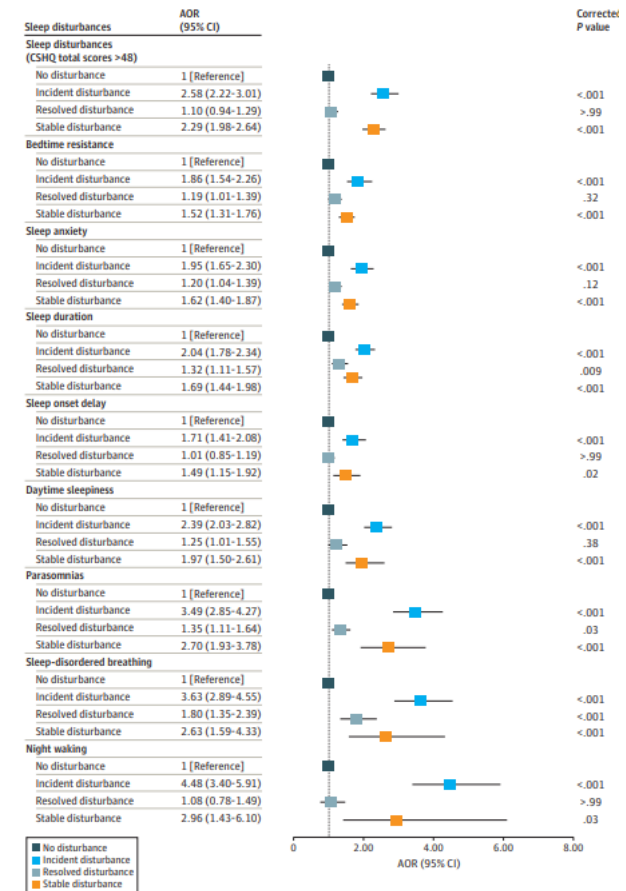
### Key Points

**Question** Is a natural history of sleep disturbances associated with resolved and incident emotional and behavioral difficulties (EBDs) during preschool years?

**Findings** In this cohort study of 17 182 preschool-aged children in Shanghai, China, incident and stable sleep disturbances were negatively associated with resolved EBDs but positively associated with incident EBDs after adjustment. Resolved sleep disturbances were positively associated with resolved EBDs.

**Meaning** These findings underscore the association between sleep disturbances and EBDs among preschool-aged children and the importance of sleep health in promoting their mental well-being.

Figure 2. Odds of Incident Emotional and Behavioral Difficulties for Children With Transition of Different Sleep Disturbances



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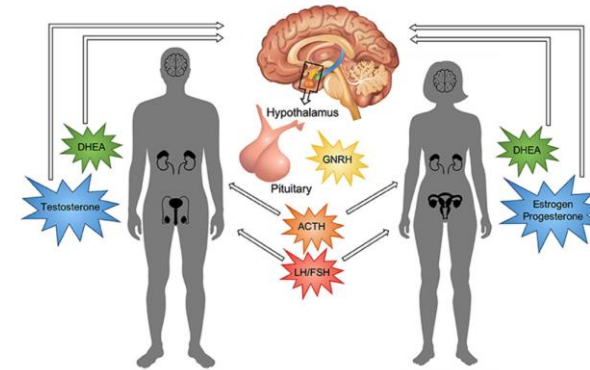
# Adolescenza: un momento «critico» di cambiamento

## Adolescence

Historically defined by WHO as the period between ages 10 and 19 years.<sup>16</sup> It is derived from the Latin *adolescere*—the present participle *adolescens* means growing up, whereas the past participle *adultus* means grown up.

*Sarab-Jayne Blakemore The Lancet Vol 393, 2019*

- Cambiamenti negli ormoni e nel corpo



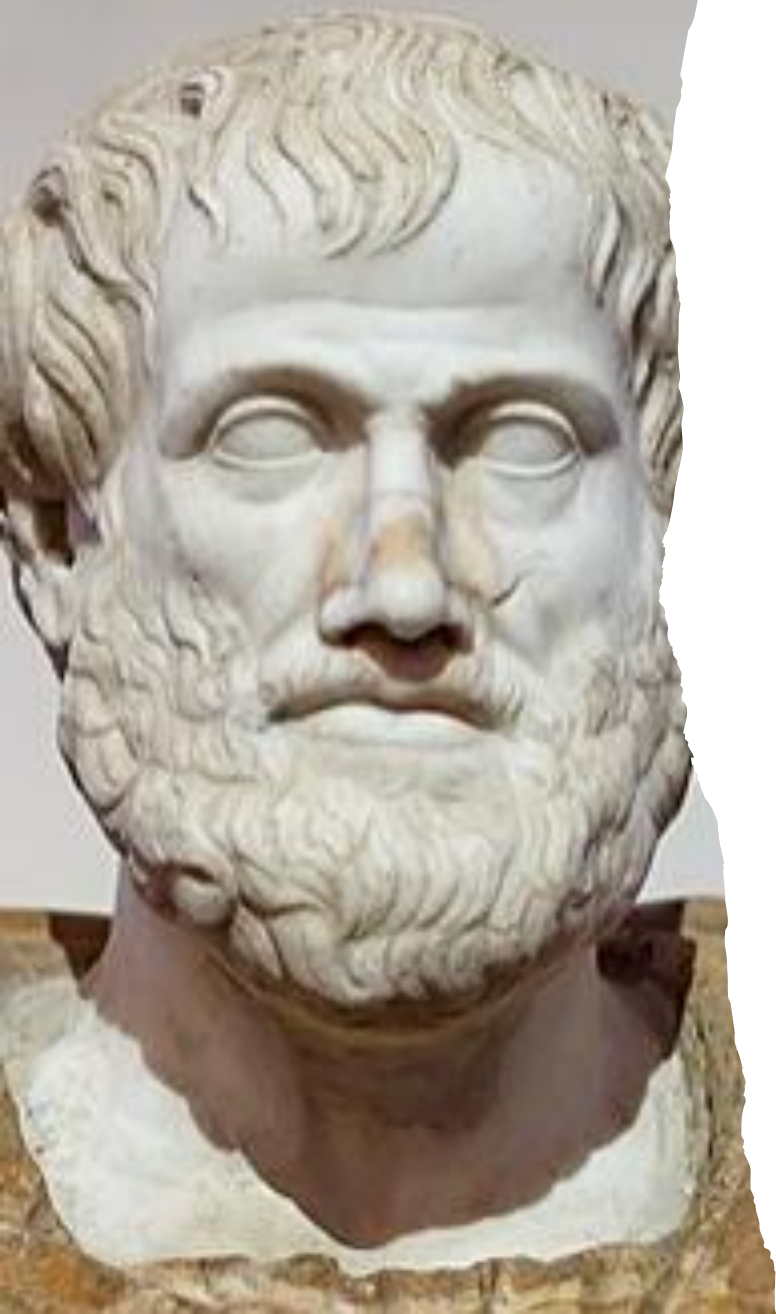
- Cambiamenti nel cervello e nella mente

