Dynamic Causal Graph-Based Learning Approach for Predicting Cognitive Impairment in Middle-Aged and Older Adults

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Abstract

The increasing prevalence of dementia and cognitive impairments in the aging global population poses significant challenges to healthcare and society. Detecting cognitive impairment is crucial for managing diseases like Alzheimer's, yet current research faces limitations such as reliance on cross-sectional studies and a lack of understanding of causal relationships. In response, our study introduces a dynamic causal graph-based learning approach for predicting cognitive impairment risk in middle-aged and older adults. Employing a longitudinal perspective, we uncover causal structures through causal discovery methods, offering profound insights into cognitive changes over time. Our model, utilizing dynamic input variables, outperforms traditional algorithms while enhancing interpretability. This innovative approach not only improves prediction accuracy but also contributes to a deeper comprehension of the causal mechanisms underlying cognitive impairment. The longitudinal insight offers a comprehensive understanding of evolving factors associated with cognitive changes, making our model valuable for both research and practical applications.

Keywords: Artificial Intelligence; Causal Reasoning; Cognition of Time; Cognitive Architectures; Dynamic Systems Modeling

Introduction

The escalating prevalence of dementia and its associated cognitive impairments in our aging global population presents formidable healthcare and socioeconomic challenges(Organization et al., 2012; Walsh et al., 2024). Cognitive impairment, an intermediate stage between normal aging and dementia, represents a decline in cognitive functions that is noticeable but does not severely impair daily activities(American Psychiatric Association, Association, et al., 2013). Often, individuals remain unaware of neurodegeneration until cognitive impairment progresses to a point where it results in disability and dependency(Petersen, 2011). Dementia significantly affects the elderly population, as seen in China, where over 360,000 new diagnoses of cognitive impairment are reported annually. Projections suggest that by 2060, China will have approximately 48.68 million individuals with cognitive impairment(Prince et al., 2016). Therefore, early detection of cognitive impairment is crucial in slowing the progression of diseases like Alzheimer's.

However, the existing researches expose certain constraints. The majority of studies rely on cross-sectional research, which lack a longitudinal perspective capable of offering profound insights into cognitive changes over an ex-

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tended period. Moreover, the current state of knowledge regarding causal relationships in the progression of cognitive impairment is limited. While statistical knowledge suffices for prediction and diagnosis, a comprehensive understanding of causation is indispensable for guiding effective actions and interventions (Danks & Davis, 2023).

In response to these challenges, our study introduces a novel dynamic causal graph based learning approach that integrates causal discovery to predict the risk of developing cognitive impairment in middle-aged and older adults. We capture the interactions among variables and reveal dynamic causal structures by generating causal graphs. Leveraging the insights gained from the causal discovery phase, our model significantly reduces the number of input variables, outperforming mainstream algorithms that rely on all variable inputs. By incorporating a temporal dimension, this approach not only aids in elucidating the mechanisms underlying cognitive impairment but also provides interpretable outcomes for the model. The structure of the model is shown in Figure 1. The contributions of this work can be summarized as follows:

- **Dynamic causal graph generation.** We construct a module to get dynamic subset of features that captures the most resilient relationships influencing Cognitive Impairment.
- **Enhancing model performance with interpretability.** We present a novel prediction model DGCog that integrates dynamic causal graph, leading to a reduction in input variables and superior performance compared to traditional algorithms. Simultaneously, this approach enhances our comprehension of causal relationships in the progression of cognitive impairment.
- **Offering longitudinal Insight.** Longitudinal data analysis offers a more profound understanding of the evolving factors associated with cognitive impairment.

