Specific Aims

Alzheimer's disease (AD) progression reflects complex interactions between neural changes and declining real-world function. This study aims to establish clinically useful biomarkers by integrating neuroimaging and actigraphy data using advanced analytical methods (Zhanga et al., 2023; Wen et al., 2020; Geraci et al., 2024). We propose two complementary aims to address gaps in early detection and prediction of AD progression (Nadeem et al., 2024; Varatharajah et al., 2019).

Aim 1: Investigate relationships between neuroimaging biomarkers and activity patterns in AD progression.

We hypothesize that neural degradation patterns, particularly default mode network (DMN) connectivity loss and hippocampal atrophy, are significantly associated with reduced sleep quality and daytime activity levels measured by actigraphy (Greicius et al., 2004; Ju et al., 2013; Lim et al., 2013). Using existing datasets from ADNI (neuroimaging, n = 300, including cognitively normal, MCI, and AD participants) and NSRR (actigraphy, n = 500, age ≥65), we will conduct cross-sectional regression analyses controlling for age and clinical stage. Primary outcomes will be standardized beta coefficients quantifying the strength of associations between imaging markers (DMN connectivity, hippocampal volume) and actigraphy metrics (sleep efficiency, daytime activity counts) (Müller et al., 2020), We will evaluate results using rigorous statistical thresholds (FDR-corrected $p < 0.05$) and report effect sizes to assess clinical relevance.

Aim 2: Develop and validate a multimodal predictive model for cognitive decline.

We hypothesize that combining neuroimaging and actigraphy data will significantly improve the prediction of MCI-to-AD conversion compared to models using either data type alone (Varatharajah et al., 2019; Nadeem et al., 2024). Focusing on the ADNI-MCI longitudinal cohort (n = 150 with both imaging and actigraphy), we will implement supervised machine learning (including SVMs and neural networks) using carefully selected features from both modalities (Zhanga et al., 2023; Wen et al., 2020). Model performance will be assessed by its ability to predict 2-year cognitive decline, with the primary outcome being the AUC-ROC value. We will employ stratified 5-fold cross-validation and compare against unimodal benchmarks using DeLong’s test for statistical comparison of ROC curves. The final model will be evaluated for both accuracy and potential clinical utility (Geraci et al., 2024).

Meeting Logs

Meeting #1: 10:00 AM – 12:00 PM, April 10
Attendees: Aishwarya Kunam, Durga Prasad Bukka, Arun Kumar Soora, Vaibhav Thakur
Summary: Decided to refine Specific Aims by focusing on existing datasets (ADNI/NSRR) rather than new recruitment. Assigned tasks: Aishwarya to draft Aim 1 (neuroimaging-actigraphy associations), Durga to draft Aim 2 (ML prediction model), Arun to identify relevant ML papers, and Vaibhav to compile evaluation metrics.

Meeting #2: 3:00 PM – 4:30 PM, April 14
Attendees: Aishwarya Kunam, Durga Prasad Bukka, Arun Kumar Soora, Vaibhav Thakur
Summary: Shared drafts of Specific Aims. Revised hypotheses to clarify links between DMN connectivity, hippocampal atrophy, and actigraphy patterns. Finalized methods: cross-sectional regression for Aim 1 and neural networks for Aim 2. Discussed outcome measures (AUC-ROC, effect sizes) and agreed on stratified cross-validation. Aishwarya presented example papers using similar multimodal approaches.

Meeting #3: 11:00 AM – 12:30 PM, April 16
Attendees: Aishwarya Kunam, Durga Prasad Bukka, Arun Kumar Soora, Vaibhav Thakur
Summary: Reviewed feedback on Significance and Innovation sections from Step 2. Discussed the professor's comments regarding the feasibility of cross-cohort data integration. Finalized Specific aims to ensure clarity and compliance with page limits. Streamlined language to one sentence per component (hypothesis/method/outcome/evaluation). Addressed concerns about statistical power by justifying sample sizes from ADNI/NSRR. Durga formatted the section to fit the template. Planned next steps: prepare for submission and begin outlining the Methods section for the full proposal.

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