



Research article

AI-based tool for early detection of Alzheimer's disease

Shafiq Ul Rehman^{a,*}, Noha Tarek^{b,1}, Caroline Magdy^{b,1}, Mohammed Kamel^{b,1},
Mohammed Abdelhalim^{b,1}, Alaa Melek^b, Lamees N. Mahmoud^c, Ibrahim Sadek^c^a College of Information Technology, Kingdom University, Bahrain^b Systems and Biomedical Engineering, Faculty of Engineering, Cairo University, Cairo, Egypt^c Biomedical Engineering Dept, Faculty of Engineering, Helwan University, Helwan, Cairo, Egypt

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ABSTRACT

In the context of Alzheimer's disease (AD), timely identification is paramount for effective management, acknowledging its chronic and irreversible nature, where medications can only impede its progression. Our study introduces a holistic solution, leveraging the hippocampus and the VGG16 model with transfer learning for early AD detection. The hippocampus, a pivotal early affected region linked to memory, plays a central role in classifying patients into three categories: cognitively normal (CN), representing individuals without cognitive impairment; mild cognitive impairment (MCI), indicative of a subtle decline in cognitive abilities; and AD, denoting Alzheimer's disease. Employing the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset, our model undergoes training enriched by advanced image preprocessing techniques, achieving outstanding accuracy (testing 98.17 %, validation 97.52 %, training 99.62 %). The strategic use of transfer learning fortifies our competitive edge, incorporating the hippocampus approach and, notably, a progressive data augmentation technique. This innovative augmentation strategy gradually introduces augmentation factors during training, significantly elevating accuracy and enhancing the model's generalization ability. The study emphasizes practical application with a user-friendly website, empowering radiologists to predict class probabilities, track disease progression, and visualize patient images in both 2D and 3D formats, contributing significantly to the advancement of early AD detection.

1. Introduction

Alzheimer's disease (AD) is a chronic, irreversible brain disorder with no effective cure. Early detection is essential in preventing and controlling the progression of the disease, even though there are medications that can delay its progression. AD is the most common form of dementia, encompassing a range of symptoms that severely impact memory, thinking, and social abilities, greatly affecting both patients and their relatives [1]. The disease initially targets the hippocampus, the brain region responsible for memory and learning, before spreading to other outer layers of the brain [2,3]. In its early stages, individuals may struggle remembering recent situations, such as appointments or conversations. In contrast, in later stages, crucial information like one's name and family becomes increasingly difficult to recall [4]. With a staggering 55 million cases of dementia worldwide, Alzheimer's accounts for 60–70 % of those cases, causing a significant global impact. Individuals may experience Mild Cognitive Impairment (MCI) before developing AD.

* Corresponding author.

E-mail address: s.rehman@ku.edu.bh (S. Ul Rehman).¹ These authors are equally contributed.

MCI is characterized by minor cognitive problems such as memory or thinking difficulties (Fig. 1). While not all individuals with MCI develop AD, it is important to note that it is still considered a potential precursor to the disease. Thus, early identification and monitoring are critical to providing interventions that can slow its progression. It is not just the affected patients; their families and caregivers also face significant challenges in providing assistance and care as the illness advances [5].

2. Related work

This literature review explores diverse approaches to classifying Alzheimer's disease, encompassing various viewpoints and methodologies.

Sarraf and Tofighi [6] proposed a novel approach using Convolutional Neural Networks (CNN) to classify Alzheimer's disease structural MRI data. The authors achieved an accuracy of 98.84 % in predicting Alzheimer's disease from normal control brains using two CNN architectures: LeNet and GoogleNet. This study highlighted the significance of deep learning architectures in medical diagnostic imaging, particularly for brain disorders, offering promising opportunities for future research and clinical applications.

Korolev et al. [7] introduced deep 3D CNN architectures for brain MRI classification. The small training dataset limitations were addressed through advanced deep learning techniques, and an accuracy of 80 % was achieved for Alzheimer's disease versus normal control classification. The study's major advantages included its simplicity and elimination of feature generation requirements, enabling real-time MRI prediction without complex preprocessing.