Summary of structural and functional effects	Brain Structure	Brain Function	Model	Hormone(s)	Effect
	Hypothalamus	Hormone secretion; regulation of temperature, appetite, emotions, and sexual behavior	Animal (rat)	↑ Testosterone, progesterone, and estradiol	↑ New cell growth
	Pituitary	Hormone secretion; regulation of hormone production in other endocrine glands	Human (healthy adolescent)	↑ Testosterone and estradiol	↑ Grey matter volume
	Amygdala	Emotion processing; fear, aggression, sexual behaviors, and reward learning	Animal (rat/hamster)	↑ Testosterone	↑ New cell growth
			Human (healthy adolescent)	↑ Testosterone and DHEA	↑ Grey matter volume
	Human (Klinefelter syndrome)	↓ Testosterone	↓ Grey matter volume		
	Hippocampus	Learning and memory	Animal (rat)	↑ Estrogen	↑ Synaptic density
Myelin	Insulates axons; increases speed and efficiency of signal transmission in neurons	Animal (rat)	↑ Sex steroids	↑ Myelination	
		Human (healthy adolescent)	↑ Testosterone and estradiol		

- Cambiamenti nell'ambiente sociale



# Adolescenza



Socrate 470–399 a.C.

*“Hanno cattive maniere, disprezzo per l'autorità; mancano di rispetto agli anziani e amano le chiacchiere al posto dell'esercizio fisico. ....Contraddicono i genitori, trangugiano le prelibatezze a tavola, accavallano le gambe e tiranneggiano i loro insegnanti.”*

Aristotele 384–322 a.C.

*«...mancano di autocontrollo sessuale, sono volubili nei loro desideri, passionali e impulsivi. ..La giovinezza è l'età in cui le persone sono più devote ai loro amici.*



# Adolescenza: vitale per l'evoluzione

- Aumentata propensione al rischio quando si trovano in compagnia di coetanei.
  - Ricerca di nuove sensazioni.
- Esistono prove di comportamenti tipici dell'adolescenza in tutte le specie.

Developmental Psychology  
2012, Vol. 48, No. 3, 598–623

© 2011 American Psychological Association  
0012-1649/12/\$12.00 DOI: 10.1037/a0026220

The Evolutionary Basis of Risky Adolescent Behavior:  
Implications for Science, Policy, and Practice

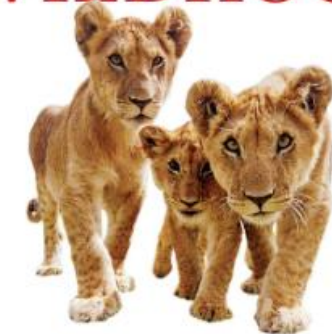
Applying an Evolutionary Approach of Risk-  
Taking Behaviors in Adolescents

