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Supplementary Materials for

Unraveling why we sleep: Quantitative analysis reveals abrupt transition from neural reorganization to repair in early development

Junyu Cao, Alexander B. Herman, Geoffrey B. West, Gina Poe, Van M. Savage*

*Corresponding author. Email: vsavage@ucla.edu

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Supporting Information (SI)

S1. Notation

Variable	Definition	Units
B_b	mass-specific metabolic rate of the brain	W/kg
B	whole body metabolic rate	W
P_R	power density	W/m^3
V_b	total brain volume	m^3
M_b	brain mass	kg
M	body mass	kg
t_A	total time awake	hr
t_S	total sleep time	hr
t_R	total REM sleep time	hr
t_{NR}	total NREM sleep time	hr
$\Delta E_{I \to \sigma}$	the energy needed to convert a unit of information acquired by sensory systems to synaptic changes in the brain	J
f_I	fraction of the total metabolic rate required for sensing that information	unitless
ν	rate of processing information of each synapse	bits/s
N_σ	total number of synapses in the brain	#
V_w	white matter volume	m^3
V_g	gray matter	m^3
ρ_σ	synaptic density	#/m^3

Table S1: Notation with units.

S2. Assumptions

Assumptions and which ones are directly empirically tested:

- Nearly all damage must be repaired or cleared in order for the brain to continue to function normally.
- Nearly all repair and clearance occurs during sleep. Data support this for adults across species.

- Sleep is driven by the brain and not the body. Data across species support this.
- Local neural reorganization associated with changes in synaptic density primarily occurs during REM or NREM sleep. Data support all occurring during REM sleep during development, especially before 2 to 3 years of age.
- Idealized synaptogenesis occurs uniformly across the brain.
- Information processing is directly tied to energy use.
- Brain metabolic rate is proportional to the number of synapses and to the volume of white matter, in agreement with empirical data.
- Empirical data show that there is a phase transition in the function of sleep occurring between 2 and 3 years of age.
- The energy required to convert information into synaptic connections, the fraction of metabolic rate needed to sense information, the power density needed for repair, and the efficiency of repair, are all invariant with respect to body size.
- Brain metabolic rate scales with brain size as if brain is autonomous organ. Empirical data support this with approximate exponent of $3/4$.

S3. Equation for mass dependence of total sleep time, t_S

We can solve Eq. (1) in the main text by substituting $t_S = 24$ hours $- t_A$ to obtain

$$t_S = \frac{24 c_1 M_b^{\alpha-1}}{1 + c_1 M_b^{\alpha-1}} \tag{8}$$

where $c_1 \equiv \frac{cB_{b,0}}{P_R}$ with parameters as defined in the main text and $B_{b,0}$ representing the normalization constant for relating brain metabolic rate, B_b to brain mass, M_b. Across species, the scaling exponent is sublinear, $\alpha < 1$, so $\alpha - 1 < 0$, resulting in $t_S \sim 24$hours when M_b becomes

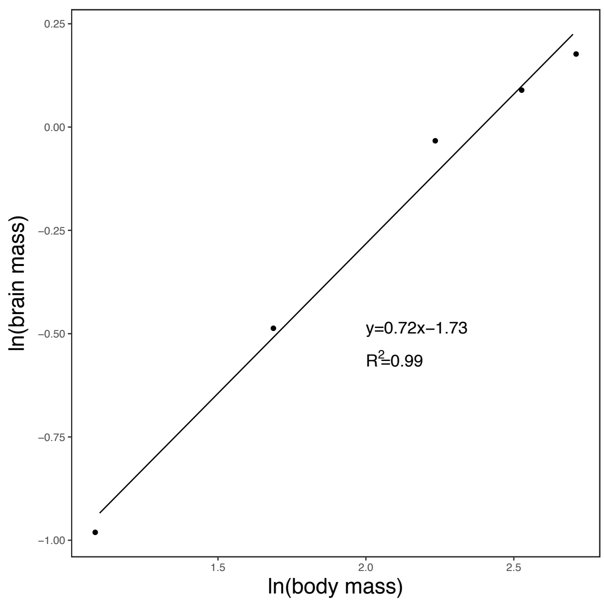

Figure S1: Plot of the logarithm of brain mass versus the logarithm of body mass before the transition with the measured slope 0.72.

increasingly smaller and $t_S \sim M_b^{\alpha-1} \to 0$ when M_b becomes increasingly larger. In strong contrast, within species, the scaling exponent is superlinear, $\alpha > 1$, so $\alpha - 1 > 0$, resulting in $t_S \sim 24$hours when M_b becomes increasingly larger and $t_S \sim M_b^{\alpha-1} \to 0$ when M_b becomes increasingly smaller. These limits make it strikingly clear that these predictions are the opposite of real patterns of sleep during growth.

S4. Scaling of brain mass with body mass during early development

We note that data confirm that the brain mass of infants scales with their body mass as a power law whose exponent is 0.72, as shown in Fig. (S1), and that this value is very close to the value of $3/4$ that was used in our predictions for the scaling of sleep properties.

