جامعة الشارقة
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Research Abstract Form

2nd Women in Research Forum

Quwa: Empowering Women in Research & Innovation

Research Project Title : Diagnostics of dementia from structural and functional markers of brain atrophy with deep learning
عنوان البحث باللغة العربية:

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1. Research Project Overview & Objectives [should relate to Community Impact, Innovation or Industry Partnership]

Summary. The world-wide population faces the problem of aging and age-related diseases. In the UAE for instance, the life expectancy increased from 74.3 in 2000 up to 78.18 in 2021 [1]. Societal aging leads to the rise of the incidence of Nerodegenerative Disorders(NDs). NDs are incurable conditions that result in death of neurons and a progressive deterioration, i.e. dementia. Dementia is characterized by a disturbance of higher mental function, such as reasoning, planning, judgment, and memorization. The most common reason for dementia is Alzheimer's Disease (AD). Currently, 50 million people worldwide are suffering from dementia, and this number is predicted to double every 20 years to reach over 130 million by 2050 [2]. Brain atrophy is a morphological basis of both aging and NDs. Therefore, it is important to identify markers of specific types of brain atrophy, i.e. to segregate pathology versus age-related conditions.

The relationship between brain structural changes and man's functional performance is not straight-forward. Neural plasticity accounts for this phenomenon. The plasticity is a specific feature of biological systems to adjust to pathology. However, the process of adjusting the system may cause diminishing to the potential outcomes of the disease. So, clinical appearance may not be reflective of a real structural impairment and visa versa. For example, there is no clear association between functional performance and structural changes in AD and Mild Cognitive Impairment (MCI). In addition, the pathophysiological mechanisms are complex and therefore they remain unstudied despite a success of today's neuroscience. The future diagnostic should be based on the whole range of possible diagnostics modalities. Therefore, the challenge of the polymodal diagnostics is to find an informative value of structural attributes, functional features, clinical risk factors and demographics attributes. Without the combination of all these attributes the final prediction of the disease and its course (e.g., disease severity, outcomes, a response to therapy) will not be accurate.

An association between brain structural and functional changes is a topic of ongoing studies. Many authors have demonstrated a boost in the predictive performance of the diagnostic methods when cognitive features were ensembled with structural ones [3-4]. However, only a few works have focused on the prediction of cognitive status from brain structural images. Hypothetically, as dementia has been associated with structural and functional (cognitive) changes, the combination of neuroimaging and neuropsychological data seems feasible. Structural MRI is shown to be a valid marker of AD [5] and AD-related NDs at the late stages of the disease. However, reliable means of identifying cognitively normal individuals at higher risk of developing AD are more likely to derive from psychophysiological testing (e.g., event-related potentials) [6-7]. Ultimately, the full understanding of the pathophysiological mechanisms underlying the AD-related functional

impairment of the brain and its structural bases is missing [8]. Therefore, new findings may have a huge impact on earlier detection, diagnosis, and treatment of NDs.

Importance and significance. An association between the brain structural changes and man's functional performance may have different characteristics in the normal healthy condition and in pathology such as neurodegenerative disorder (ND). By utilizing deep learning (DL), one may predict the cognitive status of a person from the brain MRI acquisition. Then the obtained data may be compared with the results of conducted cognitive tests. The larger is the gap between the predicted value and the observed one, the higher is the probability of dementia . **We hypothesize** that the brain structural-functional association (SFA) may be described with distinct patterns specific to either normal or accelerated aging. DL may provide new insight into these patterns.

Our main objective in this research work is to improve the diagnostics of NDs by applying DL techniques to the combination of radiological and neurofunctional data. To address the main goal we will perform the following tasks:

i. develop a method to calculate the cognitive status from structural data obtained from different sources on a dataset of mentally healthy people;
ii. predict the cognitive scores from the MRI acquisitions in another dataset of cognitively preserved people tested with executive functioning tasks;
iii. correlate the predicted cognitive scores with the reaction time and accuracy metrics in executive functioning tasks;
iv. assess the generalizability and transferability of the model for its implementation into practice.

New contribution of the proposed work. Currently brain atrophy is commonly detected at a late stage while early neuronal functional impairment is misdiagnosed and mistreated. As pathophysiological mechanisms of brain atrophy are complex, they remain unstudied despite the success of today's neuroscience. Therefore, we believe that addressing the above mentioned objectives may contribute significantly to the earlier detection, diagnosis, and treatment of age-related degenerative diseases.

Expected outcome. The scientific research findings of the proposed project are expected to be published in leading conference and journal.

