

Research questions and working hypothesis

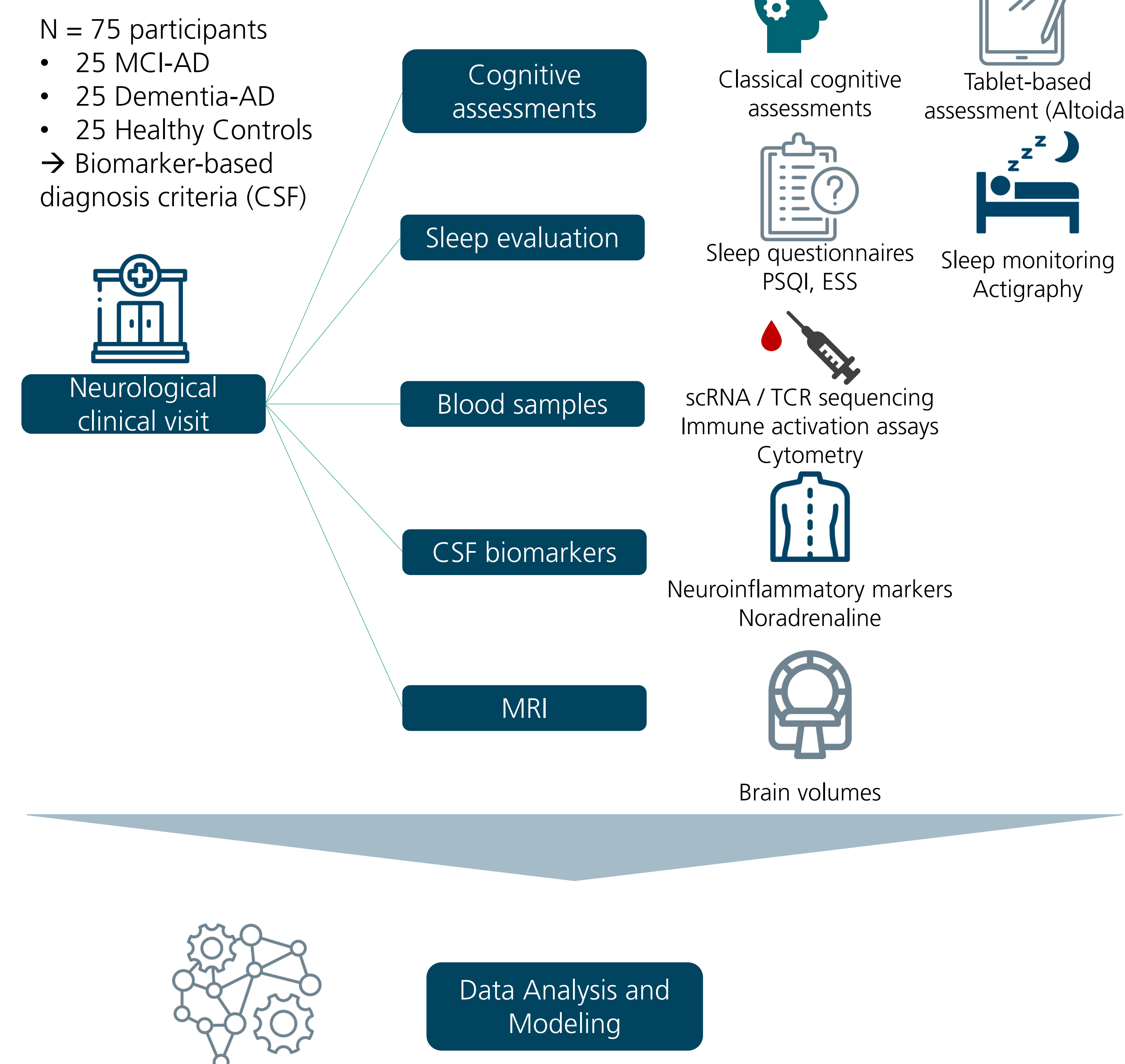
- **Sleep-wake alterations** are common symptoms in Alzheimer's Disease (AD):
 - nighttime awakenings, nocturnal wandering, excessive daytime sleepiness
- Happen early in the disease course and correlate with more rapid decline and caregiver burden
- Early **degeneration of the arousal system** (esp. Locus coeruleus):
 - Leads to dysregulation of the noradrenergic system
 - Depletion of noradrenaline (neurotransmitter with neuroprotective effects) leads to both sleep-wake dysregulation and activation of neuroinflammatory pathways contributing to disease progression
- Sleep disturbances themselves increase **systemic inflammation**, which is a well-known driver of AD pathogenesis
- Understanding the **mechanisms linking cognitive impairment, sleep disturbances and inflammation could facilitate earlier diagnosis of AD**



Aims

- Explore the potential of **digital sleep monitoring** for **early diagnosis**
- Investigate the **correlation** between digitally assessed **sleep perturbances** and **immune biomarkers**
- Explore new **blood-based candidate biomarkers** based on insights of the role of peripheral cytotoxic lymphocytes in AD