Front. Psychol., 10 January 2022

Barbara Natterson-Horowitz  
and Kathryn Bowers

NEW YORK TIMES bestselling authors of ZOObIQUITY

## WILDHOOD



The Epic Journey from  
Adolescence to Adulthood  
in Humans and Other Animals

**L'assunzione del rischio è vitale per l'evoluzione**

# Equilibri adattivi/disadattivi e squilibrio nelle emozioni

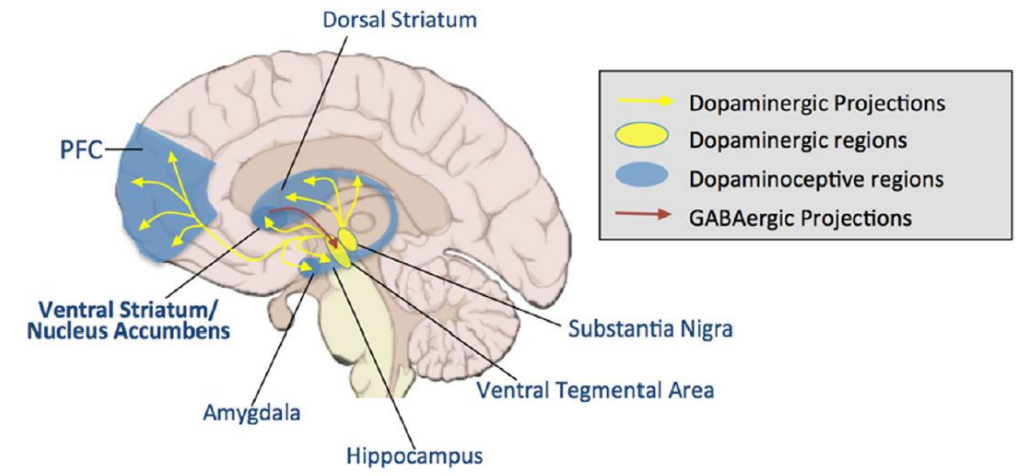
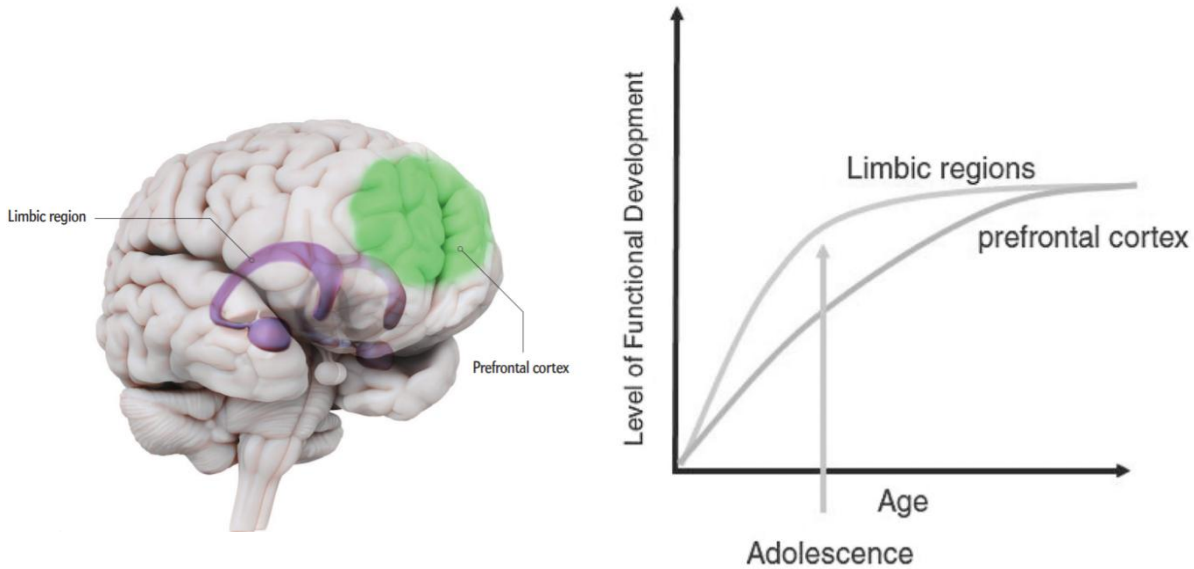
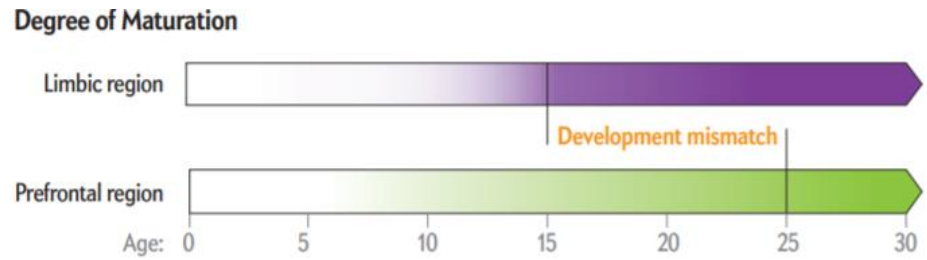


Fig. 1. Dopaminergic pathways in the brain.



Ventral striatum reactivity can be both a source of vulnerability and opportunity.

Vulnerability	Opportunity
<p><i>Orientation toward negative rewards</i></p> <ul style="list-style-type: none"> <li>• Drug experimentation</li> <li>• Risky sexual behaviors</li> </ul>	<p><i>Orientation toward positive rewards</i></p> <ul style="list-style-type: none"> <li>• Academic motivation</li> <li>• Passions and hobbies</li> </ul>
<p><i>Sensitivity to social threat</i></p> <ul style="list-style-type: none"> <li>• Heightened depression</li> <li>• Negative peer influence</li> </ul>	<p><i>Sensitivity to social connection</i></p> <ul style="list-style-type: none"> <li>• Healthy peer relations</li> <li>• Prosocial behaviors</li> </ul>



# Stato di emergenza per la salute mentale

## Child and Adolescent Mental Health: A National Emergency

October 25, 2021

Leah Kuntz

The American Academy of Child and Adolescent Psychiatry, American Academy of Pediatrics, and Children's Hospital Association have declared a national emergency for children and adolescent mental health. Children and families in the United States have experienced "enormous adversity and disruption," which was only exacerbated by the COVID-19 pandemic.

"This [worsening crisis in child and adolescent mental health](#) is inextricably tied to the stress brought on by COVID-19 and the ongoing struggle for racial justice and represents an acceleration of trends observed prior to 2020. Rates of childhood mental health concerns and suicide rose steadily between 2010 and 2020 and by 2018 suicide was the second leading cause of death for youth ages 10-24. The pandemic has intensified this crisis," the groups wrote.<sup>1</sup>

