POSTER NUMBER

Identifying endogenous and environmental factors driving sleep and circadian phenotypes by combining data with a mathematical model to improve sleep timing in an older population

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Sleep and circadian rhythmicity are **disrupted in dementia,** with more than **70% of people living with dementia** (PLWD) experiencing disturbances such as early bedtimes and a long time in bed [1].

Sleep and circadian phenotypes are driven by both **physiological factors** and **environmental light exposure**.

We combined **readily collectable data** with a **new mathematical model to extract physiological parameters that determine sleep phenotypes** for the subsequent design of interventions.

Collect light exposure and sleep timing data

- Thirty-five older adults (65-83 y) monitored their light exposure and sleep for a period of 7-14 days at home.
- Before giving participants the light sensors, we assessed the sensor accuracy in our laboratory, Fig 1.
- Fig 2 shows examples of collected data for 5 different phenotypes.

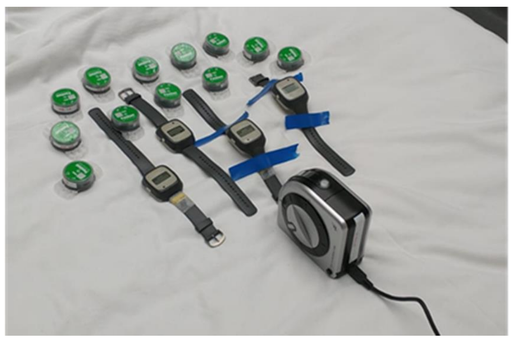


Fig 1: Calibration of light sensors in the Surrey Sleep Research Centre

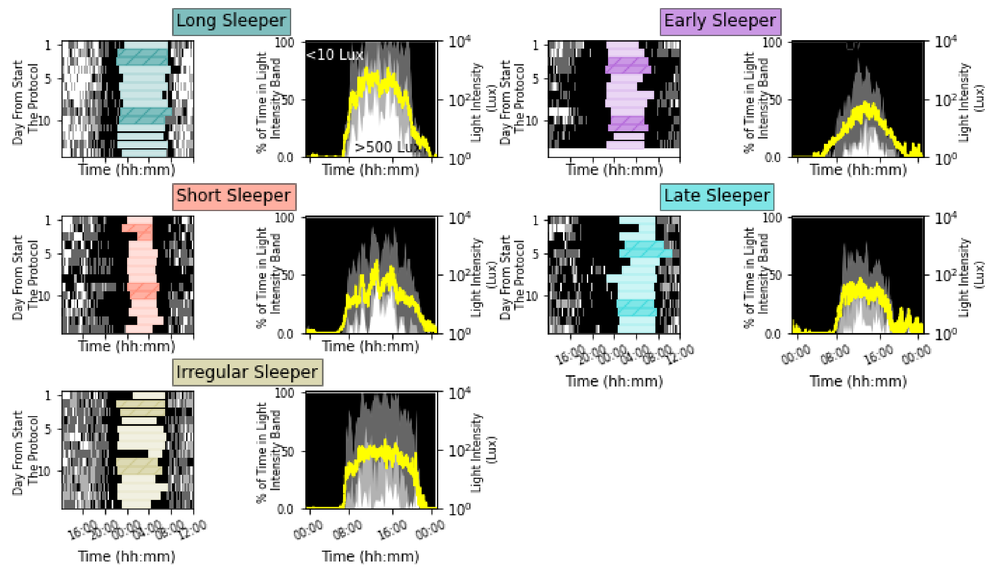


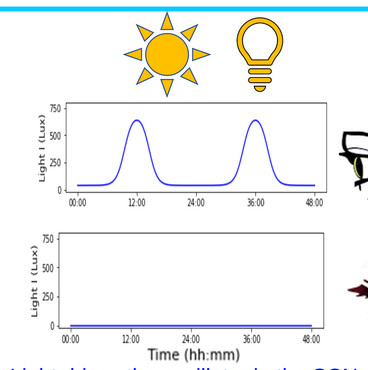
Fig 2. Sleep schedule and light exposure for different sleep phenotypes