Materials and Methods

Participants and Data Sources

Our study is a longitudinal investigation based on data obtained from the China Health and Retirement Longitudinal Study (CHARLS)(Zhao, Hu, Smith, Strauss, & Yang, 2014). CHARLS is a high-quality, publicly available longitudinal survey representative of individuals aged 45 and older and their spouses across China. CHARLS conducts face-to-face computer-assisted personal interviews (CAPI) with respondents every 2 years. Physical measurements are taken during each 2-year follow-up, with blood samples collected once every two follow-up periods. Utilizing a multi-stage probability sampling method, the CHARLS team surveyed residents across 28 provinces in China. The baseline survey took place in 2011, followed by subsequent rounds in 2013, 2015, 2018, and 2020. After excluding participants lost to follow-up and those with missing data, a cohort of 3,660 individuals (1,877 males, 1,783 females, average age 62) was selected for our longitudinal investigation. The study protocol of CHARLS received approval from the Peking University Biomedical Ethics Committee(`https://opendata.pku.edu.cn/dataverse/CHARLS`).

Cognitive Impairment Labeling

In this study, we employ a range of variables based on previous research for cognitive classification. These variables include demographics, family structure and dynamics, health status and functioning, past and present general health, physician-diagnosed chronic illnesses, lifestyle and behaviors, and emotional status, among others.

As illustrated in Figure 1 'Label Setting', this study evaluates cognitive function using a global cognitive score composed of 2 main components: Episodic Memory (EM) and Mental Intactness (MI) (McArdle, Fisher, & Kadlec, 2007). EM was assessed through recall and delayed recall tests of memory using 10 words, wherein participants were asked to recall 10 Chinese words immediately and after a 5-minute delay. MI was evaluated based on information from the Telephone Interview of Cognition Status form, which included self-rated memory, awareness of today's date, day of the week, and current season, along with tests of serial subtractions of 7 from 100 and the ability to reproduce a picture of two overlapped pentagons. In the analysis, a global cognitive score was computed by combining scores from EM and MI tests. A higher score generally indicates better cognitive function among middle-aged and elderly individuals. Raw scores were transformed into z-scores based on the baseline mean and standard deviation of each respondent in the cohort. Cognitive impairment at baseline was defined as a global cognitive score in the bottom 10 percent of the distribution, using established methodologies (Chen, Ho, & Chau, 2023).

Dynamic Causal Graph based Learning

To enhance the applicability of deep learning algorithms, we preprocess the data into temporally structured sequences. The missing values are imputed using the prior round value. In predicting cognitive impairment, it's crucial to go beyond investigating causes and equally important to explore effects. These features provide essential signals for cognitive decline development.

Causality learning. In the field of causal discovery, constraint-based and score-based methods work well in theory but fall short in real-world scenarios when inferring causal graphs(Ng, Zhu, Chen, & Fang, 2019). Recent research has explored the integration of graph neural networks, aiming to capture the intricacies of nonlinear causal relationships and improve practical performance(Deng, Zheng, Tian, & Zeng, 2022; Zanga, Ozkirimli, & Stella, 2022). The gradient-based method demonstrates enhanced accuracy and computational efficiency in practical scenarios, proving adept at navigating the complexities inherent in causal relationships. Therefore, we apply Graph Autoencoder (GAE)(Ng et al., 2019) and Causal Generative Neural Net-