STUDENT WELL-BEING

## Children, Teens Are in a 'Mental Health State of Emergency,' Child Health-Care Groups Warn



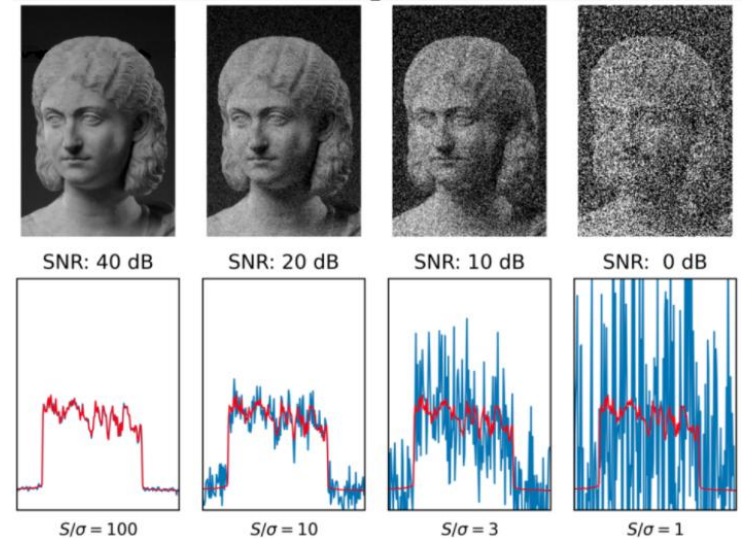
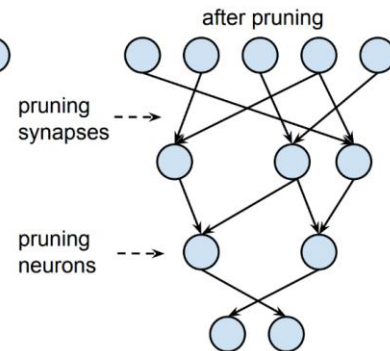
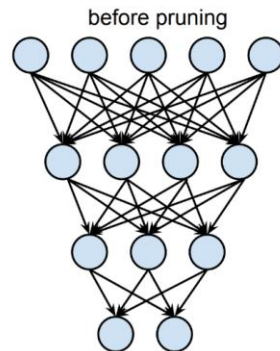
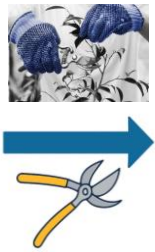
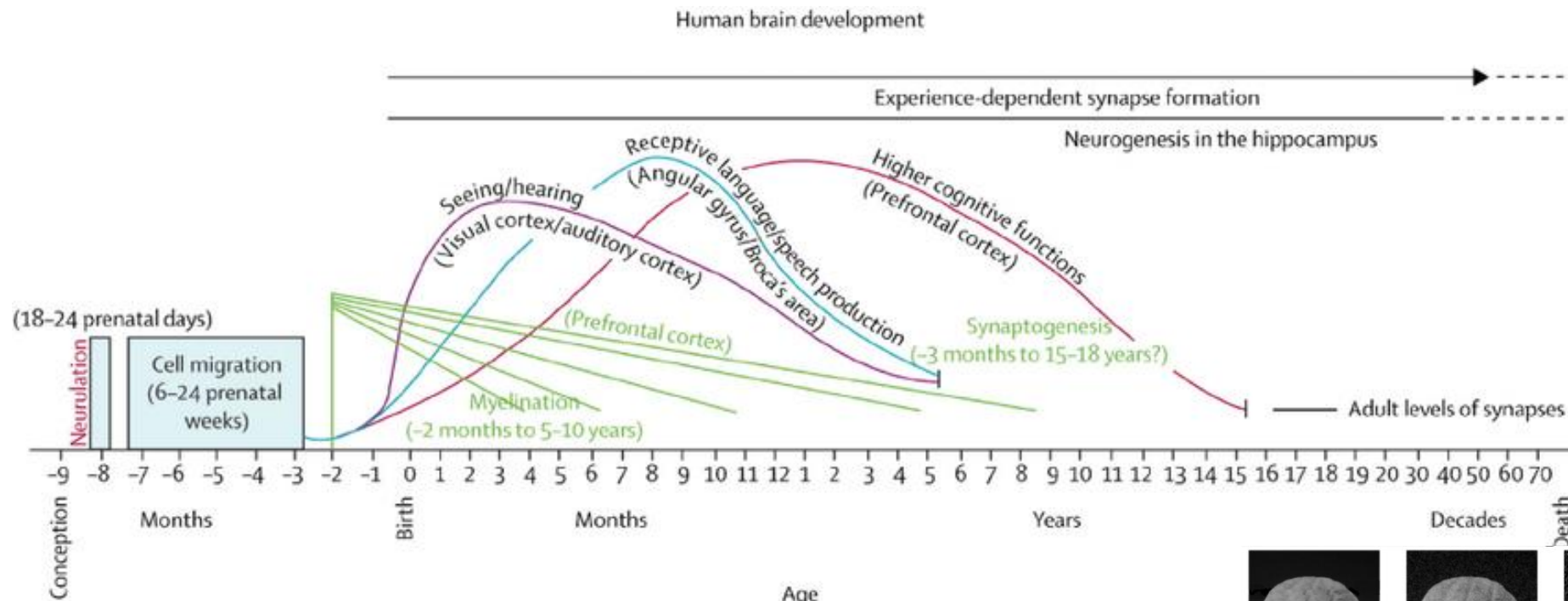
By [Alyson Klein](#) — October 19, 2021 ⌚ 2 min read