S5. Determination of transition age

Surveying the plots of our data, we note the sharpest and most dramatic transition of any of the sleep variables is for the ratio of either NREM sleep time or REM sleep time to awake time, strongly supportive of a transition in sleep function. Indeed, this ratio remains unchanged as a function of brain mass during the earliest stages of development until a transition occurs after which it steeply decreases. Thus, beyond this transition the fraction of REM sleep sharply decreases as a function of brain mass and age. Fig. (2) in the main text displays the data for this relationship and the dramatic transition from one scaling regime to another is clearly evident. Our fitting procedure identifies the transition age as 2.4 years old. Notably, there is a similar transition at roughly the same age in the ratio of sleep time to awake time (Fig. (3A) in main text) and of REM sleep time to awake time (Fig. (3C) in main text). Because the ratio of sleep to awake time and REM to awake time are primary drivers of sleep relationships within our models, these findings are consistent with a general shift in all sleep properties at a common age. For this reason, we use the following equations to determine the transition point.

$$\begin{aligned}\min_{k_1,k_2} \quad J(k_1,k_2) &= \sum_{i=1}^{t}(y_i - k_1(x_i - x_0) - y_0)^2 \\ &\quad + \sum_{i=t}^{T}(y_i - k_2(x_i - x_0) - y_0)^2 \end{aligned} \tag{9}$$

Taking the derivative of J, we have

$$\begin{cases} \frac{\partial J}{\partial k_1} = 2\sum_{i=1}^{t}(y_i - k_1(x_i - x_0) - y_0)(x_0 - x_i) = 0 \\ \frac{\partial J}{\partial k_2} = 2\sum_{i=t}^{T}(y_i - k_2(x_i - x_0) - y_0)(x_0 - x_i) = 0 \end{cases}$$

which implies that the optimal k_1 and k_2 with the corresponding transition point (x_0, y_0) are

$$k_1 = \frac{\sum_{i=1}^{t}(y_i - y_0)(x_i - x_0)}{\sum_{i=1}^{t}(x_i - x_0)^2} \text{ and } k_2 = \frac{\sum_{i=t}^{T}(y_i - y_0)(x_i - x_0)}{\sum_{i=t}^{T}(x_i - x_0)^2}$$

S6. Raw data for scaling of number of synapses in early development

Our plots for number of synapses, N_σ, in the main text were calculated from raw data for synaptic density, ρ_σ, and gray matter volume, V_g. Plots of the raw data for these two parameters are shown in Fig. (S2). Based on the scaling exponents of 0.39 and 0.91 measured in these plots, we would predict that $N_\sigma \propto M_b^{0.39} M_b^{0.91} = M_b^{1.30}$, which is consistent with the measured scaling exponent for N_σ of 1.23 ± 0.09 from Fig. 1B in the main text.

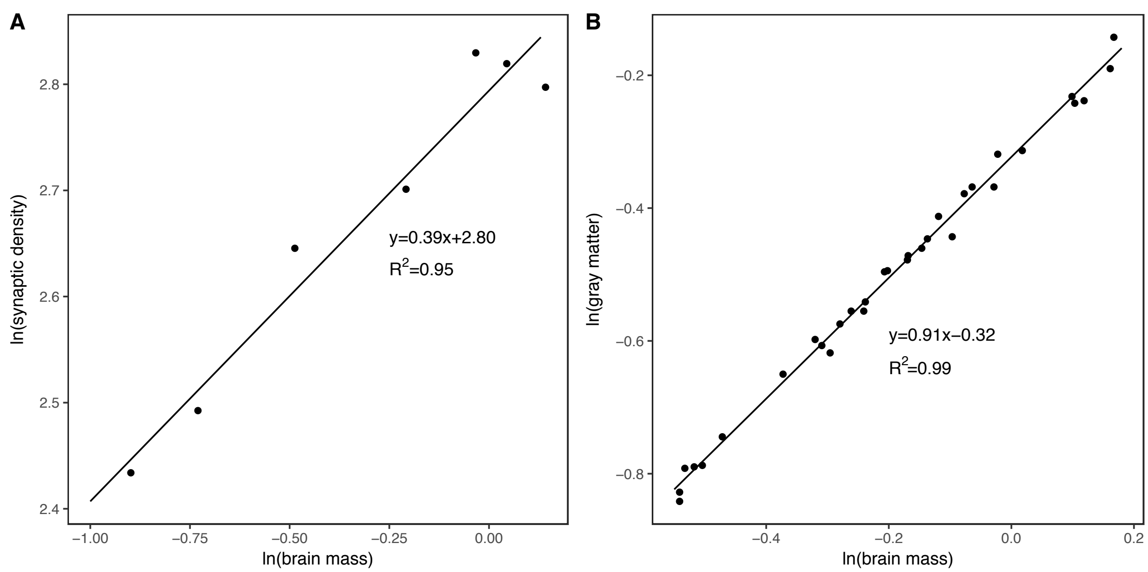

Figure S2: Relationships to calculate how number of synapses changes with brain mass. A. Plot of the logarithm of synaptic density versus the logarithm of brain mass before transition with measured slope 0.39. B. Plot of the logarithm of gray matter versus the logarithm of brain mass before transition with measure slope 0.91.

