journal homepage: www.intl.elsevierhealth.com/journals/cmpb

Ontology driven decision support for the diagnosis of mild cognitive impairment

Xiaowei Zhang[a], *Bin Hu*[b,a,c,*], *Xu Ma*[a], *Philip Moore*[c], *Jing Chen*[a]

[a] *School of Information Science and Engineering, Lanzhou University, Lanzhou, China*
[b] *College of Electronic Information and Control Engineering, Beijing University of Technology, Beijing, China*
[c] *School of Computing, Telecommunications and Networks, Birmingham City University, UK*

ARTICLE INFO

Article history:
Received 22 July 2013
Received in revised form
13 November 2013
Accepted 27 December 2013

Keywords:
Alzheimer dementia
Mild cognitive impairment
Diagnosis
Ontology
Magnetic resonance imaging (MRI)
Decision tree

ABSTRACT

In recent years, mild cognitive impairment (MCI) has attracted significant attention as an indicator of high risk for Alzheimer's disease (AD), and the diagnosis of MCI can alert patient to carry out appropriate strategies to prevent AD. To avoid subjectivity in diagnosis, we propose an ontology driven decision support method which is an automated procedure for diagnosing MCI through magnetic resonance imaging (MRI). In this approach, we encode specialized MRI knowledge into an ontology and construct a rule set using machine learning algorithms. Then we apply these two parts in conjunction with reasoning engine to automatically distinguish MCI patients from normal controls (NC). The rule set is trained by MRI data of 187 MCI patients and 177 normal controls selected from Alzheimer's Disease Neuroimaging Initiative (ADNI) using C4.5 algorithm. By using a 10-fold cross validation, we prove that the performance of C4.5 with 80.2% sensitivity is better than other algorithms, such as support vector machine (SVM), Bayesian network (BN) and back propagation (BP) neural networks, and C4.5 is suitable for the construction of reasoning rules. Meanwhile, the evaluation results suggest that our approach would be useful to assist physicians efficiently in real clinical diagnosis for the disease of MCI.

1. Introduction

Mild cognitive impairment (MCI) is currently thought of as a transition phase between normal aging and dementia, especially Alzheimer's disease (AD). MCI refers to the clinical state of individuals who have impaired memory but are otherwise functioning well and do not meet clinical criteria of dementia. By cognitive impairment, we typically refer to a person's ability to remember, read, write, solve problems, perform calculations, and navigate around their environment. A common indicator of the early onset of AD involves an insidious progression of forgetfulness. For a discussion on the progressive development of dementia see Vickland and Brodaty [1] in which the 7 tier model applies a taxonomy for dementia with prevalence statistics.

With the rapid aging of society, the cognitive impairment and dementia have high incidence and this seriously impacts on the elderly's health and quality of life. At the Mayo Alzheimer's Disease Research Center (ADRC), studies manifest that when subjects are followed for 6 years, approximately 80% of patients with MCI will convert to AD [2]. Obviously, people with MCI have been the high-risk group for AD, therefore recognition of MCI serves as an important tool for the

* *Corresponding author at*: College of Electronic Information and Control Engineering, Beijing University of Technology, Beijing, China. Tel.: +86 931 8912779; fax: +86 931 8912779.
E-mail address: bh@lzu.edu.cn (B. Hu).
0169-2607/$ – see front matter © 2014 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.cmpb.2013.12.023

investigation of treatments aimed at managing AD and improving the quality of life (QoL) for both patients with dementia and carers.

AD can be diagnosed clinically with reasonable accuracy at the dementia stage when there is impairment in a patient's function at a social level. However, diagnosing the early onset of AD represents a difficult clinical decision and is frequently a matter of clinical judgment. Generally, the identification of MCI can be made by neuropathological confirmation of individuals who have been studied in life and meet criteria for MCI. The diagnostic criteria for MCI, as formulated by ADRC, are as follows [3]:

1. Memory complaint by patient, family or physician.
2. Normal activities of daily living.
3. Normal general cognitive function.
4. Objective impairment in one area of cognitive function as evidenced by scores >1.5 SD of age-appropriate norms or abnormal memory function for age.
5. Clinical dementia rating score of 0.5.
6. Not demented.

