Associations between sleep, brain, and cognitive performance using the ENIGMA-Sleep data

Hanwen Bi[1,2], Robin Bülow[3], Michele Deantoni[4], David Elmenhorst[1], Eva-Maria Elmenhorst[5], Ralf Ewert[3], Fabio Ferrarelli[6], Stefan Frenzel[3], Hans J. Grabe[3,7], Sanne J.W. Hoepel[8], Felix Hoffstaedter[1,2], Neda Jahanshad[9], Ahmadreza Keihani[6], Vincent Küppers[1,10], Annemarie I. Luik[8], Ahmad Mayeli[6], Nasrin Mortazavi[4], Gustav Nilsonne[11,12], Julia S Rupp[6], Amin Saberi[13,1,2], Christina Schmidt[4], Kai Spiegelhalder[14], Sandra Tamm[11,12], Sophia I. Thomopoulos[9], Paul M. Thompson[9], Sofie Valk[13,1,2], Gilles Vandewalle[4], Henry Völzke[3,15], Antoine Weihs[3], Joseph Wexler[11,16], Katharina Wittfeld[3,7], Simon B. Eickhoff[1,2], Kaustubh R. Patil[1,2], Federico Raimondo[1,2], Masoud Tahmasian[1,2], for the ENIGMA-Sleep Working Group

[1]Research Center Jülich, Jülich, Germany; [2]Heinrich-Heine University Düsseldorf, Düsseldorf, Germany; [3]University Medicine Greifswald, Greifswald, Germany; [4]University of Liège, Liège, Belgium; [5]German Aerospace Center, Cologne, Germany; [6]University of Pittsburgh, Pittsburgh, United States; [7]German Centre for Neurodegenerative Diseases (DZNE), Greifswald, Germany; [8]Erasmus MC University Medical Center Rotterdam, Rotterdam, Netherlands; [9]University of Southern California, Marina del Rey, United States; [10]University of Cologne, Cologne, Germany; [11]Karolinska Institute, Stockholm, Sweden; [12]Stockholm University, Stockholm, Sweden; [13]Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany; [14]University of Freiburg, Freiburg, Germany; [15]German Center for Cardiovascular Research (DZHK), Greifswald, Germany; [16]Stanford University, Stanford, United States

Background

- Sleep disturbance is considered a potential risk factor for cognitive decline and dementia[1,2].
- Large-scale studies are needed to reveal the relationship and neurobiological mechanism.
- Previous large-scale studies (N ≈ 40,000 & 500,000) using the UK-Biobank data highlighted a significant, non-linear relationship between sleep duration and cognitive performance but with a **small effect size**[3,4].

Gap:

- These studies were primarily cross-sectional and limited to a UK-based sample, thereby constraining the generalizability of the findings.
- Machine learning methods enable individual-level predictions and can validate models on unseen data, thus providing a more robust analytical framework.

Aim:

In this study, we performed machine learning (ML) analysis based on both self-reported and objective sleep duration and sleep efficiency and brain structure data using the ENIGMA-Sleep[5] data to predict cognitive scores at the individual level.

Sleep + Brain → Cognitive Performance

Methods

ENIGMA-Sleep Datasets

SHIP-Trend:

- N = 831 (396 Female, 435 Male)
- Age 21-81 (52.7 ± 13.5)
- Stroop interference score 1-113 (20.2 ± 11.4)

Liege:

- N = 192 (99 Female, 93 Male)
- Age 50-82 (64.0 ± 7.1)
- Stroop interference score -0.02-0.57 (0.22 ± 0.14)

Features

Sleep measurements:

- Sleep duration & efficiency from polysomnography (PSG) & Pittsburgh Sleep Quality Index (PSQI)

