Patient-centered Deep Learning Model and Diagnosis Service for Persons with Alzheimer's Disease

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Abstract

Because pharmaceutical companies have failed to develop Alzheimer's disease (AD) cure and treatment as of today, AD early detection and intervention becomes increasingly clear to be the best choice of improving quality of life for persons with AD at least in the near future. Thus, developing patient-centric predictive models and enabling self-diagnosis services are of great potential. This paper presents how recurrent neuron neatwork (RNN) models can be adopted in the AD early diagnosis modeling (AD-EDM). In particular, we show that the improved prediction accuracy of RNN AD-EDM can contribute to the delivery of self-diagnosis services for preclinical/early AD patients. By leveraging the fast development of big data technologies and machine learning methods, our AD-EDM tools will make a difference in discovering non-pharmacologic therapy solutions to slow AD progression.

Keywords
Alzheimer's disease (AD); deep learning; recurrent neuron network; Tensorflow; self-service

1. Introduction

About 5.5 million Americans currently live with Alzheimer's disease (AD), which is the only top ten cause of death that cannot be prevented, cured, or slowed. AD is the most common form of dementia and the sixth leading cause of death in the US (Alzheimer's Association, 2017). On January 8, 2018, Pfizer announced to halt research into AD and Parkinson's treatments after high-profile disappointment in years of research. In fact, pharmaceutical companies worldwide have failed to develop any new drug since the last new drug that treats only the symptoms of AD was approved by the FDA 14 years ago (Johnson, 2018). The high-profile failures of developing AD treatments thus propel the idea of seeking alternative solutions for persons with AD and their caregivers in the near future (Crous-Bou et al., 2017; Loewenstein et al., 2017; Qiu et al., 2017; Qiu et al., 2018).

AD early prediction and intervention have been studied, aimed at postponing AD onset or slowing down its progression (Oaklander, 2016; Park, 2016). Studies have shown that appropriate and positive interventions, such as providing AD patients with the effective levels of lifestyle changes and brain training, surely contribute to slowing AD progression. However, preclinical AD patients are often reluctant to take diagnostic tests. Most of them usually lack motivation to take diagnostic tests due to believing that ongoing cognition declines are a result of a natural aging process. In addition, AD tests are expensive and time-consuming (Bradford et al., 2009). In fact, completing these tests at an AD center is expensive and time-consuming, which typically includes brain scans such as magnetic resonance imaging (MRI) and positron emission tomography (PET) scans and neuropsychological tests such as the Clinical Dementia Rating (CDR), Geriatric Depression Scale (GDS), and Mini-Mental State Examination (MMSE).

Obviously, patient-centered while cheap and convenient AD services are necessary to change this (Gerteis et al., 1993; Barry and Edgman-Levitan, 2012; Wang et al., 2018), especially for persons with probable AD at their preclinical/early stages. To promote patient-centered AD diagnosis services, it is essential to have ways to correctly and timely detect and diagnose patients with signs of AD at the preclinical/early stages so that appropriate and personalized interventions can be prescribed to the patients when helps or treatments are more effective.

In our early study that focused on predicting or classifying AD patients at their preclinical/early stages using a large dataset of 123417 medical records from the National Alzheimer's Coordinating Center (NACC) (Wang et al., 2018). In this paper, we will present how a deep learning based model facilitates the delivery of self-diagnosis services for persons with AD at their preclinical/early stages. The remaining paper is organized as follows. Section 2 provides a brief background of this study. Section 3 then shows how deep learning models can be adopted in support of patient-centered diagnosis service for persons with AD at their preclinical/early stages. At last, we conclude this paper in Section 4 with a brief summary and future research directions.

2. Brief Background Review

Scientists and doctors have been suspected that proteins known as β-amyloid and *tau* form "plaques and tangles" that can build up over time in the brain, clogging and interfering with neurotransmitters. Despite a lot of studies of AD medicine and treatments based on those suspects of β-amyloid and *tau*, there is no success of finding an AD cure. AD treatment studies require an immense investment of time and money. For instance, pharmaceutical companies, Eli Lilly, Merck, and Pfizer, have spent billions of dollars and many years in the drug development and clinical trials, all of which ended in failures (Johnson, 2018). As a result, there are currently just a few FDA-approved drugs that help ease AD symptoms rather than stopping AD.