Build personalised HCL model and extract parameters that determine sleep phenotypes

$$\tilde{I} = \mathcal{H}(1/2 - S)\, I(t)$$

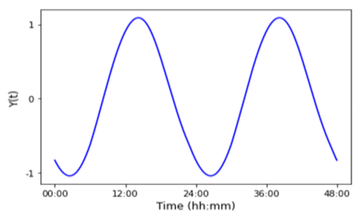
$$\hat{B} = \alpha_0 \left(\frac{\tilde{I}}{I_0}\right)^p G(1-n) \qquad \frac{dn}{dt} = \lambda\left(\alpha_0 \left(\frac{\tilde{I}}{I_0}\right)^p (1-n) - \beta n\right)$$

- We constructed a new mechanistic mathematical model for sleep timing including known physiological factors (sleep homeostasis and circadian rhythmicity) and environmental light exposure, Fig 3.
- For each participant, we fitted the model to their average sleep timing and duration data to find personalised homeostatic (μ) and circadian parameters (c_a).



Light drives the oscillator in the SCN

$$C(t) = \left(c_0 + \alpha_1 x - \alpha_2 y + \beta_1 x^2 - \beta_2 xy + \beta_3 y^2 + \delta(-cy + sx)^3\right)$$



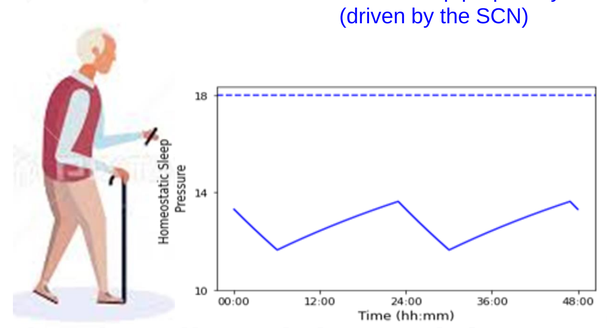
Circadian sleep propensity (driven by the SCN)

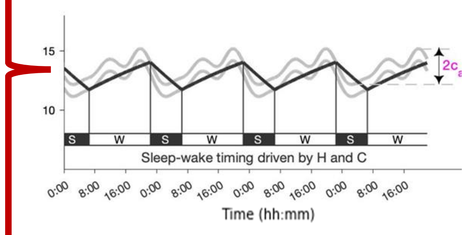
$$\kappa\frac{dx}{dt} = \gamma\left(x - \frac{4x^3}{3}\right) - y\left(\left(\frac{24}{f\tau_c}\right)^2 + kB\right)$$

$$\kappa\frac{dy}{dt} = x + B,$$

$$\frac{dH}{dt} = \begin{cases} \frac{\mu - H}{\chi_w} & \text{during wake} \\ -\frac{H}{\chi_s} & \text{during sleep} \end{cases}$$

Homeostatic sleep pressure H (driven by the sleep-wake cycle)





Sleep-wake timing determined by H and c_a

Fig 3: The Homeostatic Circadian Light model

Understand driving factors of sleep phenotypes

- Sleep phenotypes relate to model parameters and light exposure patterns Fig 4.
- The effect of light exposure patterns on sleep timing depends on the personal parameters values.

