Mathematical and computational methods for comparing anatomical structures in MRI brain scans of Alzheimer's Disease and healthy controls

Mattan J. Pelah, Monica K. Hurdal

Florida State University, Department of Mathematics, Tallahassee, FL

ABSTRACT

According to the Centers for Disease Control (CDC), as many as 5.8 million Americans are afflicted with Alzheimer's Disease (AD), a condition which results in significant and progressive cognitive impairments. While research on AD progresses steadily, the total number of cases is projected to nearly triple to 14 million by the year 2060 [1]. This project applies a mathematical method derived from planar geometry, called 'circle packing.' Anatomical structures from the human brain are extracted from Magnetic Resonance Imaging (MRI) data from AD patients and compared with healthy controls. Conformal (angle preserving) maps are then created using mathematical techniques. The resulting conformal maps can be used to define a coordinate system from which the features representing anatomical landmarks can be described and used to identify significant disparities between the two sample groups. Using this innovative method of studying brain anatomy, we hope to make significant new discoveries about characteristic anatomical features affected by AD (see Fig. 1). The methods being developed may potentially be applied to analyses on brains affected by other common neurodegenerative diseases, such as Parkinson's disease, and in various brain regions (e.g., [2]).

INTRODUCTION

- The structure of the brain is hard to study using traditional methods due to the physical characteristic of folds and fissures.
- Creating flat conformal maps, using 'circle packing,' can be useful for studying the brain:
  - a) They allow specific analysis of internal structures that would normally be inaccessible non-invasively.
  - b) They allow for coordinates that facilitate quantitative analysis. (See Fig. 2)
  - c) They are mathematically unique.
- Anatomical data is obtained from MRI images.
- The software program FreeSurfer [3] is used to reconstruct the brain surface and CirclePack [4] creates flat conformal maps.
- General hypothesis: <u>There will be a significant difference in the intrinsic mathematical values, such as conformal invariants, of the AD vs healthy control imaging data set.</u>

METHODS

- Applied and received permission to access the Alzheimer's Disease Neuroimaging Initiative (ADNI) data archive, which provides both healthy and non-healthy imaging specimens [5].
- ADNI has an immense number of diverse and extensive imaging data using different techniques; this study focuses on a small set of AD and healthy control baseline MRI images.
- Images are processed using FreeSurfer, removing the skull, segmenting the cortex and subcortical structures, outlining the white matter, defining the gray matter thickness, and inflating into a 3D rendering.
- Mathematics [6] applied in Ken Stephenson's CirclePack software enables the cortical surface to be conformally mapped to a surface of constant curvature using circle packing, essentially unfolding it while retaining the angular relationships.
- The 2D conformal maps will then be displayed and analyzed, comparing the two groups.

RESULTS

Results are preliminary as additional data processing steps are required. The processing is computationally intensive and therefore very slow; however, we are optimistic about obtaining further findings.