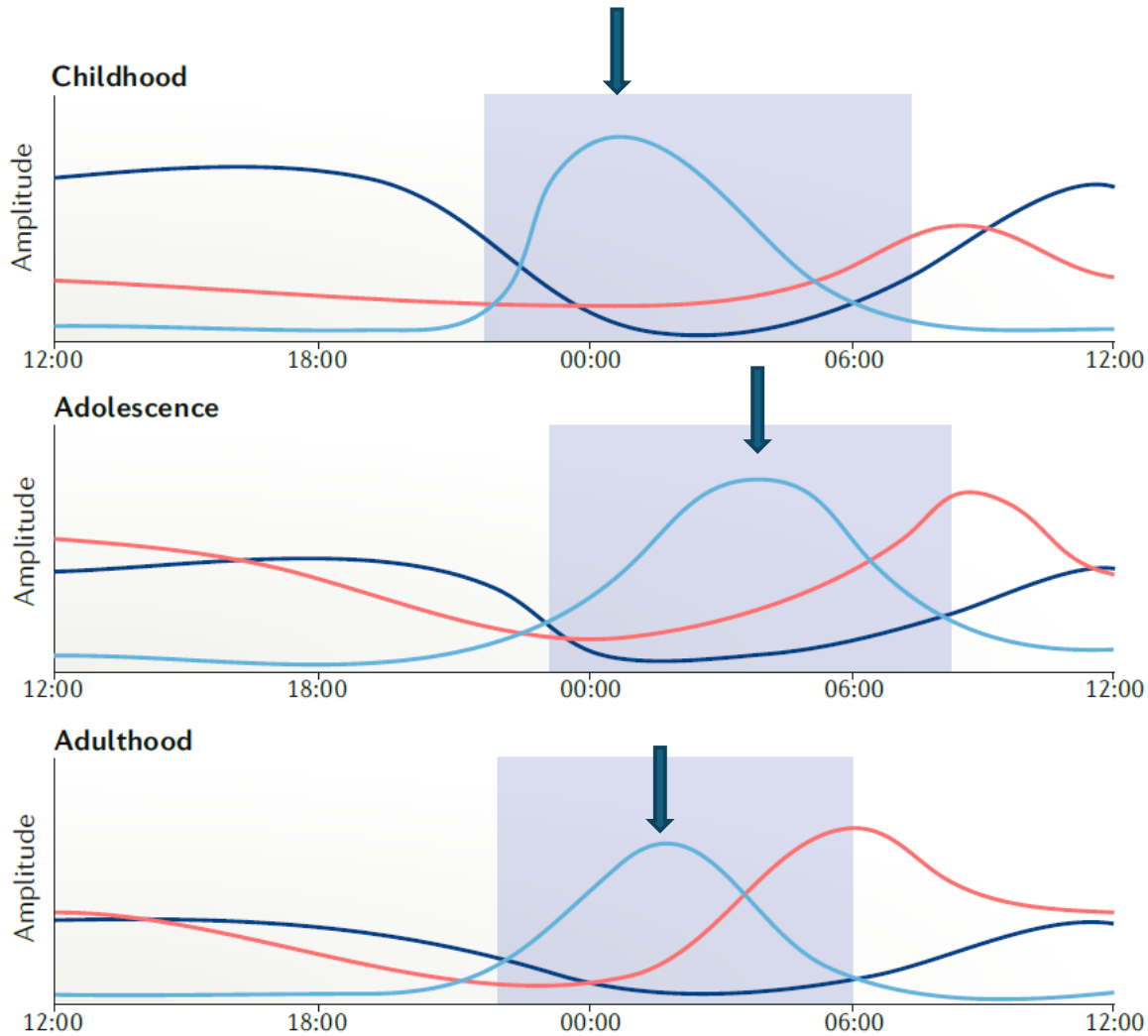
— ma\_rishy/Stock/Getty

There's been a quieter, parallel pandemic happening alongside COVID-19: a spike in significant mental health problems among young people, spurred by isolation, uncertainty, fear, and grief.

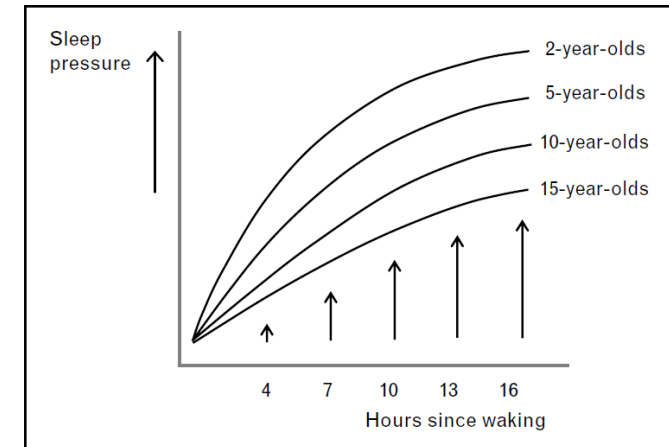
# Pruning sinaptico nell'adolescenza



# La transizione dell'adolescente verso un cronotipo più serale



- Ormoni gonadici e maturità sessuale.
- Fattori ambientali, come la pressione sociale dei coetanei e/o il minore coinvolgimento dei genitori nelle routine serali
- Gli adolescenti potrebbero essere più sensibili alla capacità della luce di spostare i ritmi in determinati momenti della giornata.



Proposed developmental changes in accumulation of sleep pressure as a function of time since waking depicted for different ages. Sleep pressure accumulates more slowly during the day with increasing age.

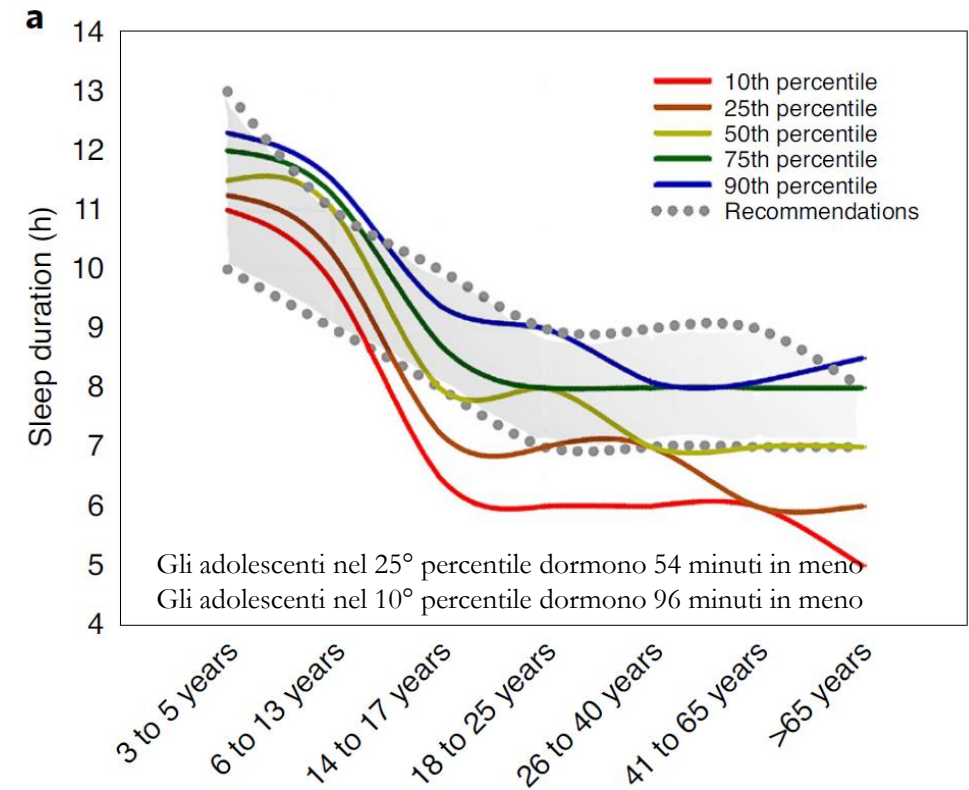
# Deprivazione di sonno negli adolescenti

Supplementary Table 3. Sleep duration according to recommendations

Age group	N	Recommended	Sleeping less, %	Sleeping more, %	Acceptable	Sleeping less, %	Sleeping more, %
1-2 yrs	9	11-14 hrs	-	-	9-16 hrs	-	-
3-5 yrs	1,266	10-13 hrs	1.0	0.1	8-14 hrs	0	0
6-13 yrs	8,377	9-11 hrs	5.4	24.3	7-12 hrs	0.6	1.3
14-17 yrs	513	8-10 hrs	51.5	0.4	7-11 hrs	17.9	0
18-25 yrs	5,192	7-9 hrs	14.3	3.1	6-11 hrs	2.8	0.3
26-40 yrs	38,635	7-9 hrs	20.1	0.7	6-10 hrs	3.7	0.1
41-64 yrs	93,837	7-9 hrs	27.8	0.8	6-10 hrs	7.1	0.1
>65 yrs	8,195	7-8 hrs	35.4	10.6	5-9 hrs	4.7	2.0
Total	156,025	-	24.5	2.6	-	5.6	0.2

Recommendations are by the American National Sleep Foundation.