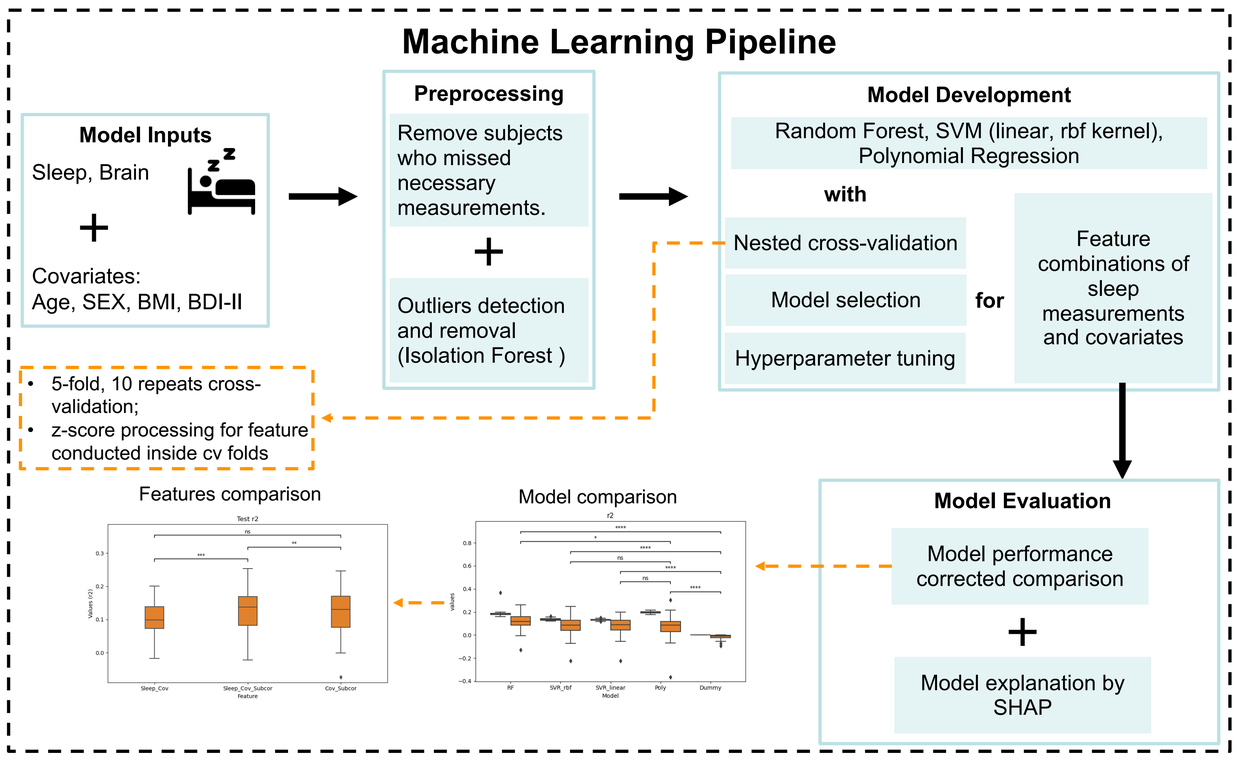
Brain structure data:

- Cortical thickness & surface area (Desikan-Killiany, Schaefer 400 atlas)
- Subcortical volumes (Aseg)

Covariates:

- Age, Sex, BMI, Depression score

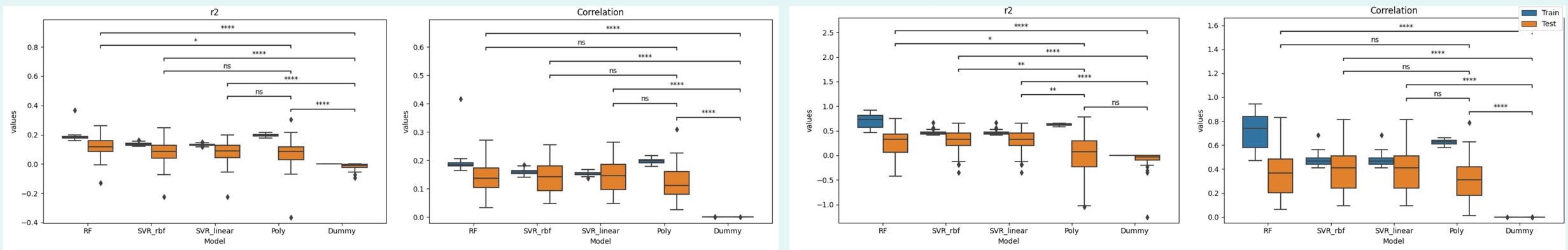
Machine Learning Pipeline



Results

Random Forest and SVM-rbf showed weak but stable prediction to Stroop Interference Score in both SHIP-Trend (left) and Liege (right) datasets.

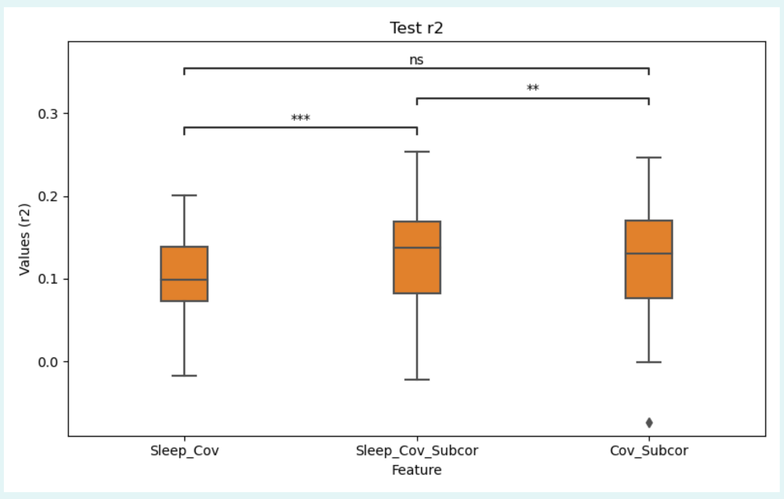
- Non-linear models showed successful prediction compared to dummy regressor (predict target's mean value). ML models are better than poly-regression.