Janghel and Rathore [8] suggested a deep learning-based approach for AD detection, employing the ADNI database with fMRI and PET images. The authors applied 3D to 2D conversion and image resizing before using the VGG-16 CNN architecture. The study achieved an average accuracy of 99.95 % for fMRI and 73.46 % for PET dataset classification, outperforming existing methods and improving CNN model performance.

Mukhtar and Farhan [9] proposed a CNN-based deep learning approach for predicting the conversion from MCI to AD using various features, including MRI, genetics, and neuropsychological assessment scores. The CNN model achieved an accuracy of 94 % for predicting MCI to AD conversion. The proposed technique showed promise for assisting medical practitioners in the timely and accurate prognosis of AD, providing opportunities for early detection and intervention.

Raju et al. [10] proposed a multi-class classification approach for AD using 3DCNN features and a Multilayer Perceptron classifier, achieving an accuracy of 96.66 %. The authors implemented a patch-based method, 3D-CNN for feature extraction, and a multilayer neural network for classification. The generated heat map helped identify atrophic brain regions contributing to AD, MCI, and NC prediction, aiding physicians in distinguishing Alzheimer's-related dementia from aging-related issues. However, the authors acknowledged the potential for further improvement by including multimodal images such as PET, fMRI, and cerebral spinal fluid to enhance the algorithm's diagnostic capabilities.

Almubark et al. [11] developed a Multilayer Perceptron (MLP) neural network to classify AD, MCI, and CN subjects based on neuropsychological test data from the ADNI database, achieving an average accuracy of 86.26 % for the multi-class classification. The results demonstrated the potential of using MLP neural networks with neuropsychological test data for early AD detection, providing a reliable and cost-effective method suitable for large-scale cognitive screening. Future work will focus on identifying individuals with MCI who are more likely to develop AD within a defined period and exploring other artificial neural networks for AD diagnosis and prediction, including the combination of brain imaging and behavioral data with machine learning and deep learning techniques for insights into the progression of AD stages [11].

Table 1 summarizes the works mentioned above, outlining the image modalities, the classifiers employed, the classification groups considered, and the corresponding accuracy achieved in each study.

Compared to the cited studies, our research introduces a unique approach to early Alzheimer's disease (AD) detection by leveraging the synergistic power of the hippocampus and the VGG16 model with transfer learning. While Sarraf and Tofighi [6] and Janghel and Rathore [8] utilized Convolutional Neural Networks (CNNs) for AD classification, our study distinguishes itself by integrating the hippocampus approach, a region crucially impacted in the early stages of AD, enhancing the interpretability of our model's predictions. Additionally, unlike Mukhtar and Farhan [9], who focused on predicting the conversion from Mild Cognitive Impairment

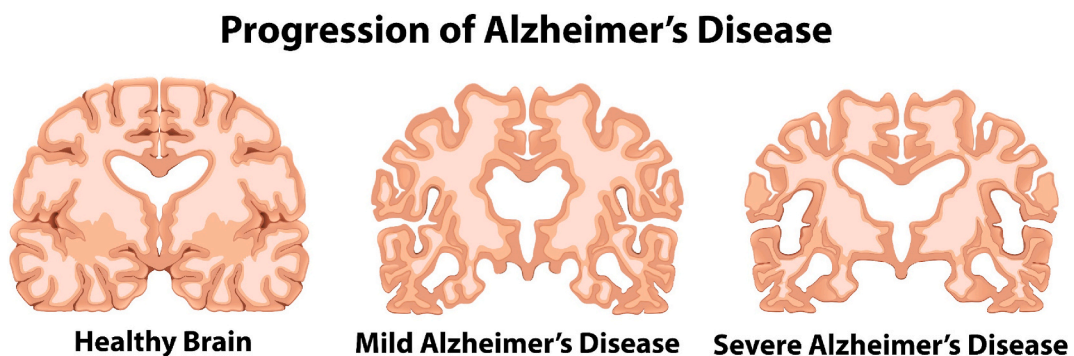


Fig. 1. Diagram illustrating AD progression, including the healthy brain, mild AD, and severe AD.

Table 1
Summary of different methods used to detect AD, including the classifiers used and their overall accuracy.