Più della metà (51,5%) dei soggetti di età compresa tra 14 e 17 anni riferisce



nature human behaviour ARTICLES  
https://doi.org/10.1038/s41562-020-00965-x

## Sleep characteristics across the lifespan in 1.1 million people from the Netherlands, United Kingdom and United States: a systematic review and meta-analysis

Desana Kocavska<sup>1,2,3,4</sup>, Thom S. Lysen<sup>5</sup>, Aafje Dotinga<sup>6</sup>, M. Elisabeth Koopman-Verhoeff<sup>3,7</sup>, Maartje P. C. M. Luijk<sup>8,9</sup>, Niki Antypa<sup>10</sup>, Nienke R. Biermasz<sup>11</sup>, Anneke Blokstra<sup>12</sup>, Johannes Brug<sup>13,14</sup>, William J. Burk<sup>15</sup>, Hannie C. Comijs<sup>16</sup>, Eva Corpeleijn<sup>17</sup>, Hassan S. Dashti<sup>18,19</sup>, Eduard J. de Bruin<sup>20</sup>, Ron de Graaf<sup>21</sup>, Ivonne P. M. Derks<sup>22</sup>, Julia F. Dewald-Kaufmann<sup>23,24</sup>, Petra J. M. Elders<sup>25</sup>, Reinoldus J. B. J. Gemke<sup>26</sup>, Linda Grievink<sup>27</sup>, Lauren Hale<sup>28</sup>, Catharina A. Hartman<sup>29</sup>, Cobi J. Heijnen<sup>30</sup>, Martijn Huismans<sup>31</sup>, Anke Huss<sup>32</sup>, M. Arfan Ikram<sup>33,34</sup>, Samuel E. Jones<sup>35</sup>, Mariska Klein Velderman<sup>36</sup>, Maaike Kontig<sup>37</sup>, Anne Marie Meijer<sup>38</sup>, Kim Meijer<sup>39</sup>, Raymond Noordam<sup>40</sup>, Albertine J. Oldehinkel<sup>41</sup>, Joost Oude Groeninger<sup>42</sup>, Brenda W. J. H. Penninx<sup>43</sup>, H. Susan J. Picavet<sup>44</sup>, Sara Pieters<sup>45,46</sup>, Sijmen A. Reijneveld<sup>47,48</sup>, Ellen Reitz<sup>49</sup>, Carry M. Renders<sup>50,51</sup>, Gerda Rodenburg<sup>52</sup>, Femke Rutters<sup>53</sup>, Matt C. Smith<sup>54</sup>, Amika S. Singh<sup>55</sup>, Marieke B. Snijder<sup>56,57</sup>, Karien Stronks<sup>58</sup>, Margreet ten Have<sup>59</sup>, Jos W. R. Twisk<sup>60</sup>, Dike Van de Mheen<sup>61,62</sup>, Jan van der Ende<sup>63</sup>, Kristiaan B. van der Heijden<sup>64,65</sup>, Peter G. van der Velden<sup>66</sup>, Frank J. van Lenthe<sup>67</sup>, Raphaële R. L. van Litsenburg<sup>68,69</sup>, Sandra H. van Oostrom<sup>70</sup>, Frank J. van Schalkwijk<sup>71,72</sup>, Connor M. Sheehan<sup>73</sup>, Robert A. Verheij<sup>74</sup>, Frank C. Verhulst<sup>75</sup>, Marijke C. M. Vermeulen<sup>76,77</sup>, Roel C. H. Vermeulen<sup>78</sup>, W. M. Monique Verschuren<sup>79</sup>, Tanja G. M. Vrijkotte<sup>80</sup>, Alet H. Wijga<sup>81</sup>, Agnes M. Willemien<sup>82,83</sup>, Maïke ter Wolbeek<sup>84</sup>, Andrew R. Wood<sup>85</sup>, Yilza Xerxa<sup>86</sup>, Wichor M. Bramer<sup>87</sup>, Oscar H. Franco<sup>88,89</sup>, Annemarie I. Luijk<sup>90</sup>, Eus J. W. Van Someren<sup>4,91,92</sup> and Henninze Tiemeier<sup>1,2,93,94</sup>

