EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE BASED ON THE SUPERVISED RECONFIGURABLE GROWING NEURAL GAS. TOWARDS AN EHEALTH SOLUTION

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Introduction

The growing number of older people implies a higher prevalence of geriatric diseases, among others, dementia. Around 70% of dementia cases are Alzheimer's Disease (AD), about 47 million (Zhu and Sano 2006; Reitz and Mayeux 2014). AD is a neurodegenerative disease that affects the daily living activities of the patient. Mild Cognitive Impairment (MCI), on the contrary, is a construct whose patients do not get the daily activities impaired (R. C. Petersen 2004). Several levels exist in AD and the prodromal one coincides with MCI.

Early diagnosis of AD is a very complex problem due to the lack of both standardized diagnostic criteria and a specific biomarker (Ronald C. Petersen et al. 2014). Computational methods, including Artificial Neural Networks (ANNs) and Deep Learning (DL) have been used or developed for both the diagnosis and prognosis of AD and MCI (Cabrera-León et al. 2024).

Patients with AD require frequent visits to medical infrastructures to control the progress of the disease, places that can be far or unavailable when required or for extended periods. Use of eHealth solutions that integrate different capabilities can help overcome these issues.

In this work we propose an e-Health system to aid in the early diagnosis and prognosis of AD that can be used in any clinical setting, from primary to specialized care. It incorporates the concept of Universal Health since it allows to improve medical assistance in the neurological and geriatric field in disadvantaged or geographically remote areas, due to the capabilities of this system to access diagnosis at any time and from any point. The proposed intelligent early diagnosis support system is based on our ontogenetic neural architecture, the Supervised Reconfigurable Growing Neural Gas (SupeRGNG).

Methodology

The eHealth solution will comprise several modules, similar to those found in (Suárez-Araujo et al. 2004; P. G. Báez et al. 2015; Patricio García Báez et al. 2009; Suárez Araujo et al. 2011). The main ones are the diagnostic and the prognostic ones. For the former, the SupeRGNG will be used. The integration of the SupeRGNG in this multilingual and modular eHealth solution will allow transnational usage of the system for the early diagnosis of AD.

Additionally, this eHealth solution will include prognostic capabilities. This way, this other module will allow predicting the patient's future cognitive impairment severity solely based on the data collected in previous clinical visits.

Regarding the diagnostic system that will be integrated in the eHealth solution, data from the ADNI database (University of Southern California 2004) was used to train the SupeRGNG in which it will be based. 345 MCI and 150 AD were selected from the ADNI2 study.

Fast Correlation-Based Filtering (FCBF) (Yu and Liu 2003) was used for feature selection, allowing reducing the input data from 202 multimodal features (including quantitative neuroimaging, Cerebrospinal Fluid, blood, genes, and neuropsychological tests) to just 6 attributes from 3 of the former modality. These tests, which cover both cognitive and functional domains, were the Mini-Mental State Examination (MMSE) (Folstein, Folstein, and McHugh 1975), the Functional Activities Questionnaire (FAQ) (Pfeffer et al. 1982), and the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) (Rosen, Mohs, and Davis 1984).

The SupeRGNG is a supervised ontogenetic ANN based on the unsupervised Growing Neural Gas (Fritzke 1995). Both networks, as other ontogenic neural architectures do, are able not only to change their connections during learning, as other ANNs do, but also to automatically adapt their topology to the problem (Fiesler 1994). These characteristics made them quite suitable for clustering, data visualization and vector quantization. Its main difference is the reconfigurable capability: the network decides to disconnect wrongly-connected clusters and reconnect previously-erroneously-disconnected clusters.

Results

SupeRGNG yielded superb performance results according to several metrics in the MCI-AD classification task: accuracy, sensitivity, and specificity values of 0.98, and an AUC value of 0.97. In the same classification task, the SupeRGNG obtained similar or even outperformed a solution that used the same dataset and was based on the Modular Hybrid Growing Neural Gas (Sosa-Marrero et al. 2021) and several DL-based solutions that used neuroimaging data from the ADNI database (Hosseini-Asl et al. 2018; Basaia et al. 2019; Song et al. 2021; Urooj et al. 2021; Rashid et al. 2022). The SupeRGNG results were stable too.