Workplan strategy



Machine Learning with actigraphy data from sleep monitoring for prediction of diagnosis

Statistical correlation analysis between CSF neuro-inflammatory biomarkers, sleep and diagnosis

Differential gene expression analysis and pathway overrepresentation analysis of scRNA seq data

Artificial Intelligence (AI) for modeling of conditional statistical dependencies between cognition, sleep disturbances, CSF markers and biological mechanisms

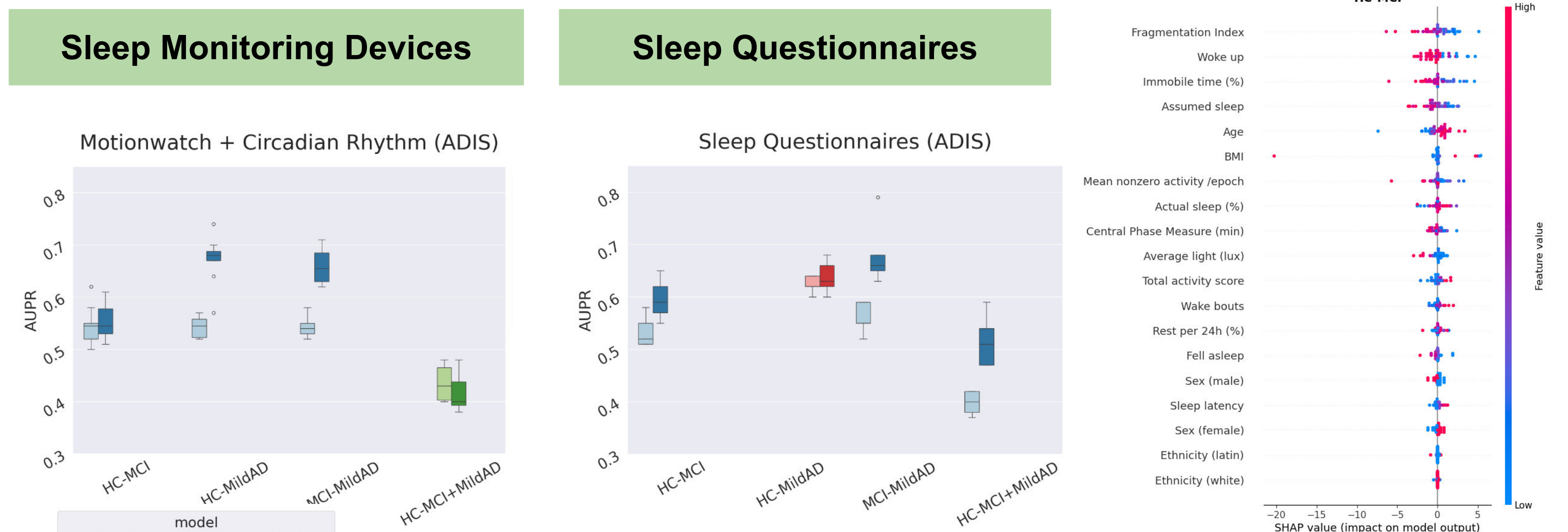
Agent-based modeling of cell-cell interactions between T-cells and Natural Killer cells

Significance and impact

- Limited efficacy and strong adverse effects of currently available treatments for patients at progressed stages of AD.
- Early intervention is of utmost importance to intervene in the progression of the neurodegenerative disease.
- Identification of **minimally invasive** and **cost-effective biomarkers** and development of **algorithms for an early diagnosis** are needed.
- Tools for patient stratification would **accelerate and enhance success** chances of **clinical trials**.