Approach	Image Modality	Classifier	Classification Group	Accuracy
[6]	MRI & fMRI	CNN (LeNet-5 and GoogleNet)	CN vs. AD	98.84 %
[7]	MRI	3D CNN (ResNet and VGGNet)	CN vs. AD	80 %
[8]	fMRI & PET	SVM, Linear Discriminate, K-means clustering and Decision tree	CN vs. AD	For fMRI Dataset: 99.95 % For PET Dataset: 73.46 %
[9]	MRI	CNN	MCIc vs. MCInc	94 %
[10]	MRI	3D-CNN	MCI vs. CN vs. AD	96.66 %
[11]	MRI	MLP	MCI vs. CN vs. AD	84.28 %

(MCI) to AD using diverse features, our model contributes by providing accurate classification into three distinct classes: cognitively normal (CN), MCI, and AD. Furthermore, in contrast to the patch-based method implemented by Raju et al. [10], our study employs advanced image preprocessing techniques, ensuring a streamlined and efficient process for early AD detection. The proposed solution stands out by achieving high accuracy rates and incorporating a user-friendly website for practical clinical applications, distinguishing it as a comprehensive and impactful contribution to the field.

3. Methodology

Our primary objective was to develop a method for early AD detection, considering the absence of a cure. Extensive research has shown that AD affects the hippocampus in its early stages [2,3]. As a result of our understanding, we intentionally trained our model using MRI images by selecting brain image slices that specifically include the hippocampus. This involved the deliberate selection of MRI slices from each case or subject, where we identified the start and end indices of the hippocampus region, encompassing all slices in between for our analysis. The number of slices per case varied based on hippocampal size, and each case ensured that all its slices were allocated to the same data split (train, validation, or test), with shuffling for optimal model training. We employed the VGG-16 model and transfer learning to take advantage of its pre-training on ImageNet. To enhance the model's performance, we fixed the first three layers as they had already learned the fundamental features and focused on fine-tuning the remaining layers using our dataset. A fully automated website allows radiologists to upload DICOM or Nifti images easily. The model will then provide predictions for the stage of the disease and offer 2D and 3D visualizations for a thorough analysis.

3.1. Dataset acquisition

For our study, we utilized the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset [12,13], a longitudinal multicenter study aimed at developing biomarkers for the early detection and tracking of Alzheimer's disease (AD). ADNI, established over a decade ago, has significantly advanced AD research by facilitating data sharing among researchers worldwide. We specifically selected 339 AD cases, 452 CN (cognitively normal) cases, and 807 MCI (mild cognitive impairment) cases from the ADNI dataset. The AD group had a mean age of 76, ranging from 57 to 90, and a female-to-male ratio 171:168. The CN group exhibited a mean age of 76, ranging from 62 to 91, and a female-to-male ratio of 235:217. In the MCI group, the mean age was 75 years, with ages ranging from 55 to 91 and a female-to-male ratio of 309:498. We chose the "MPR; GradWarp; B1 Correction; N3; Scaled" preprocessed images for analysis to ensure standardized preprocessing. Our focus was on the T1-weighted modality and MRI imaging to comprehensively examine the structural changes associated with AD.

3.2. Preprocessing

In our data preprocessing pipeline, we followed several steps to prepare the brain images for further analysis.

- **Image Registration:** Our data contains images with different orientations, so we performed image registration using the MNI152 template [14]. This step ensured a standardized orientation for all the images, allowing for consistent analysis.
- **Hippocampus Mask:** Using FSL [15,16], a software library for MRI brain imaging data analysis, we employed its tools to segment the hippocampus and generate a hippocampus mask. This mask was crucial for selecting the slices of the original brain volume that contained the hippocampus.
- **Brain Surface Extraction:** After obtaining the selected slices as a volume from FSL, we re-entered it into the software to perform skull stripping. This process helped extract the brain surface and remove any extraneous non-brain tissues, which are considered noise to the model.
- **Background Removal:** We performed background removal to eliminate background noise or non-brain regions, focusing on the brain structures of interest.
- **Histogram Equalization:** To enhance the contrast and improve visualization, we applied histogram equalization to the slices. This technique equalizes the distribution of pixel intensities, enhancing the image contrast and highlighting structural details.