Although the situation of seeking AD pharmacologic therapies seems depressing, pharmaceutical companies continue to work hard to seek pharmacologic solutions. In the meantime, a growing number of researchers have been focusing on studies of risk factors and non-pharmacologic therapies for AD patients at their preclinical/early stages (Crous-Bou et al., 2017). It is worth mentioning that the A4 study at Brigham and Women's Hospital in Boston shows great potential in the AD early prediction and intervention research, which could shed light on finding a drug for preclinical AD. Therefore, it is vital to develop a simple and convenient predictive model to support AD early diagnoses. We are confident that a cheap and convenient system to enable preclinical/early AD self-diagnosis will make a difference (Qiu et al., 2017; Wang et al., 2018).

Recently, recurrent neuron neatwork (RNN) models have begun to gain a strong presence in healthcare applications as RNN modeling is effective at discovering temporal patterns in data, such as classifying diagnoses and predicting mortality, health decline, and length of stay for Pediatric Intensive Care Unit patients (Aczpn et al., 2017; Lipton et al., 2015; Wang et al., 2017). These studies applied various RNN models for medical prediction tasks by taking advantage of temporal relations in patient's medical data. In particular, a Long Short-Term Memory (LSTM) RNN model has been successfully used for AD progression predictive modeling (Wang et al., 2017).

As discussed in Qiu et al. (2017) and Wang et al. (2018), deep learning approaches have so far relied on either an extensive dataset or lab-based biomarker data for AD predictive modeling (Bhatkoti and Paul, 2016; Suk et al., 2014). The dataset provided by NACC is comprehensive, which includes patients' demographic and physical information, medication, health history, visit time, biomarker results, and the results from Global Staging CDR, GDS, and Functional Activities Questionnaire (FAQ) tests. We extracted a refined dataset with only a handful patients' medical and functional activities data for building a deep learning model to enable early diagnosis of AD. As a result, we can develop a convenient and simple website to allow early AD patients to complete preliminary diagnoses at home. We discuss next how we can build a prototype to showcase a potential implementation of the developed deep learning model.

3. Prototyping a self-diagnosis platform for persons with AD at the preclinical/early stages

In Wang et al. (2018), we showed how RNN models could be applied to AD early detection modeling (AD-EDM). The Global Staging Clinical Dementia Rating (CDR) score is a clinical and symptomatic metric to assess the dementia levels (Williams et al. 2013), which was adopted to model AD progression stages. A person with AD can be at five different stages with respect to CDR score: 0 (no impairment), 0.5 (questionable impairment), 1 (mild impairment), 2 (moderate impairment), and 3 (severe impairment). Although biomarkers and brain imaging approaches are widely used in AD labs and test centers, CDR is effective while easy and cheap for persons with probable AD at the preclinical/early stage (Qiu et al., 2017).