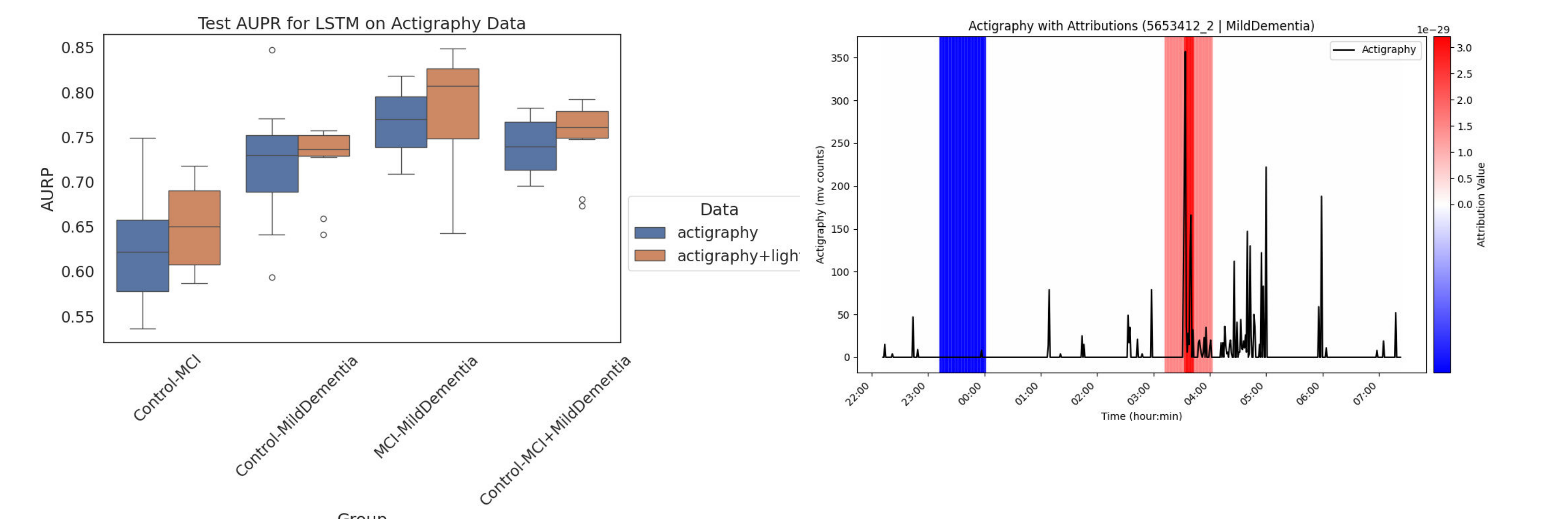
Project outcomes so far

- Sleep monitoring via smart devices performs at least as well as traditional sleep questionnaires in identifying MCI and MildAD patients.



Explainability analysis with SHAP values for classifying MCI patients.

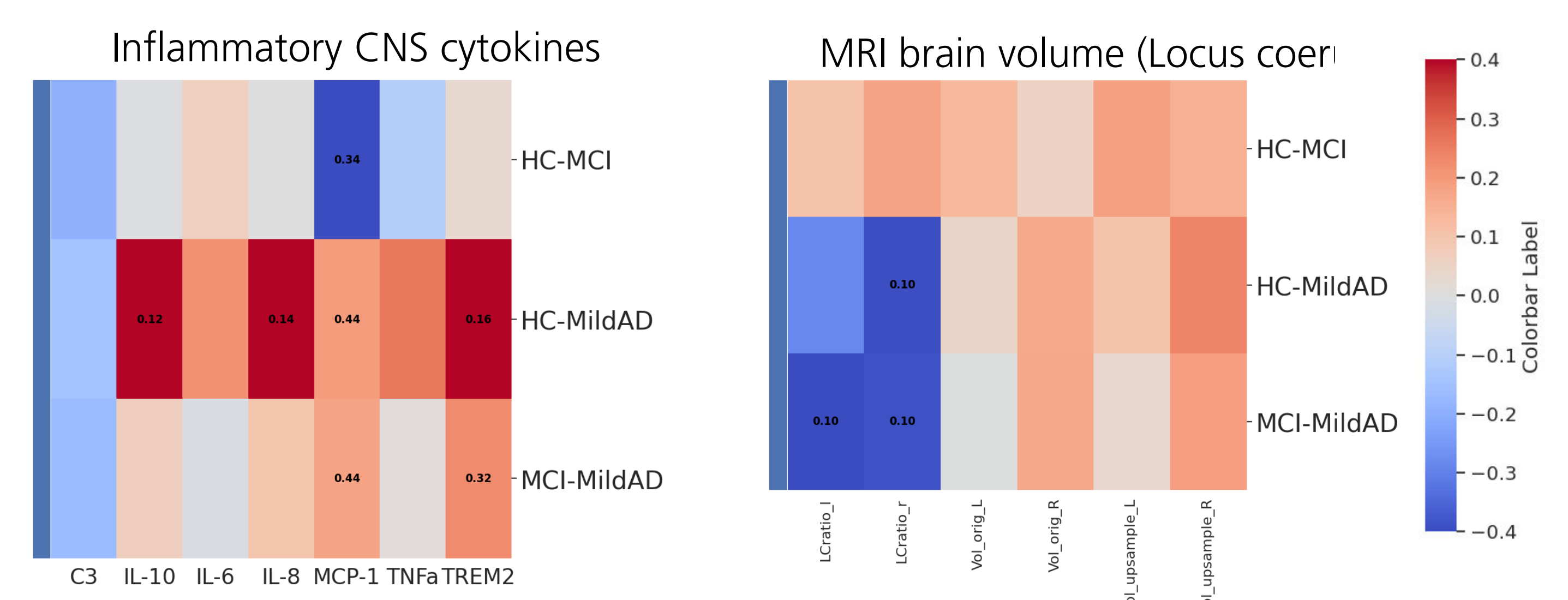
- Longitudinal sleep modeling with raw actigraphy data outperforms traditional sleep questionnaires at identifying AD patients.



LSTM classifier performance with actigraphy (+ambient light) data.

Explainability analysis with Integrated Gradients for a Mild-Dementia participant.

- Link between disruption in sleep patterns (monitoring device Motionwatch 8) and



Next steps and future challenges

- Biotech: single-cell sequencing and T-cell receptor sequencing
- Data Science & Modeling: investigation of scRNA sequencing data of peripheral blood mononuclear cells for biomarker discovery