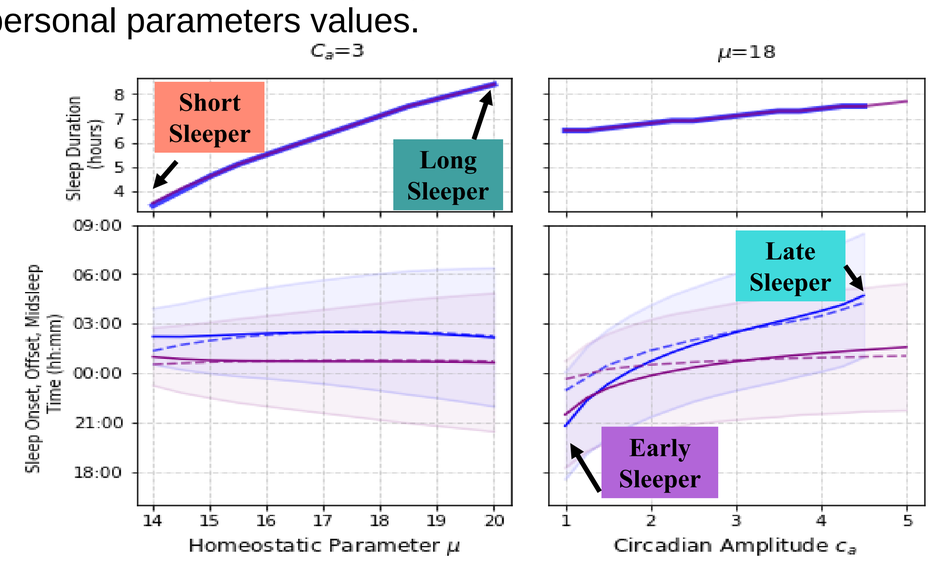


Fig 4. Sleep duration and timing depend on the personal parameters and light exposure (In blue a baseline light profile, in purple a profile with less light in the evening).

- We successfully retrieved 'personal' model parameters that accurately captured sleep duration and timing for 32 of the 35 participants Fig 5.
- We found the homeostatic parameter derived by fitting to the home data correlated with a biomarker of sleep homeostasis (slow wave activity) found in a subsequent laboratory assessment Fig 6.

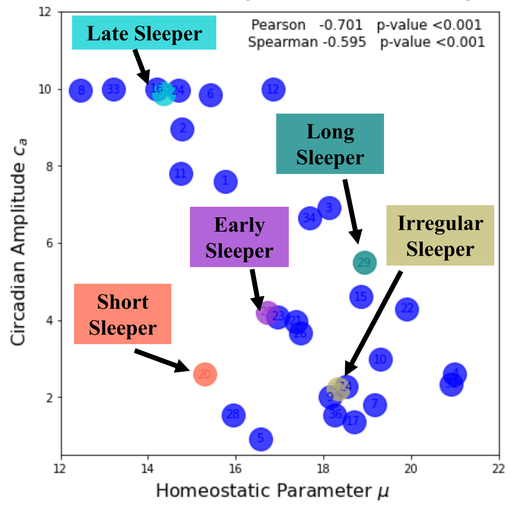


Fig 5. Personalised parameters were found for 32 of the 35 participants

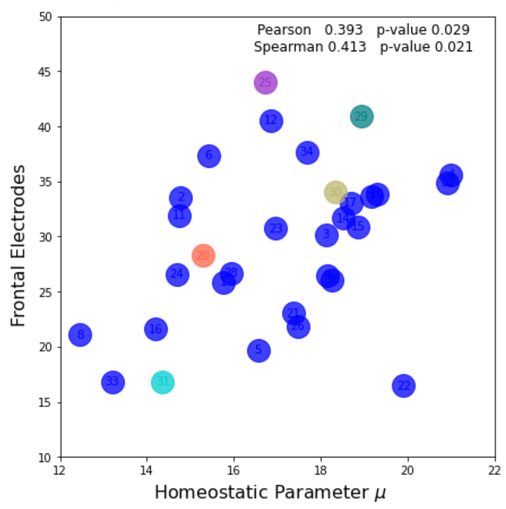


Fig 6. Correlation between homeostatic parameter and SWA

References

[1] Rongve A, Boeve BF, Aarsland D. "Frequency and correlates of caregiver-reported sleep disturbances in a sample of persons with early dementia", *J Am Geriatr* Soc. 58: 480–486, (2010).

Acknowledgments

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Within individuals, **understanding the relative contributions of different driving** factors will facilitate the design of **effective, personalised interventions.**

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