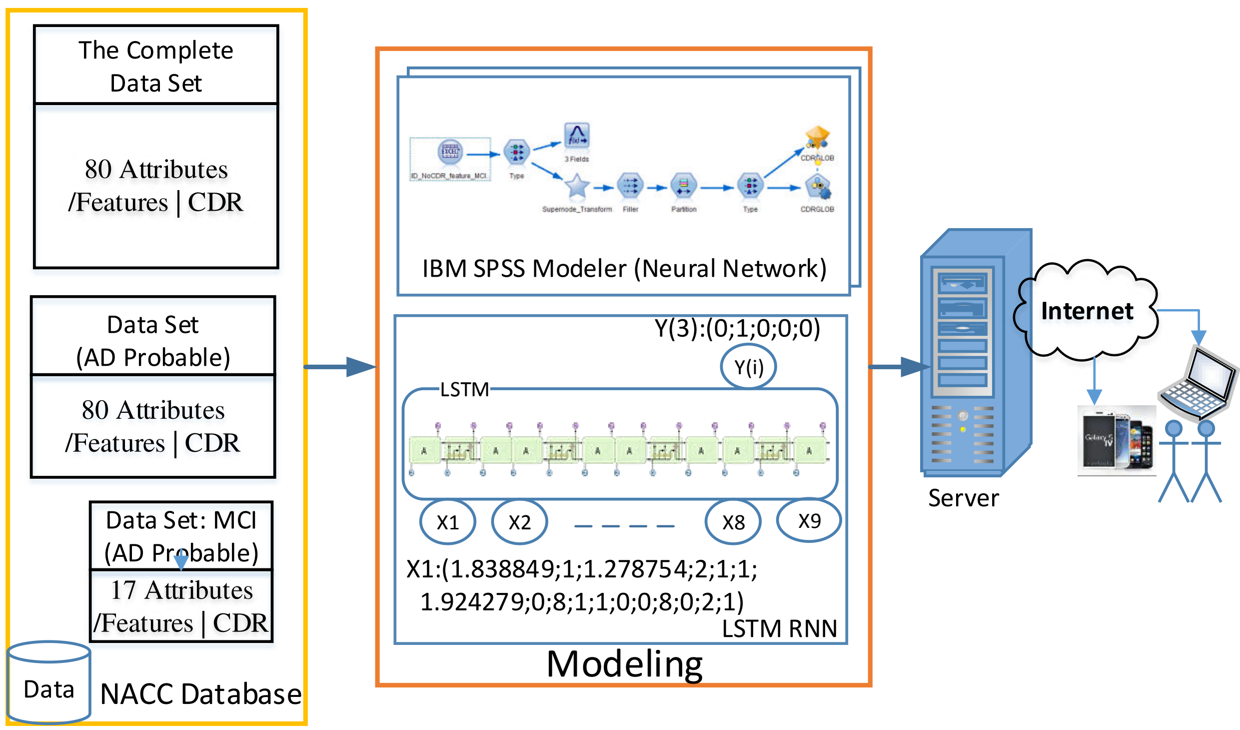

Figure 1. Overview of approaches to develop home-based AD diagnosis tools

Figure 1 illustrates there are numerous ways of implementing AD-EDM prototypes. In this paper, we show one prototype that supports patient-centered self-diagnosis services at home. A deep learning based diagnosis model is developed using a recurrent neuron network (RNN) with long short-term memory (LSTM) cells. A website prototype has been developed with the support of a built AD-EDM model.

As illustrated in Figure 1, we identified 17 significant features that are easily collected at home by persons with AD or their caregivers. Those 17 features are listed in Table 1, which essentially involve the data relevant to persons' medical histories and their body functional capabilities. In Wang et al. (2018), we built an RNN with LSTM cells, presenting how a deep learning approach towards diagnosing preclinical/early AD patients can be implemented. We utilized Google's Tensorflow Deep Learning library (Google, 2018) to explore the possibility of an improved diagnosis model. The input can be easily scaled. Thus, the needed input features with all historical visits and irregular diagnosis time intervals for patients can be well accommodated (Wang et al., 2017).

Table 1. Significant impacting features

Inputs	Meaning
AGE	Age
SEX	Gender
EDUC	Years of Education
INDEPEND	Level of independence
ANYMEDS	Taking any medications
HYPERTEN	Hypertension
BPDIAS	Blood pressure (sitting), diastolic
COMFORT	Behavior, comportment, and personality
BILLS	In the past four weeks, did the subject have any difficulty or need help with: Writing checks, paying bills, or balancing a checkbook
TAXES	In the past four weeks, did the subject have any difficulty or need help with: Assembling tax records, business affairs, or other paper
SHOPPING	In the past four weeks, did the subject have any difficulty or need help with: Shopping alone for clothes, household necessities, or groceries
GAMES	In the past four weeks, did the subject have any difficulty or need help with: Playing a game of skill such as bridge or chess, working on a hobby
STOVE	In the past four weeks, did the subject have any difficulty or need help with: Heating water, making a cup of coffee, turning off the stove
MEALPREP	In the past four weeks, did the subject have any difficulty or need help with: Preparing a balanced meal
EVNETS	In the past four weeks, did the subject have any difficulty or need help with: Keeping track of current events
REMDATES	In the past four weeks, did the subject have any difficulty or need help with: Remembering appointments, family occasions, holidays, medications
TRAVEL	In the past four weeks, did the subject have any difficulty or need help with: Traveling out of the neighborhood, driving, or arranging to take public transportation

Figure 2 shows the interface used in our developed website prototype. Once the data are correctly provided and submitted, a diagnostic test result will be generated as shown in Figure 3. An appropriate guidance will be also made available. As a DEMO site, appropriate medical guidance from a variety of trusted websites is incorporated, which are clustered based on ages, genders, and AD stages. As a result, by simply clicking "HERE For HELP" as shown in Figure 3, personalized medical guidance can be timely provided for users with probable AD at the preclinical/early stages.