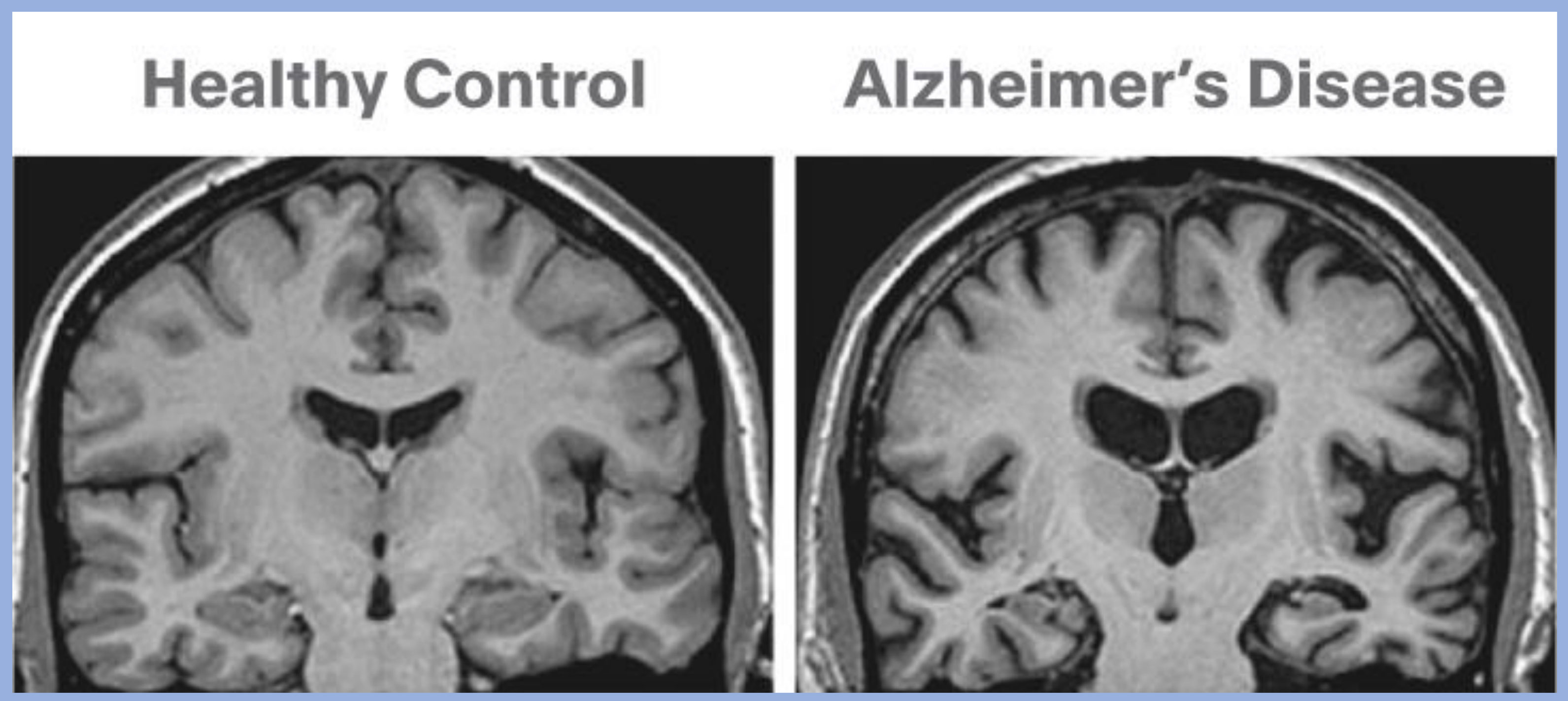


Figure 1. This image shows the noticeable difference in spatial regions in the MRI scans of the brain of a healthy control (left) and with Alzheimer's Disease (right). Taken from [7].