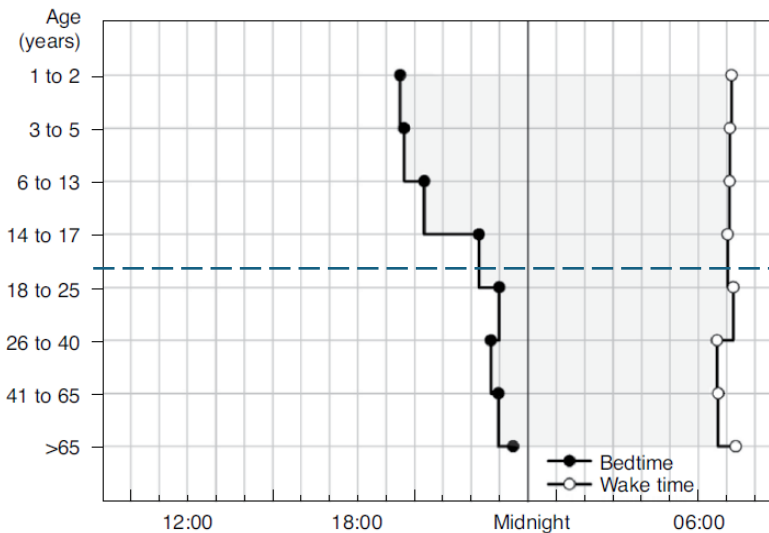
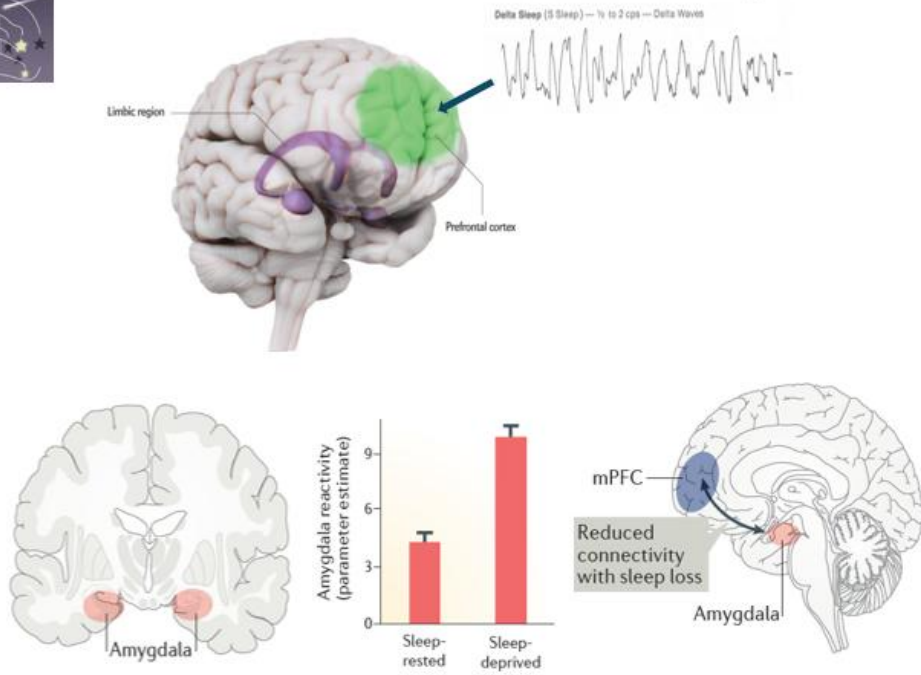


Fig. 3 | Sleep timing across lifespan. Night-time sleep timing across the lifespan (n=106,282).

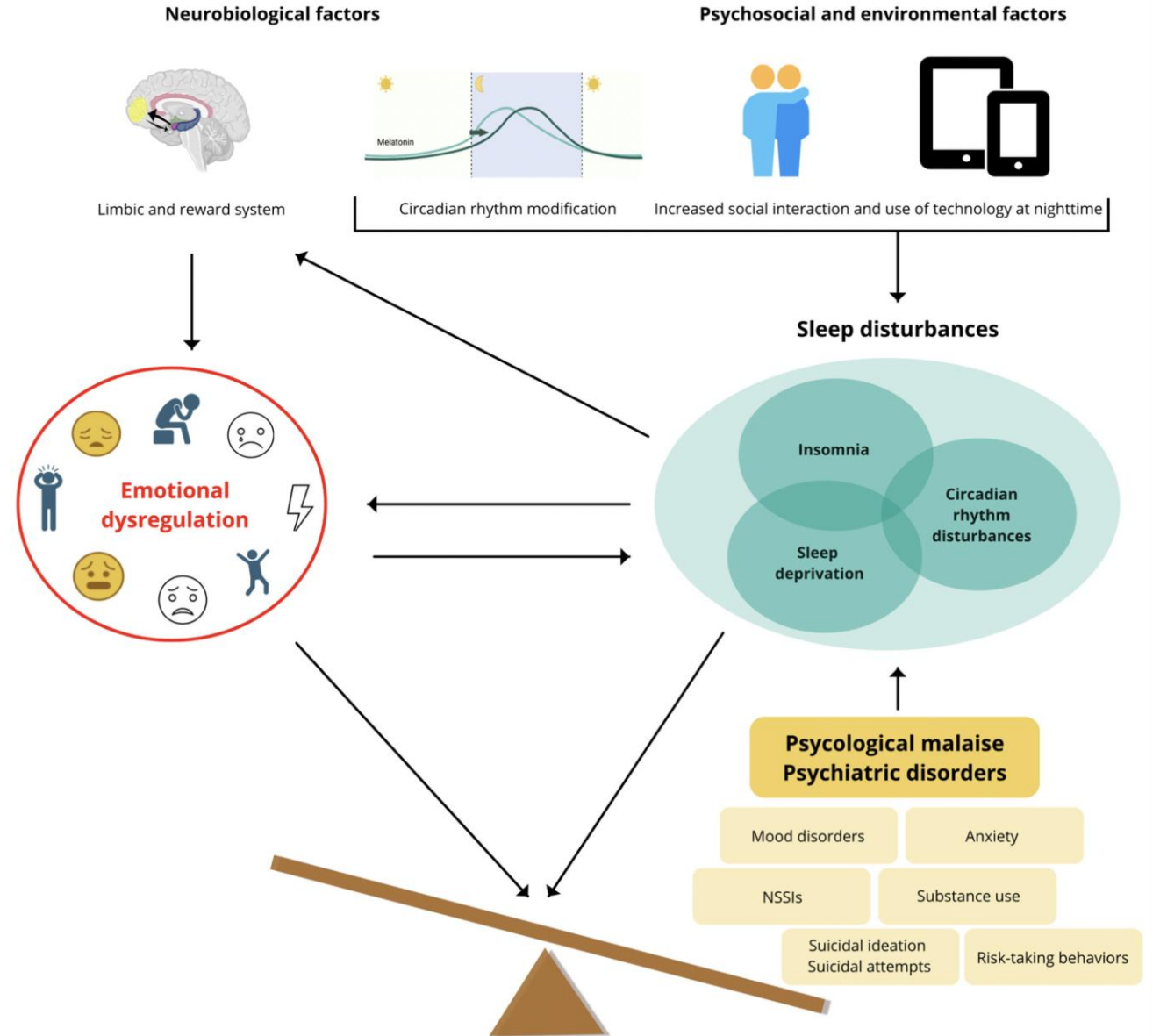
# Sonno e salute mentale nell'adolescenza