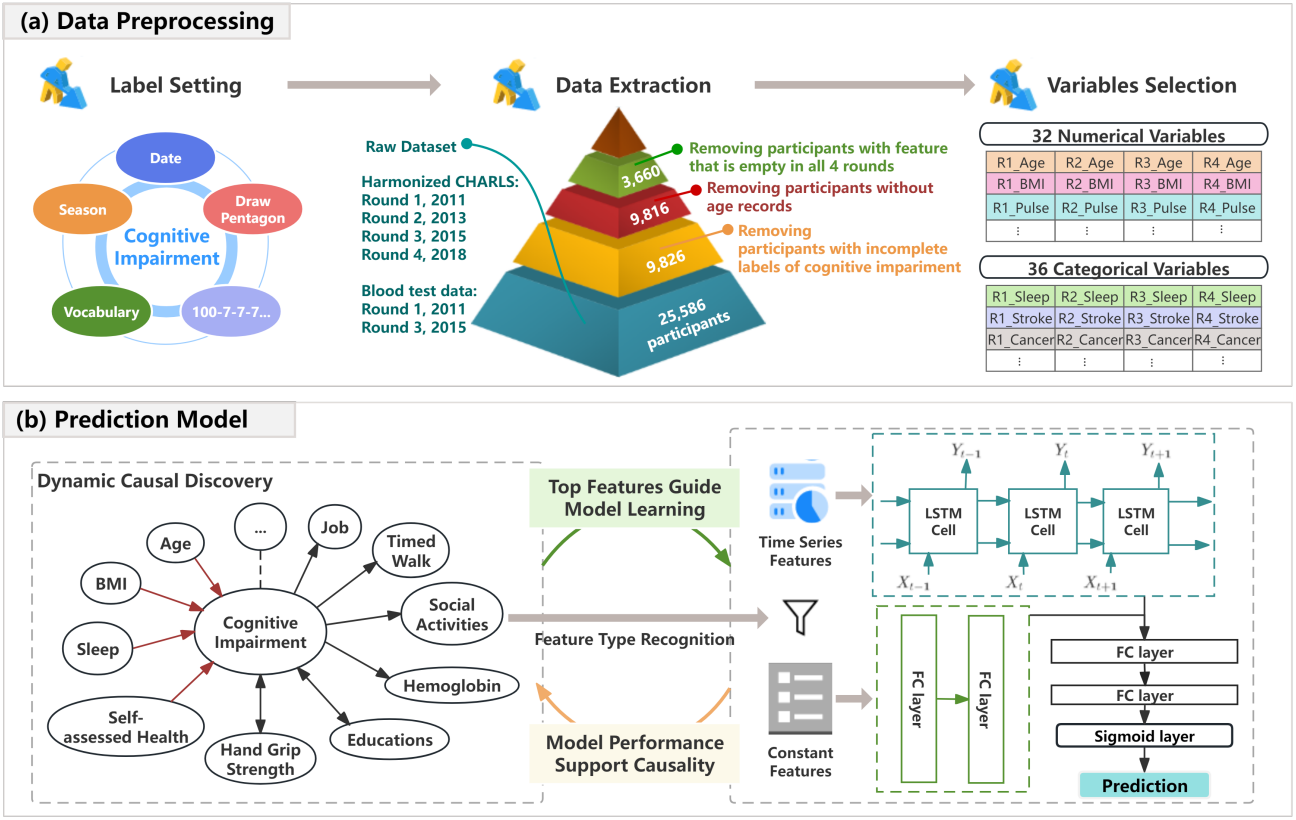

Figure 1: Cognitive impairment prediction framework in CHARLS. **(a)** shows how to process data, variables and label. **(b)** shows the structure of our prediction model.

works (CGNN)(Goudet et al., 2018) methods to generate causal structure. GAE is applied to capture latent representations of variables and their relationships within a causal graph, aiding in the identification of causal structures. CGNN integrates causal modeling principles with graph neural networks, providing a nuanced understanding of complex systems compared to conventional causal discovery methods.

To enhance the interpretability and efficiency of our model in the face of complex survey data, we adopt a focused strategy targeting robust causal edges associated with Cognitive Impairment. Utilizing Directed Acyclic Graphs (DAGs) derived from both GAE and CGNN, we conduct an analysis of edge frequency and weight. This involves calculating the occurrence rate of each edge with Cognitive Impairment and considering edge weights. The edges are subsequently ranked based on a composite measure of frequency and weight, denoted as the Causal Probability ($CP = \langle x, Y \rangle$), where CP represents the probability of causal relationship between a feature x in the feature set X and the label Y (cognitive impairment). Let x_i be a feature in X, $p(x_i \to Y)$ and $p(x_i \leftarrow Y)$ denote the probabilities of x_i causing or being caused by Y, respectively. The Causal Probability is then defined as:

$$CP(x_i, Y) = \langle x_i, Y \rangle = p(x_i \to Y) \cdot p(x_i \leftarrow Y) \quad (1)$$