Conclusions

Early diagnosis of AD is a challenging task. Our novel ontogenetic neural architecture, the Supervised Reconfigurable Growing Neural Gas, has demonstrated its adequacy for the fast and reliable early diagnosis of AD on both primary and specialized care despite only using data from several non-invasive, easy-to-obtain and inexpensive neuropsychological tests. Thanks to the good data preprocessing conducted and the reconfigurable characteristic of the SupeRGNG, it yielded superior performance results. This performance was usually like, but sometimes better than, some state-of-the-art approaches that made use of the expensive and computer-intensive combination of neuroimaging data and Deep Learning methods.

The integration of our lightweight intelligent computing system in a modular eHealth solution with multi-language capabilities will aid in the early and differential diagnosis of AD and MCI in any transnational medical setting, including sociosanitary institutions. Controlling the evolution of the subjects with AD or MCI help improving the quality of life of both these patients and their caregivers.

Among future works, we may mention the following ones: using data from other modalities, adapting the eHealth solution to both PC and mobile infrastructures, including the solution in the regional or national health systems, and integration in the eHealth solution of models specialized in tackling other illnesses.

Bibliography

1. Báez, P. G., C. F. Viadero, N. R. Espinosa, M. A. Pérez del Pino, and C. P. Suárez-Araujo. 2015. "Detection of Mild Cognitive Impairment Using a Counterpropagation Network Based System. An e-Health Solution." In *2015 International Workshop on Computational Intelligence for Multimedia Understanding (IWCIM)*, 1–5. https://doi.org/10.1109/IWCIM.2015.7347094.

2. Báez, Patricio García, Miguel Angel Pérez del Pino, Carlos Fernández Viadero, and Carmen Paz Suárez Araujo. 2009. "Artificial Intelligent Systems Based on Supervised HUMANN for Differential Diagnosis of Cognitive Impairment: Towards a 4P-HCDS." In *International Work-Conference on Artificial Neural Networks*, 981–88. Springer.

3. Basaia, Silvia, Federica Agosta, Luca Wagner, Elisa Canu, Giuseppe Magnani, Roberto Santangelo, and Massimo Filippi. 2019. "Automated Classification of Alzheimer's Disease and Mild Cognitive Impairment Using a Single MRI and Deep Neural Networks." *NeuroImage: Clinical* 21 (January). https://doi.org/10.1016/j.nicl.2018.101645.

4. Cabrera-León, Ylermi, Patricio García Báez, Pablo Fernández-López, and Carmen Paz Suárez-Araujo. 2024. "Neural Computation-Based Methods for the Early Diagnosis and Prognosis of Alzheimer's Disease Not Using Neuroimaging Biomarkers: A Systematic Review." *Journal of Alzheimer's Disease* 98 (3). https://doi.org/10.3233/JAD-231271.

5. Fiesler, E. 1994. "Comparative Bibliography of Ontogenic Neural Networks." In *ICANN '94*, edited by Maria Marinaro and Pietro G. Morasso, 793–96. London: Springer. https://doi.org/10.1007/978-1-4471-2097-1_188.

6. Folstein, M.F., S.E. Folstein, and P.R. McHugh. 1975. "'Mini-Mental State'. A Practical Method for Grading the Cognitive State of Patients for the Clinician." *Journal of Psychiatric Research* 12 (3): 189–98. https://doi.org/10.1016/0022-3956(75)90026-6.

7. Fritzke, Bernd. 1995. "A Growing Neural Gas Network Learns Topologies." *Advances in Neural Information Processing Systems*, 625–32.

8. Hosseini-Asl, Ehsan, Mohammed Ghazal, Ali Mohmoud, Ali Aslantas, Ahmed Shalaby, Manuel Casanova, Gregory Barnes, Georgy Gimel'farb, Robert Keynton, and Ayman El-Baz. 2018. "Alzheimer's Disease Diagnostics by a 3D Deeply Supervised Adaptable Convolutional Network." *Frontiers in Bioscience* 23 (January): 584–96. https://doi.org/10.2741/4606.

9. Petersen, R. C. 2004. "Mild Cognitive Impairment as a Diagnostic Entity." *Journal of Internal Medicine* 256 (3): 183–94. https://doi.org/10.1111/j.1365-2796.2004.01388.x.

10. Petersen, Ronald C., Barbara Caracciolo, Carol Brayne, Serge Gauthier, Vesna Jelic, and Laura Fratiglioni. 2014. "Mild Cognitive Impairment: A Concept in Evolution." *Journal of Internal Medicine* 275 (3): 214–28. https://doi.org/10.1111/joim.12190.