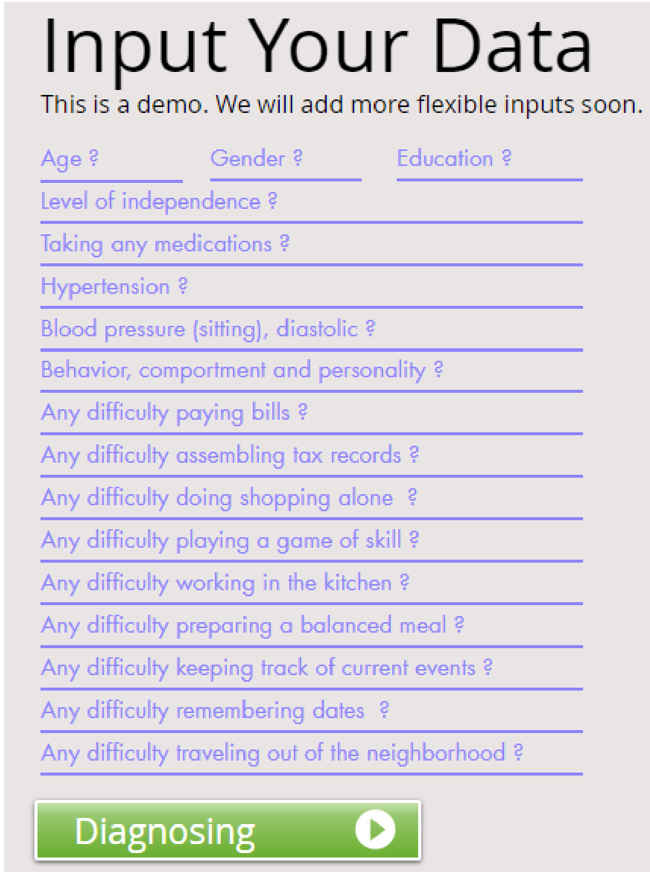

Figure 2. Data inputs collected from end users

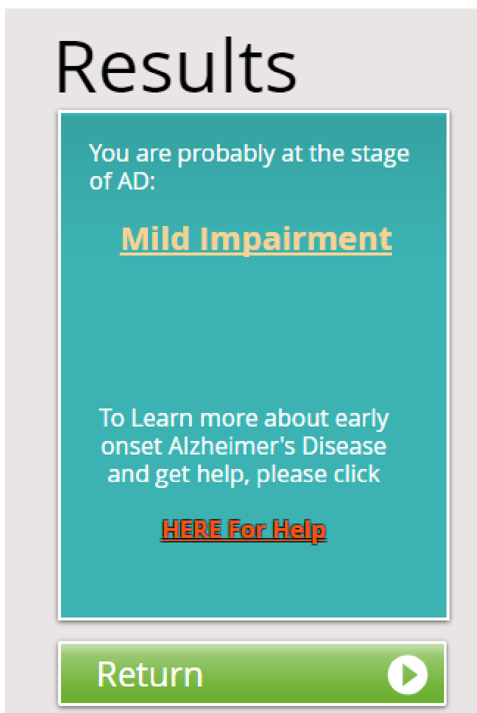

Figure 3. A corresponding diagnostic result generated from collected inputs from an end user

4. Final Remarks

This short paper showed that the LSTM RNN approach to AD-EDS seems very promising. It becomes clear that we can utilize the developed deep learning model by well incorporating it into a mobile-friendly website. As a result, self-diagnosis tools can be made available to the public, which surely promote and support patient-centered approaches in the field of AD. By leveraging the technology advances in "speech-to-text" and deep learning, we can enhance the method of acquiring inputs substantially to make the prototype easy to use by end users.

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Biographies

Robin G. Qiu, professor of information science, earned his Ph.D. in industrial engineering from Penn State and his M.S. and B.S. from Beijing Institute of Technology, China. He teaches courses on data analytics, information science, software engineering, computer security, and enterprise service computing. Dr. Robin G. Qiu research includes Service Science, Smart Service Systems, Big Data, Data/Business Analytics, Service Operations and Management, Information Systems and Integration, Supply Chain Management, and Control and Management of Manufacturing Systems. Dr. Qiu served as the editor-in-chief of INFORMS Service Science. He is an associate editor of IEEE Transactions on Systems, Man, and Cybernetics, and IEEE Transactions on Industrial Informatics, and has more than 160 publications.

Jason L. Qiu is currently a fulltime student at Methacton School District. He likes coding and computer science. His *MMSE Modeling: A Patient-centric Approach to Mitigating Alzheimer's Disease Progression* won the Excellence in Student Science Research Award, Merck and Company Honorable Mention Award in 2017.