By selecting the top n edges based on the ranking of CP, we curate a subset of features that encapsulates the most robust relationships contributing to Cognitive Impairment. This refined set of features, denoted as X_{top}, is then employed in training our model, streamlining the input space and focusing on key variables. This selection process ensures that the model prioritizes the most influential features in contributing to the prediction of Cognitive Impairment. X_{top} is defined as:

$$X_{Top} = \{x_i \,|\, \langle x_i, Y \rangle \in Top_n\} \quad (2)$$

With the accumulation of survey data, we adopt a dynamic approach to model the evolving causal relationships. Specifically, let $G^{(N)}$ denote the causal graph obtained at Round N, where N is the round index. The cumulative causal graph at Round $N+1$ ($G^{(N+1)}$) is determined by the union of the causal graph from the previous round ($G^{(N)}$) and the DAG learned from the most recent round ($G_{new}^{(N+1)}$):

$$G^{(N+1)} = G^{(N)} \cup G_{new}^{(N+1)} \quad (3)$$

The newly acquired causal knowledge from each round continuously incorporates into the evolving causal graph. The union operation ensures that the causal graph dynamically adapts and expands with the accumulation of survey data

over successive rounds, capturing the changing landscape of causal relationships.

Prediction model. The proposed model DGCog is designed to predict Cognitive Impairment with neural network. The architecture of our model is designed to accommodate inputs comprising both historical round data and discovered CP score. The model incorporates an LSTM (Long Short-Term Memory) layer designed to capture sequential dependencies within the historical round data. On the other hand, certain features, such as 'Gender', remain constant throughout the historical rounds. To effectively handle these fixed features, they are fed into an MLP. The outputs from both the LSTM and the MLP are concatenated, forming a comprehensive feature vector. This combined representation is then passed through a final fully connected layer, followed by a sigmoid activation function to facilitate binary classification.

The predicted probability P is calculated as the output of the neural network f_ϕ, where $P = f_\phi(Input)$. The network parameters ϕ are updated during the training phase by minimizing the Binary Cross-Entropy (BCE) Loss function L_{pred}. The BCE Loss function is defined as:

$$L_{pred}(P,Y) = -\frac{1}{N}\sum_{i=1}^{N}[Y_i \cdot \log(P_i) + (1-Y_i)\cdot \log(1-P_i)] \quad (4)$$

Here, P_i represents the predicted probability for the i-th sample, Y_i is the corresponding true label (binary), and N is the total number of samples. This loss function quantifies the discrepancy between the predicted probability distribution and the actual labels, guiding the iterative parameter updates during training to improve the model's ability to accurately predict the probability of Cognitive Impairment based on the selected features from the curated subset X_{top}.

Results

In this study, we evaluate the performance of models: Logistic Regression (LR), Random Forest (RF), eXtreme Gradient Boosting (XGBoost), an Ensemble model and DGCog across 4 rounds of data. For ensemble learning approach, we utilize stacking framework with XGBoost and RF as base models, and LR serves as the meta-model. The hyperparameters for baseline models are optimized using the GridSearchCV technique. Data instances are divided into 3 sets based on unique IDs, maintaining a ratio of 6:1:3 for training, validation, and testing.

Our network is implemented using PyTorch and CUDA, and trained on an NVIDIA Titan XP GPU. The metrics include: Area Under the Receiver Operating Characteristic Curve (AUROC), Area Under the Precision-Recall Curve (AUPRC), Accuracy, Precision, F1-Score and Recall.

Persistent Indicators in Prediction Model

Our DGCog has exhibited increasing effectiveness through successive causal iterations, as highlighted by the recurrent identification of specific features across four rounds of data collection. These variables encompass a broad range of categories including demographic data (Age, Gender, Educational Level, Job), health status (Self-assessed Health, IADL, Heart Disease), lifestyle activities (Smoking, Sleep, Social Activities), blood tests (Creatinine, Hemoglobin, Fasting Blood Glucose, Uric Acid, Blood Weight), and physical examinations (Waist Circumference, Diastolic Pressure, Hand Grip Strength, BMI, Weight). Significantly, these elements are not mere transient correlates; they are pivotal indicators of cognitive health trajectories. As depicted in Figure 2, their enduring association with cognitive outcomes underscores their potential as robust markers for monitoring and predicting cognitive impairment.