ns: p <= 1.00e+00; *: 1.00e-02 < p <= 5.00e-02 ; **: 1.00e-03 < p <= 1.00e-02; ***: 1.00e-04 < p <= 1.00e-03; ****: p <= 1.00e-04 (same below)

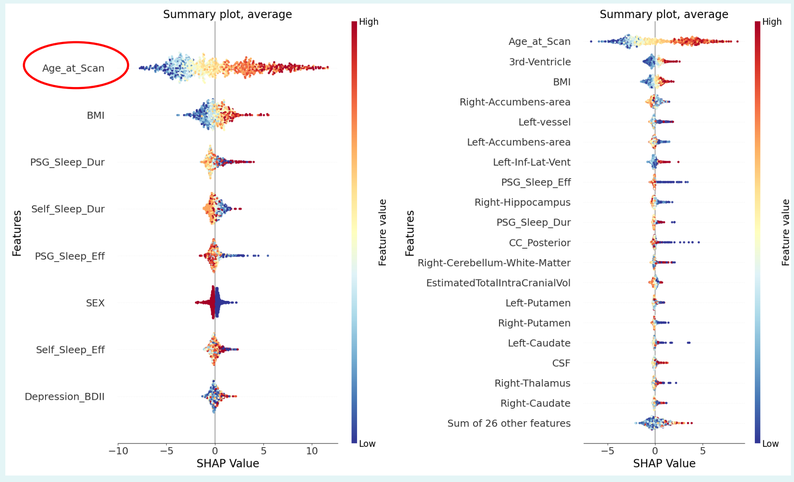
Model comparison by features in SHIP-Trend by Random Forest

- Stroop interference score can be predicted with sleep, subcortical, and demographic data by ML model.

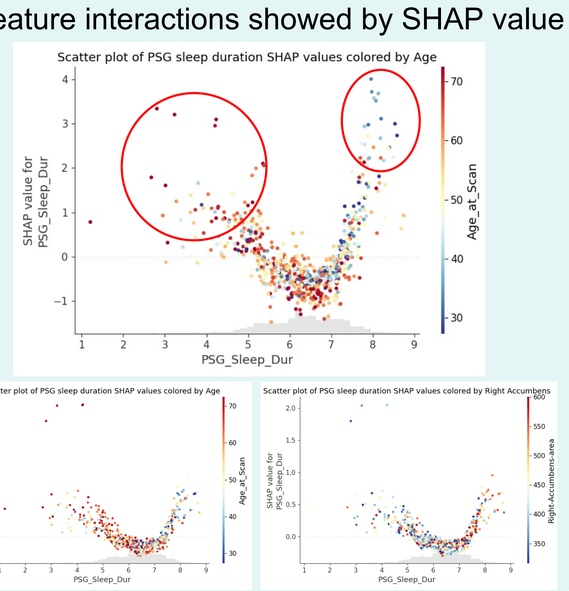


Model explanation by SHAP in SHIP-Trend by Random Forest

- Feature importance based on SHAP value (left: Sleep + Covs; Right: Sleep + Covs + Subcortical)



- Feature interactions showed by SHAP value



Conclusion

- Stroop interference and reaction time scores can be weakly but stably predicted by sleep measurements, brain structure, and demographic data based on non-linear ML models.
- The nonlinear relationship between sleep measurements and cognitive measurements can be revealed by model explanation.
- Model explanation showed:
  - Predicted variance is driven by the interaction between sleep, brain, and demographic data (mainly age).
  - Older subjects with shorter sleep and younger subjects with longer sleep contribute to the prediction.

References: 1. F. Emamian, et al. Front. Aging Neurosci. 8, 78 (2016); 2. R. S. Osorio, et al. Neurology 84.19, 1964-1971, 2015; 3. Y. Li, et al. Nat. Aging. 2.5 (2022); 4. S. D. Kyle, et al. Sleep Med. 38, 85-91 (2017); 5. M. Tahmasian, et al. J. Sleep Res. 30.6, e13347 (2021).

Contact: h.bi@fz-juelich.de; m.tahmasian@fz-juelich.de