2. Research Methodology & Expected Results

DATA: In this research we will use two publicly available datasets:

i. **Alzheimer's disease neuroimaging initiative (ADNI)** dataset [9] includes 400 subjects with mild cognitive impairment (MCI), 200 subjects with early AD, and 200 elderly control subjects with an age range from 55 to 90 years. From the comprehensive ADNI dataset we acquire final diagnosis clinical reports, demographic data (i.e., age, gender, ethnicity), morphometric data (i.e., volumes of brain areas that can be mostly affected by ND), cognitive assessment data (i.e., MMSE, RAVLT, TMT (part B), DSST, ADAS-cog tests) and pre-processed T1-weighted MRI files.
ii. **Psychophysiological outcomes of brain atrophy (POBA)** dataset consists of 231 cases of MRI examination and psychophysiological tests [10] of people of different age range from 4 to 84 years. From the comprehensive POBA dataset we acquire the functional assessment with the psychophysiological tests, demographic data, morphometric data, and raw T1-weighted and FLAIR MRI files.

PROPOSED METHOD: The proposed method to address the main objective of the study is illustrated in Figure 1.

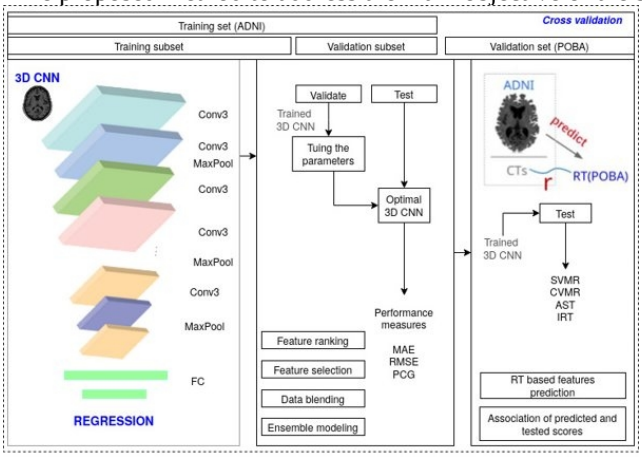

Figure 1. Overview of the methodology of the study

The poposed method starts by first pre-processing the structural data before employing the Deep Learning(DL) techniques which include the following:

i. Register all T1w MRI images to an MNI152 space by employing the FLIRT tool from the FSL package [11].
ii. Conduct additional bias field correction N4 to correct low frequency intensity non-uniformity [12].
iii. Normalize the intensities of the voxels by scaling them to the standard normal distribution parameters.
iv. Extract non-brain tissues from the image by utilizing BET (Brain Extraction Tool) from the FLS package [11].
v. Perform background removal and optionally crop the image within the limits of the brain tissues.
vi. Downsample the images

Then, to identify the patterns of brain atrophy related to normal aging, we will utilize different deep learning models to predict the cognitive tests results (ADAS-cog, MMSE, RAVLT, TMT, DSST) from the brain structural MRI images using 2D- and 3D-CNN models applied to benchmark dataset (ADNI). Then, we will calculate the expected cognitive decline score on POBA dataset. Afterwards, we will assess the strength of the relationship between the predicted rate of cognitive decline and the executive functioning tests (i.e., decision-making time, simple visual motor reaction, complex visual-motor reaction, reaction to a moving object). This will allow us to assess the generalizability and transferability of the proposed model.

From the currently available literature, it is indicated that ML methods to predict the risk of dementia are not yet ready for routine use. Better interdisciplinary collaborations and internationally agreed (by clinicians and computer science/engineers) validation protocols and clinical trials are needed. Development and application of DL methods in neuroimaging require interdisciplinary work, clinically relevant annotated data sets, varied imaging types. Proposed algorithms should be focused on relevant disease outcomes to ensure that the resulting machine learning methods are robust and reliable. By conducting this reaserch we believe **to contribute to improving the current state of early diagnostics of dementia-related diseases** (MCI, Alzheimer's).

Metrics of success. The set of methods we will propose in this research work (e.g. deep machine learning methods) are known to be effective techniques for improving the current diagnostic approaches. In this case, we will consider the performance of the proposed models are satisfactory if the specificity and sensitivity of the classification models are higher than 85% and the fraction of the MAE over the range of the predicted feature is less than 10% based on the regression models.

List of resources. The research in this study will be carried out using:

i. programming language Python, and its libraries for Computer Vision, Data visualization, Data Processing, such as NumPy, SciPy, Matplotlib, PIL, Pillow, OpenCV, scikit-learn just namely the few.
ii. Neurodocker container with functioning Python, Nipype, FSL, ANTs, FreeSurfer, and SPM12 software package.
iii. tensorflow-gpu container from tenforflow-gpu docker image with NVIDIA® CUDA® Toolkit and cuDNN from nvidia-docker image.
iv. an open source software library for high performance numerical computation TensorFlow with high-level API Keras.
v. Linux Ubuntu 18.04 Nvidia DGX-1 deep learning server with 40 CPU cores and 8x NVIDIA Tesla V100 GPU with 32 GB memory each accessed with web-based multi-user concurrent job scheduling system [13].

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