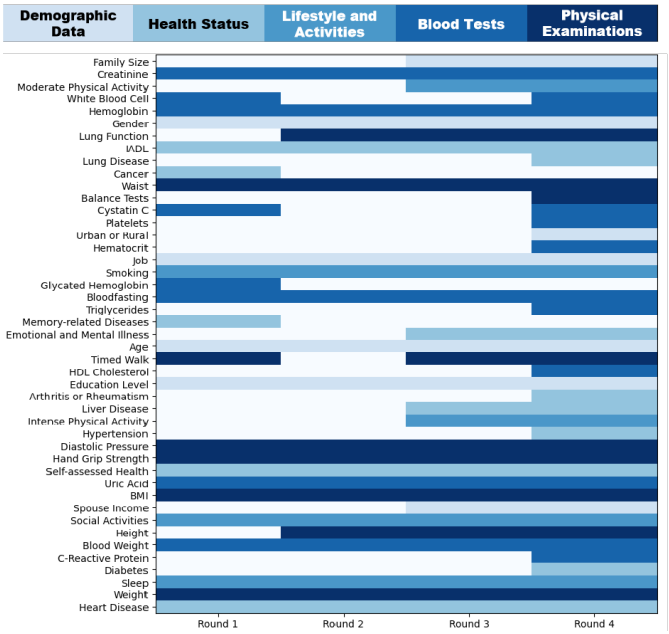

Figure 2: River plot for 4 rounds of variables. Different colors represent the categories to which the variables belong. The presence of this color indicates that the variable is a predictor variable in this round.

Performance in Predicting Cognitive Impairment

Model performance on different feature sets: We assess the performance of 2 feature sets: models leveraging dynamic top causality features (TopF) and models incorporating all available features (AllF). In Round 1, TopF's AUROC ranges from 0.7422 to 0.7687, AUPRC from 0.1901 to 0.2232, while AllF achieves higher AUROC (0.8316 to 0.839) and AUPRC (0.299 to 0.3412). From Round 2 onwards, TopF consistently outperforms AllF. Notably, in Round 2, TopF's AUROC ranges from 0.8266 to 0.845, surpassing AllF's AUROC (0.8163 to 0.8367). This trend persists in subsequent rounds 3 and 4, underlining the efficacy of prioritizing top causality features for enhanced model performance.

Table 1: Performance evaluation for Round 4 on full feature set and dynamic top causality feature set is presented, showcasing mean values for each metric, with corresponding 95% confidence intervals (CI) in parentheses. The best value of each metric is highlighted in bold.

All features						
	ROC_AUC	**PRC_AUC**	**Accuracy**	**Precision**	**Recall**	**F1**
LR	**0.8538 (0.8529-0.8548)**	**0.6466 (0.6432-0.6501)**	0.8142 (0.8106-0.8179)	0.6247 (0.615-0.6343)	0.5395 (0.5308-0.5482)	0.5792 (0.5714-0.587)
RF	0.8412 (0.8377-0.8448)	0.6064 (0.5914-0.6213)	**0.8201 (0.8124-0.8279)**	0.6364 (0.6187-0.654)	**0.5577 (0.5308-0.5846)**	**0.5959 (0.5753-0.6165)**
XGBoost	0.8472 (0.8422-0.8523)	0.6186 (0.6025-0.6348)	0.8137 (0.8051-0.8224)	0.6315 (0.6084-0.6546)	0.5115 (0.4826-0.5405)	0.564 (0.5395-0.5885)
Ensemble	0.8477 (0.8445-0.851)	0.6189 (0.6061-0.6317)	0.8199 (0.8128-0.827)	**0.6467 (0.6291-0.6644)**	0.5288 (0.5077-0.55)	0.5811 (0.5629-0.5994)
Dynamic Features						
	ROC_AUC	**PRC_AUC**	**Accuracy**	**Precision**	**Recall**	**F1**
LR	0.858 (0.8571-0.8589)	0.6337 (0.6311-0.6363)	0.8163 (0.8133-0.8192)	0.6341 (0.6256-0.6427)	0.5308 (0.5231-0.5385)	0.578 (0.5711-0.5849)
RF	0.8373 (0.8335-0.8412)	0.5975 (0.5864-0.6085)	0.8185 (0.8119-0.8252)	0.6318 (0.6141-0.6496)	0.5625 (0.5403-0.5846)	0.5939 (0.5778-0.6099)
XGBoost	0.8497 (0.8442-0.8552)	0.6091 (0.5947-0.6236)	0.8206 (0.8119-0.8293)	0.6495 (0.6268-0.6723)	0.5317 (0.5057-0.5577)	0.5858 (0.5626-0.6091)
Ensemble	0.8483 (0.8449-0.8517)	0.6145 (0.6047-0.6243)	0.8237 (0.8155-0.832)	**0.6506 (0.6299-0.6713)**	0.5518 (0.5267-0.5769)	0.5975 (0.5765-0.6184)
DGCog	**0.8787(0.8786 - 0.8787)**	**0.7215(0.7213 - 0.7218)**	**0.8252(0.8252 - 0.8252)**	0.6107(0.6104 - 0.6109)	**0.8530(0.7060 - 1.0000)**	**0.6563(0.6538 - 0.6588)**