As can be seen from the above, clinicians diagnose MCI mainly based on their observations and experience, and it is usually difficult to complete accurate diagnosis due to the very mild symptoms of cognitive impairment. Recently brain informatics may be able to provide some reliable information of MCI detection. Brain structure changes associated with MCI have been researched widely, for example, the cortical thickness of MCI patients has been found significantly reduced because of the gray matter atrophy according to structural magnetic resonance imaging (MRI) studies [4]; and distributed and progressive changes of white matter fibers have been found in diffusion tensor imaging (DTI) studies [5]. Present findings suggest that most DTI-derived changes in MCI are largely secondary to gray matter atrophy [6]. In order to make prior diagnosis of disease and shun subjectivity and superficiality, an objective method able to diagnose MCI automatically using MRI may provide significant diagnostic benefits.

Studies have shown that a computer-based system, which intelligently filters and assesses relevant parameters, may foster an objective and correct diagnosis [7]. Decision-support, which takes computer as a tool, can help physicians diagnose more objectively as it can analyze data derived from medical tests and then present results to physicians using an appropriate visualization to enable diagnosis more easily and efficiently. Therefore, clinicians who are less well trained or experienced may also identify MCI with the help of decision-support tools. Accordingly, a knowledge-based decision support for identifying MCI is needed to support neurologists in the automatic classification of NC and MCI patients.

Ontology expressed using the Web Ontology Language (OWL) and playing a central role in the development of the Semantic Web [8] provides an explicit specification of conceptualizations and relationships among them in specific domains of interest [9]. Ontology is often used in decision support system as a tool of knowledge representation [10] and it provides convenience of knowledge acquisition, knowledge sharing, and knowledge reuse [11,12]. The main advantages of applying ontology technologies are as follows: (1) knowledge can be managed organically and hierarchically. (2) Semantic representation of knowledge provides the ability to share data across heterogeneous medical information systems. (3) It can be realized the decidability and consistency on expressed knowledge.

In our proposed method, we calculate the mean values of cortical thickness in different anatomical regions of brain as features, anatomical regions correspond to 90 non-cerebellar regions-of-interest (ROI) using the automatic anatomical labeling (AAL). AAL provided by the Montreal Neurological Institute (MNI) is an anatomical parcellation including 116 areas (45 anatomical volumes in each hemisphere and 26 areas of cerebellum) [13]. Then these features are stored into a domain ontology. We use ontology technique to manage and represent specialized knowledge explicitly to assist physicians distinguishing MCI patients from NC with the help of reasoning rules.

In conclusion, this approach enables the classification of NC and MCI patients based on cortical thickness in 'real-world' clinical conditions. The ontology and rule set are both flexible and extensible; these traits provide our approach with the capability to generalize to many other classification problems. The encouraging results suggest that the system can be used effectively in auxiliary diagnosis of MCI.

This paper is organized as follows: the following section describes related work which addresses the use of cortical thickness in detecting MCI and Ontology-Based Modeling (OBM) for representing clinical knowledge. Section 3 introduces the ontology-based decision support approach in detail including descriptions of data processing, feature extraction, and knowledge modeling. Section 4 presents some numerical results when using different machine learning algorithms in this approach, followed by the conclusions in Section 5.

2. Related work

Recently, many researchers have focused on the automatic identification and diagnosis of AD [14,15]. For instance, a method using the scale-invariant feature transforms in magnetic resonance images to diagnose AD has presented in [14] with the accuracy of 86%. Cho et al. [16] proposed to classify AD and NC using cortical thickness data which has demonstrated good results (with 82% sensitivity and 93% specificity). Although these methods for AD diagnosis are effective, it also should not be ignored that the diagnosis of MCI is conducive to early detection and early treatment of AD. Studies have shown that MCI patients have a certain degree of reduction in cortical thickness [17–19]. The cortical thickness of the MCI patient decreased significantly when compared to that in NC, mainly in the medial temporal lobe region and in some regions of the frontal and the parietal cortices [20]. Yao et al. [4] indicate most significant changes in MCI patients appeared in the prefrontal gyrus, the somatosensory cortex, the Wernicke's area and the superolateral temporal lobe when compare to these areas in NC. Thus cortical thickness could provide potentially powerful information to assist in the diagnosis of MCI. Approaches of classifying MCI and NC using cortical thickness have been