3.3. Model

1) Input:

After preprocessing, the selected slices from each volume are resized to 150x150. We split the data into 80 % training, 10 % validation, and 10 % testing, generating 27,150 slices for training, 3000 for validation, and 3000 for testing. The model's inputs will be the 2D slices, and the labels will be one-hot encoded.

2) Architecture

VGG-16 model, a well-established architecture known for its excellent performance on image classification tasks, was employed as the backbone for our detection framework. To adapt the model to our specific problem, we used the concept of Transfer Learning [17, 18]. We selectively made the final 13 layers trainable to optimize our training process while keeping the initial 3 layers frozen. This approach benefited us from the pre-trained weights acquired from the ImageNet dataset. The reason we chose to freeze the first layers is that they contain the essential features that are present in all images.

Furthermore, we modified the dense layers with 1024, 512, and 3 units, respectively, after the flattened representation of the VGG16 model. These layers enable the network to capture higher-level features and enhance the discriminative capabilities for distinguishing between CN, MCI, and AD stages by using ReLU as an activation function in all the layers except the last one, which will be softmax to produce 3 probabilities, one for each class with summation of 1. Fig. 2 illustrates the VGG16 model and the modified version for a comprehensive analysis of the model's performance.

3) Output:

The model with the highest accuracy was saved and utilized to predict each slice of the volume containing the hippocampus. The average of all slices was then computed and presented to the radiologist, along with the name of the highest class.

3.4. Data augmentation

To improve the model's generalization ability and mitigate overfitting, data augmentation techniques were applied to the 2D slices [19]. We adopted a strategy of gradually increasing the augmentation factor to enhance the model accuracy. We initiated the process with a smaller range, such as 0 to 0.05, for width shifting. Subsequently, in each iteration, we incrementally increased the augmentation factor. This concept proved effective in improving the model's overall accuracy.

Additionally, we employed various augmentation strategies, including random shifts in width and height with a maximum augmentation factor of 0.1, controlled zoom at 0.1 max, rotation from 0 to 30°, and a brightness range of 0.3–1.7. The brightness factor was particularly useful in capturing variations in image quality. However, horizontal, and vertical flipping was not utilized due to the potential disruption of the anatomical structure, which could adversely affect classification performance.

3.5. Training Configuration

Optimizer and Learning Rate: The model was trained using the Adam optimizer with a batch size of 64, carefully selected to balance memory efficiency and computational performance. A learning rate schedule was employed for optimal learning, seamlessly integrating with the Adam optimizer. The initial learning rate, a crucial parameter determining step size in weight updates, was set to

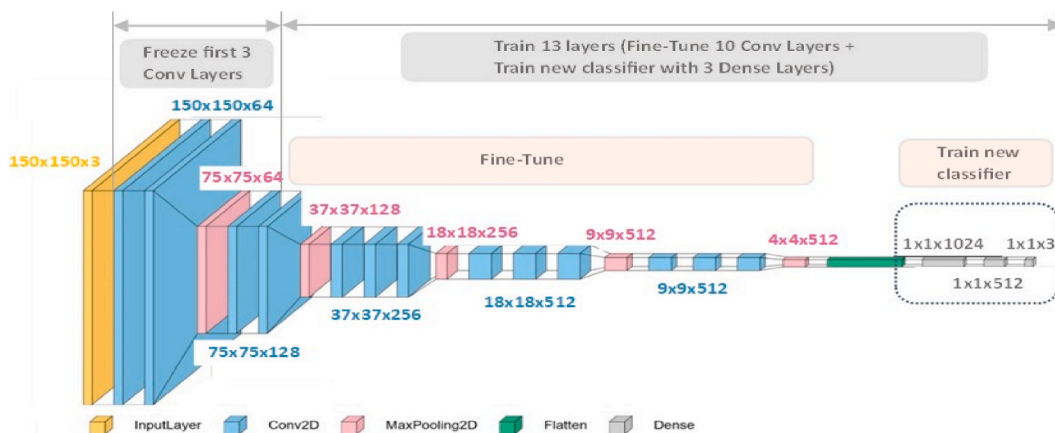


Fig. 2. VGG-16 modified architecture.

0.001, and it exponentially decayed at a rate of 0.96 during training.

Loss Function: For the loss function, we utilized categorical cross-entropy, which is suitable for multi-classification problems with three labels (CN, MCI, AD) assigned one-hot category encoding values (0s and 1s).