Figure 3: Evaluating model performance across diverse cognitive impairment sub-groups, including gender, accommodation, childhood health, and education status. AUROC values of all models and the AUPRC of DGCog within these sub-groups are shown. Childhood health comprises five categories: 'CH-MH' (Much healthier), 'CH-SH' (Somewhat healthier), 'CH-AVE' (About average), 'CH-SLH' (Somewhat less healthy), and 'CH-MLH' (Much less healthy). The education category also encompasses five groups: 'NPR' (Did Not Finish Primary School but can Read), 'ES' (Elementary School), 'MS' (Middle School), and 'LSE' (Less than lower secondary education).

Performance of DGCog across rounds: We conduct multi-round experiments on our model, observing a notable progression in performance. In Round 1, our model does not surpass the baseline, attributed to its early stage and limited data availability, resulting in an AUROC of 0.7555 (95%CI: 0.7554 to 0.7556) and AUPRC of 0.2035 (95%CI: 0.2034 to 0.2036). However, as subsequent rounds unfold and the dataset accumulates, our model's efficacy becomes increasingly evident. In Round 2, it achieves an AUROC of 0.8595 (95%CI: 0.8594 to 0.8596) and AUPRC of 0.4067 (95%CI: 0.4066 to 0.4067). This trend continues with further improvement in Round 3, reaching an AUROC of 0.9022 (95%CI: 0.9021 to 0.9023) and AUPRC of 0.5643 (95%CI: 0.5641 to 0.5646). In Round 4, our model consistently outperforms all baseline models, attaining an AUROC of 0.8787 (95%CI: 0.8786 to 0.8787) and AUPRC of 0.7215 (95%CI: 0.7213 to 0.7218). The detailed Round 4 results are presented in Table 1, highlighting the significance of temporal data accumulation and dynamic causal graph in showcasing the enhanced performance and effectiveness of our proposed model.

Comparing our results with those of recent studies provides valuable insights. (Liu, Zhang, Liu, & Chong, 2023) explored the predictive value of machine learning in cognitive impairment and found that RF showed high accuracy for various outcomes at different time points (Year 2, Year 4, and cross-sectional Year 4) with AUCs of 0.81, 0.79, and 0.80, respectively. (Pu et al., 2023) utilized the least absolute shrinkage and selection operator (LASSO) technique to select important predictors and evaluated the discriminative power of the model, achieving an AUC of 0.727. Our model's superior performance shows its potential to provide accurate predictions of cognitive impairment, especially as it continues to evolve with further data accumulation and refinement.

Cognitive Impairment Subgroup

To investigate the models' capacity in discerning subtle variations within cognitive impairments, we conducted sub-group analyses. Our evaluation systematically covers sub-groups differentiated by gender, accommodation, childhood health status, and education status, as detailed in Figure 3. We

present the AUROC scores of all models across these 4 subgroups, with distinct colors representing the models' performance at various stages within each subgroup. Additionally, we illustrate the AUPRC scores of our model across different subgroups, providing detailed insights into the predictive performance within each population subset. Notably, individuals classified as illiterate and those with less than lower secondary education demonstrate better predictive performance. Similarly, individuals whose childhood health status is categorized as "Somewhat healthier" and "About average" also exhibit good predictive performance. These findings shed light on the models' ability to capture subtle distinctions within specific demographic and health-related subgroups.