11. Pfeffer, R. I., T. T. Kurosaki, C. H. Harrah, J. M. Chance, and S. Filos. 1982. "Measurement of Functional Activities in Older Adults in the Community." *Journal of Gerontology* 37 (3): 323–29. https://doi.org/10.1093/geronj/37.3.323.

12. Rashid, Ashraf Haroon, Aditya Gupta, Jhalak Gupta, and M. Tanveer. 2022. "Biceph-Net: A Robust and Lightweight Framework for the Diagnosis of Alzheimer's Disease Using 2D-MRI Scans and Deep Similarity Learning." *IEEE Journal of Biomedical and Health Informatics* 27 (3): 1205–13. https://doi.org/10.1109/JBHI.2022.3174033.

13. Reitz, Christiane, and Richard Mayeux. 2014. "Alzheimer Disease: Epidemiology, Diagnostic Criteria, Risk Factors and Biomarkers." *Biochemical Pharmacology* 88 (4): 640–51. https://doi.org/10.1016/j.bcp.2013.12.024.

14. Rosen, W. G., R. C. Mohs, and K. L. Davis. 1984. "A New Rating Scale for Alzheimer's Disease." *The American Journal of Psychiatry* 141 (11): 1356–64. https://doi.org/10.1176/ajp.141.11.1356.

15. Song, Minseok, Hyeyoom Jung, Seungyong Lee, Donghyeon Kim, and Minkyu Ahn. 2021. "Diagnostic Classification and Biomarker Identification of Alzheimer's Disease with Random Forest Algorithm." *Brain Sciences* 11 (4): 453. https://doi.org/10.3390/brainsci11040453.

16. Sosa-Marrero, Alberto, Ylermi Cabrera-León, Pablo Fernández-López, Patricio García-Báez, Juan Luis Navarro-Mesa, and Carmen Paz Suárez-Araujo. 2021. "Detection of Alzheimer's Disease Versus Mild Cognitive Impairment Using a New Modular Hybrid Neural Network." In *Advances in Computational Intelligence*, edited by Ignacio Rojas, Gonzalo Joya, and Andreu Catala, 223–35. Lecture Notes in Computer Science. Cham: Springer International Publishing. https://doi.org/10.1007/978-3-030-85099-9_18.

17. Suárez Araujo, Carmen Paz, Miguel Ángel Pérez del Pino, Patricio García Báez, and Pablo Fernández López. 2011. "EDEVITALZH: Predictive, Preventive, Participatory and Personalized e-Health Platform to Assist in the Geriatrics and Neurology Clinical Scopes." In *International Conference on Computer Aided Systems Theory (EUROCAST 2011)*, 264–71. Springer Berlin Heidelberg. https://doi.org/10.1007/978-3-642-27579-1_34.

18. Suárez-Araujo, C. P., M. A. Pérez-del-Pino, P. García Báez, and P. Fernández-López. 2004. "Clinical Web Environment to Assist the Diagnosis of Alzheimer's Disease and Other Dementias." In https://www.semanticscholar.org/paper/Clinical-web-environment-to-assist-the-diagnosis-of-Araujo-P%C3%A9rez/fecc6e8d3480fdb9d469e6da40d7a02a445127e0.

19. University of Southern California, Laboratory of Neuro Imaging. 2004. "Alzheimer's Disease Neuroimaging Initiative (ADNI)." 2004. http://adni.loni.usc.edu/.

20. Urooj, Shabana, Satya P. Singh, Areej Malibari, Fadwa Alrowais, and Shaeen Kalathil. 2021. "Early Detection of Alzheimer's Disease Using Polar Harmonic Transforms and Optimized Wavelet Neural Network." *Applied Sciences* 11 (4): 1574. https://doi.org/10.3390/app11041574.

21. Yu, Lei, and Huan Liu. 2003. "Feature Selection for High-Dimensional Data: A Fast Correlation-Based Filter Solution." In *Proceedings of the Twentieth International Conference on Machine Learning (ICML 2003)*, 856–63. Washington DC. https://www.

aaai.org/Papers/ICML/2003/ICML03-111.pdf.

22. Zhu, Carolyn W, and Mary Sano. 2006. “Economic Considerations in the Management of Alzheimer’s Disease.” *Clinical Interventions in Aging* 1 (2): 143–54. https://doi.org/10.2147/ciia.2006.1.2.143.