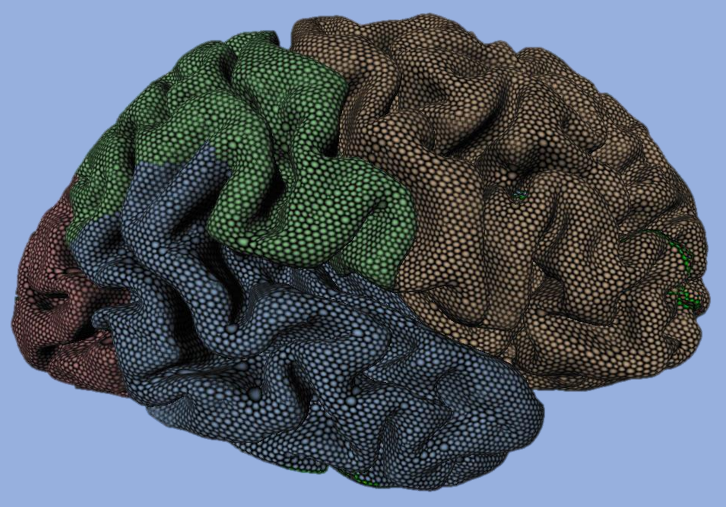
DISCUSSION AND FUTURE DIRECTIONS

- Neurodegenerative brain diseases are studied in various traditional ways, using both animal (e.g., mouse, rat or monkey) and human models, including (but not limited to) techniques such electrophysiology, lesion studies, functional capacity (e.g., cognitive testing, psychophysics) and imaging (MRI, MEG, EEG).
- The aim of this research is to study Alzheimer's Disease (AD) from MRI data using the novel mathematical technique of 'circle packing' to obtain a standardized brain representation.
- The known reduction in cognitive function and neural capacity in AD suggests that there may be differences in brain anatomy compared with normal brains [8].
- Once the results are obtained for the general hypothesis on surface area and volume, additional specific hypotheses can be created regarding the comparison of mathematical measures computed from the conformal maps, as relevant to AD and healthy controls.
- As well as studying the entire brain, additional analyses (and maps) can be carried out on specific brain regions.
- The use of mathematics in this way can create bridges between otherwise disparate areas of study to better understand AD within the context of a more fundamental mathematical structure of the brain.

Figure 2. A 'circle packing' corresponding to a flat map of the surface of the right cerebral hemisphere of a human brain (A). The 3D structure of the brain, showing the folds and major lobes, has been overlayed with circles from the flat map to illustrate the mapping correspondence (B). Taken from [9].

(A)

(B)



CONCLUSIONS

- Alzheimer's Disease (AD) is the most common form of dementia and affects millions of individuals, and their families, across the world.
- This project investigates the applications of circle packing, from planar geometry, to creating a common framework to study and compare the brains of AD with those of appropriately matched healthy controls.
- Beginning with an established dataset of raw MRI brain images, the FreeSurfer and CirclePack software packages are applied to 'flatten' the highly variable and complex 3D structure of the brain into standardized 2D conformal maps.
- The ultimate goal is for this research is to aid in a better understanding of Alzheimer's Disease, which could lead to the improvement of medical care for the most common form of neurodegenerative dementia in the world [1].

REFERENCES

[1] Alzheimer's Disease and Healthy Aging: Alzheimer's Disease and Related Dementias. Centers for Disease Control (CDC). https://www.cdc.gov/aging/aginginfo/alzheimers.htm#:~:text=In%202020%2C%20as%20many%20as,were%20living%20with%20Alzheimer's%20disease.&text=Younger%20people%20may%20get%20Alzheimer's,14%20million%20people%20by%202060. Accessed on 2/22/2022.

[2] Hurdal, M.K., Bowers, P.L., Stephenson, K., Sumners, D.W., Rehm, K., Schaper, K., & Rottenberg, D.A. (1999). Quasi-Conformally Flat Mapping the Human Cerebellum. MICCAI.

[3] FreeSurfer. https://surfer.nmr.mgh.harvard.edu/. Accessed on 2/22/2022

[4] Circle Pack. http://www.circlepack.com/software.html. Accessed on 2/22/2022.

[5] Alzheimer's Disease Neuroimaging Initiative (ADNI). http://adni.loni.usc.edu/

[6] Hurdal, M.K., Stephenson, K. Cortical cartography using the discrete conformal approach of circle packings. Neuroimage. 2004;23 Suppl 1:S119-28. doi: 10.1016/j.neuroimage.2004.07.018. PMID: 15501081.

[7] MRI Can Help Diagnose Alzheimer's Disease (Omega PDS)

https://www.omegapds.com/mri-can-help-diagnose-alzheimers-disease/. Accessed on 2/28/2022.

[8] Avila, J., Llorens-Martín, M., Pallas-Bazarra, N., Bolós, M., Perea, J. R., Rodríguez-Matellán, A., & Hernández, F. (2017). Cognitive Decline in Neuronal Aging and Alzheimer's Disease: Role of NMDA Receptors and Associated Proteins. Frontiers in neuroscience, 11, 626. https://doi.org/10.3389/fnins.2017.00626

[9] Hurdal, M.K., Visualizing Flat Maps of the Human Brain, https://www.math.fsu.edu/~mhurdal/research/visualizemaps.html. Accessed on 3/2/2022.