Discussion

In our study, we focused on improving the prediction of cognitive impairment through a deep learning model that iteratively enhanced its effectiveness over 4 data collection rounds. We identified key persistent indicators spanning demographic, health, lifestyle, and physical examination categories. Our model leverages dynamic top causality features, leading to superior performance from Round 2 onwards, as evidenced by higher AUROC and AUPRC scores compared to models using all features. Notably, the model's predictive accuracy improved with each round, achieving its best performance in Round 4. Additionally, subgroup analyses revealed nuanced predictive capabilities across different demographics, with the model showing better performance for individuals with lower education levels or average childhood health. This progression underscores the significance of our approach in enhancing the prediction and subsequent intervention of cognitive impairment, by dynamically adjusting to influential factors and capturing subtleties in various population subsets. While longitudinal data allow us to observe changes over time and improve our model iteratively, it may not always be feasible to collect such data. However, our dynamic model can also be applied to cross-sectional data, widening its applicability.

Early detection of risk factors for cognitive impairment is a fundamental strategy to prevent or minimize cognitive decline, which in turn supports preventive intervention efforts. The causality revealed in our study is substantiated by the consistent identification of factors widely documented in scientific literature as crucial for cognitive health. This reinforces the robustness and validity of the identified causal relationships. For instance, obesity, as denoted by Body Mass Index (BMI) and waist circumference, has been associated with neuroinflammation and cerebral atrophy, both of which play significant roles in the onset of cognitive decline (Ren et al., 2021). Moreover, hand grip strength serves as an indicator of overall muscular health, which, in turn, is connected to cerebral wellness via vascular and metabolic mechanisms (Fritz, McCarthy, & Adamo, 2017). The process of aging is intrinsically linked to cognitive degeneration, attributed to the cumulative impact of cellular and molecular alterations over time.

The model's interpretative capacity is particularly laudable, elucidating both direct and indirect pathways by which various factors—such as sleep patterns (Keil et al., 2023), educational attainment (Sattler, Toro, Schönknecht, & Schröder, 2012), and vascular health markers like diastolic pressure (Ou et al., 2020) and Creatinine(Wang & Lu, 2023)—influence cognitive functionality. This comprehensive analysis underscores the complex interrelation between biological markers, lifestyle factors, and socio-demographic variables in determining cognitive trajectories, thereby underscoring the need for interventions that are specifically tailored to these identified determinants.

Limitations. While the longitudinal nature of our data confers a robust temporal dimension to our findings, the model's predictive accuracy is contingent on the quality and completeness of the data inputs. Additionally, the generalizability of our results may be constrained by sample characteristics and the variability of individual responses to the identified risk factors. Hence, our conclusions necessitate validation in larger, more diverse cohorts to solidify their applicability across populations. The study is based on data from CHARLS, which may limit its generalizability to other populations. Future research could explore the application of the model to diverse datasets to enhance the generalizability of our findings.

Broader Impacts. By integrating dynamic causal graph, our research advances the interdisciplinary field of computational psychiatry, fostering a more profound understanding of cognitive impairment's underpinnings. Beyond this, our methodology has potential for application in various subfields of cognitive science. For instance, in clinical psychology, our methodology can aid in the development of personalized interventions for individuals at risk of cognitive decline. By identifying modifiable risk factors(such as physical activity and sleep quality), clinicians can tailor interventions targeting specific lifestyle changes to improve cognitive health outcomes. This research thus not only advances scientific understanding but also has the potential to inform policies and practices that could mitigate the global challenge posed by cognitive impairment and dementia.

Disciplinary Diversity & Integration. By harnessing dynamic causal computing methods, we have transcended traditional cross-sectional studies to capture the longitudinal interplay between diverse factors and cognitive impairment. This advanced application unites domains such as neurobiology, gerontology, and epidemiology, paving the way for holistic models that reflect the intricate reality of human health and disease progression.

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