Data Balancing: A data balancing technique was implemented to address the challenge of imbalanced data. The ratio of each class within the dataset was calculated, and class weights were incorporated as a parameter in the fit method. This approach assigned higher weights to underrepresented classes, allowing the model to focus more on learning from these classes during training.

Epochs and Early Stopping: For each change in the data augmentation strategy, the model was trained for 30 epochs. Early stopping was implemented to counteract overfitting, particularly in the initial epochs where the training accuracy might exceed the validation accuracy. The early stopping mechanism monitored the validation accuracy, and training was halted if signs of overfitting were detected. This helped ensure the model's generalization performance on unseen data. They were early stopping, which added adaptability to the training process, allowing it to conclude when further training might lead to overfitting.

4. Results and discussion

Our proposed model has demonstrated promising results in detecting the early stages of AD. During the training phase, we achieved a remarkable accuracy rate of 99.62 %, with a corresponding loss rate of 0.0194. In the validation phase, our model attained an accuracy rate of 97.52 %, with a loss rate of 0.086. To ensure the reliability of our findings, we conducted a 10-fold cross-validation, which revealed an average testing accuracy rate of 98.17 % and a cross-validation loss rate of 0.077 (Table 2).

These encouraging results demonstrate the potential of our approach in early Alzheimer's detection using 2D slices and highlight its applicability as a valuable tool for assisting medical professionals in diagnosing and monitoring the progression of the disease. To help utilize our trained model and make it useable by radiologists and doctors, we embedded it into a website to help diagnose, keep track of patients' records, and fully automate the prediction process (Fig. 3). Our website can be broken down into 3 main features.

1. **Diagnostic tool:** After uploading a new Nifti or Dicom image, it will be given to our trained model to diagnose the image and return the diagnosis in the form of detailed percentages.
2. **Image Viewer:** 4 views will be shown to the user for a complete visual of the brain. The 3 basic planes (Axial, Coronal and Sagittal) and a full 3D rendered view.
3. **Patient History:** The uploaded Nifti or dicom will be automatically stored along with patient data. This opens the door for an extra vital feature: the patient progression chart. This chart gives the doctor a full view of the patient's history and how the case is progressing or deteriorating.

5. Strengths

Our model exhibits a multifaceted strength anchored in the integration of innovative techniques. Utilizing the hippocampus approach, a key element in memory-related functions is a cornerstone for our competitive edge. This specialized approach, combined with advanced image preprocessing, allows for a nuanced analysis of brain structures, particularly in regions like the hippocampus affected by Alzheimer's Disease (AD). The strategic use of transfer learning further amplifies our model's performance by leveraging pre-trained features from ImageNet, facilitating generalization to the ADNI dataset, even with limited medical imaging data. This holistic integration ensures a potent and practical solution for early AD detection. The model's robustness in handling unbalanced data, achieved through specialized techniques addressing class imbalance, sets it apart from alternative approaches. Moreover, our commitment to user-friendliness is evident in developing a website that seamlessly embeds the trained model, empowering medical professionals with a diagnostic tool, comprehensive image viewer, and patient history tracker. This amalgamation of strengths positions our approach at the forefront of early AD detection, promising accuracy, reliability, and practical utility in the clinical setting.

6. Limitations

While our study demonstrates significant progress, it is crucial to acknowledge notable limitations. The high model accuracy poses a risk of overfitting to the ADNI dataset. Further validation with external datasets is imperative to ensure robustness across diverse populations. A pivotal shift in methodology involves moving from reliance on built-in tools like FSL for tasks such as skull stripping and hippocampus segmentation to adopting our trained model.

Table 2

Evaluation metrics, i.e., precision, recall, F1-SCORE for AD, CN, and MCI classes.