## The sleep-deprived human brain

Adam J. Krause<sup>1</sup>, Eti Ben Simon<sup>1</sup>, Bryce A. Mander<sup>1</sup>, Stephanie M. Greer<sup>2</sup>, Jared M. Saletin<sup>1</sup>, Andrea N. Goldstein-Piekarski<sup>2</sup> and Matthew P. Walker<sup>1,2</sup>



Krause et al., Nature Reviews Neuroscience 2017



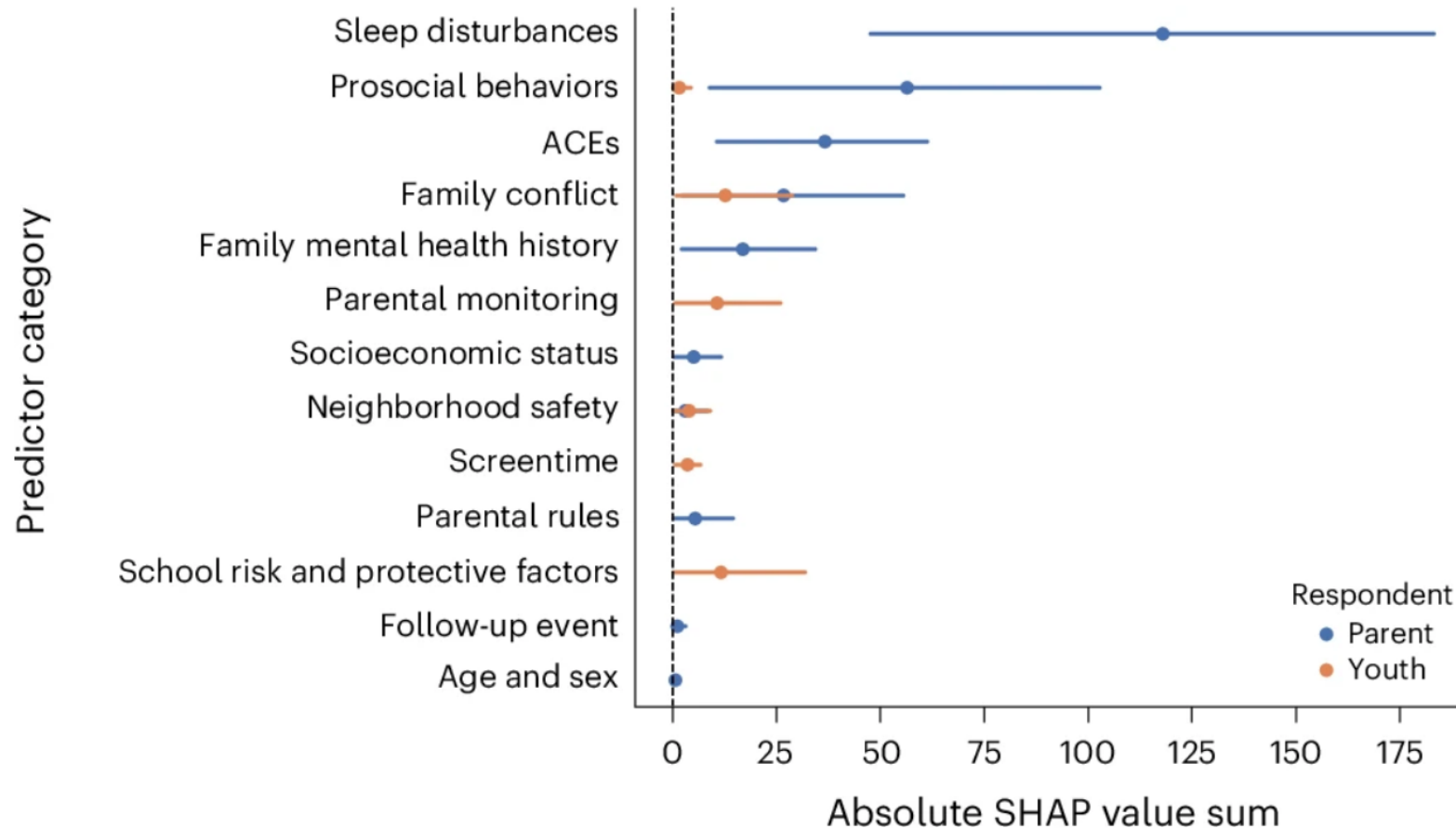
Uccella, Cordani et al, Brain Sciences, 2023

# Sonno e salute mentale nell'adolescenza

I disturbi del sonno sono emersi come un solido predittore di elevato rischio di malattia psichiatrica

## Predictor category SHAP analysis.

From: [Prediction of mental health risk in adolescents](#)



# Messaggi chiave

1

## **Due processi, un equilibrio**

Il sonno nasce dall'accoppiamento tra processo omeostatico e ritmo circadiano con il ciclo luce-buio: è la base di un sonno strutturato e di una buona vigilanza diurna.

2

## **Una maturazione precoce**

Il sistema circadiano si sviluppa dall'utero ai primi due anni di vita; nei primi mesi il sonno si consolida e nelle prime fasi di vita si dorme più che in ogni altra età.

3

## **Il sonno costruisce il cervello**

Non è solo un indicatore, ma un vero motore dello sviluppo e della plasticità cerebrale: dai twitch neonatali al pruning sinaptico e al «sonno delta» dell'adolescenza.

4

## **Dormire male fa ammalare**

Disturbi e carenza di sonno si associano a disfunzioni fisiche e neuropsichiatriche già dalla prima infanzia.

5

## **L'adolescenza è un periodo critico**

Il cronotipo si sposta verso la sera e la deprivazione di sonno è frequente: i disturbi del sonno sono un solido predittore di elevato rischio psichiatrico.

*Dormire, forse sognare*  
*Ferdinando Scianna*