S7. Scaling of brain metabolic rate during later development

Below we show a plot and measured scaling exponent for how brain metabolic rate, B_b, changes with brain size, M_b. This scaling exponent as an additional check of our theory for sleep being for neural repair during later development. We caution against much certainty or interpretation about the exact value (-2.70) of the exponent and its being significantly larger than the classic value of -0.25. Importantly, it should be noted that the range in brain mass over this time period of development is extremely small and the data are quite limited. Both of these properties of the data call into question the use of logarithmic variables to determine the exact magnitude of the scaling exponent in this case (61, 62), and the large 95% CI indicate the high degree of uncertainty in the exact value of this estimate.

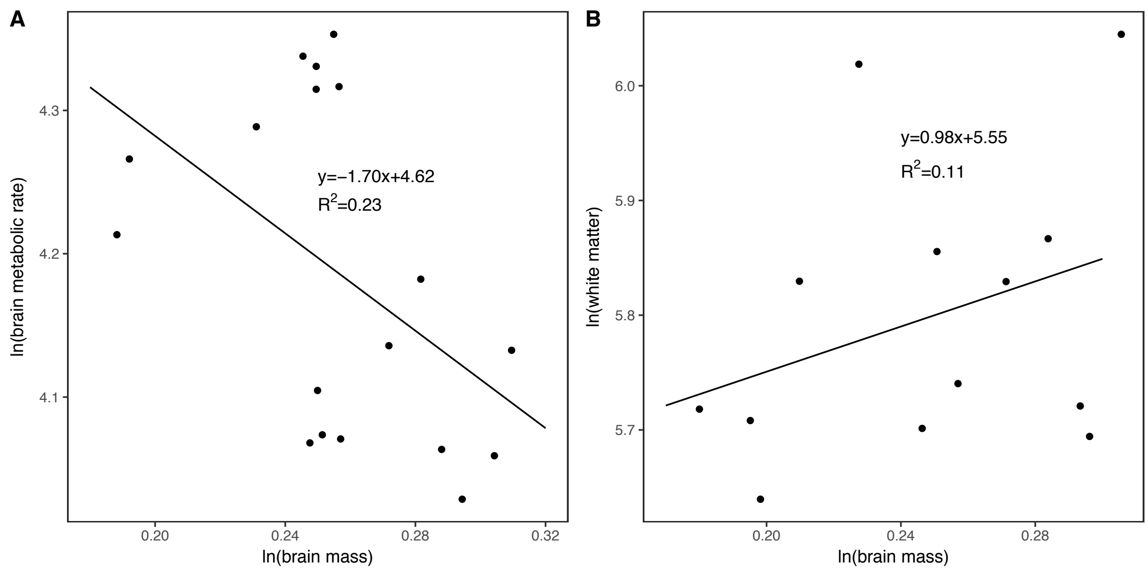

Figure S3: Scaling of brain metabolism and connections with brain mass and age after the transition. A. Plot of the logarithm of brain metabolic rate versus the logarithm of brain mass after 2.4 years old with the measured slope -1.70. B. Plot of the logarithm of the white matter volume versus the logarithm of brain mass after 2.4 years old with the measured slope 0.98.

S8. Scaling of sleep across development in other species

We collect sleep data for three other mammals: rabbit (63), rat (64), and guinea pig (65). Fig S4 is a plot of the ratio of REM sleep time to total sleep time per day versus the age (days) for these three species.

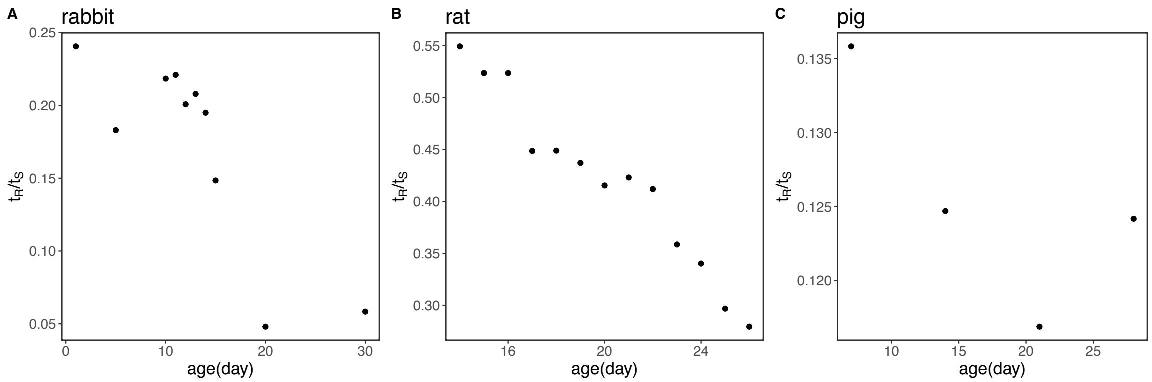

Figure S4: Plots of the ratio of REM sleep time to total sleep time per day versus the age for rabbit, rat, and pig, respectively.

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