Class	Precision	Recall	F1-score	Support
AD	0.99	0.96	0.98	946
CN	0.98	0.99	0.99	1000
MCI	0.97	0.99	0.98	1000

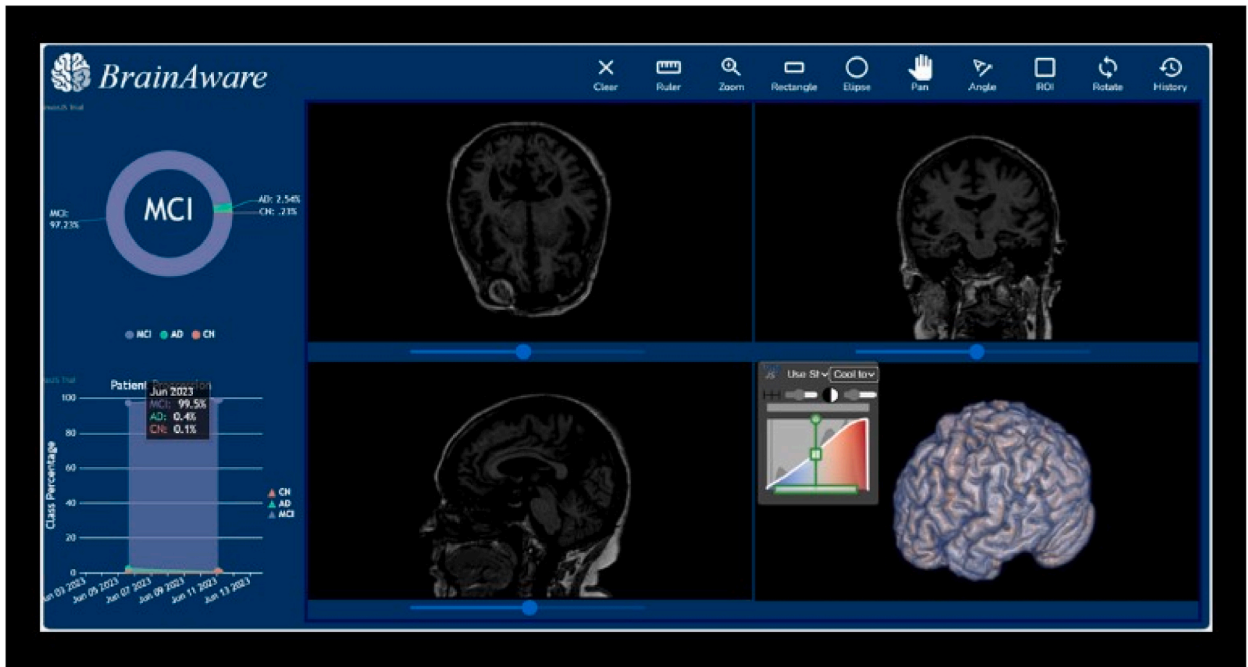


Fig. 3. The user-friendly interface used to assist clinicians.

7. Conclusion

In conclusion, our pursuit of early Alzheimer's detection through innovative approaches and technology holds significant promise in improving the lives of individuals affected by this progressive neurodegenerative disease. While a cure for Alzheimer's remains elusive, our emphasis on early diagnosis, facilitated by our product, aligns with a more practical strategy for preventing and managing risk factors. The benefits extend beyond the individual, encompassing medical advantages, opportunities for participation in clinical trials, and enhanced planning for the future. The cost-effectiveness of mitigating modified Alzheimer's risk factors also underscores the broader societal impact of our efforts. As we move forward, it is imperative to address and overcome the acknowledged limitations, ensuring the reliability and applicability of our model in diverse healthcare contexts. Through continuous refinement and validation, we strive to contribute meaningfully to the advancement of Alzheimer's research and the realization of effective early detection strategies.

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Data availability

The dataset used in this manuscript is publicly available and can be accessed at: <https://adni.loni.usc.edu/data-samples/access-data/>

CRediT authorship contribution statement

Shafiq Ul Rehman: Writing – review & editing, Funding acquisition. **Noha Tarek:** Writing – original draft, Methodology, Conceptualization. **Caroline Magdy:** Writing – original draft, Methodology, Conceptualization. **Mohammed Kamel:** Writing – original draft, Methodology, Conceptualization. **Mohammed Abdelhalim:** Writing – original draft, Methodology, Conceptualization. **Alaa Melek:** Writing – original draft, Methodology, Conceptualization. **Lamees N. Mahmoud:** Writing – review & editing. **Ibrahim Sadek:** Writing – review & editing, Methodology, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Shafiq Ul Rehman reports financial support was provided by Kingdom University. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in

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