Dementia Severity Scale Based on MRI

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In the clinical treatment of Alzheimer's disease, one of the most important tasks is evaluating its severity for diagnosis and therapy. However, traditional testing methods are deficient, such as their susceptibility to subjective factors, incomplete evaluation, low accuracy, or insufficient granularity, resulting in unreliable evaluation scores.

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1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disease with an insidious onset. It is the most common cause of dementia and one of the most expensive and deadliest diseases of the century ^[1]. Clinical manifestations include memory impairment, aphasia, apraxia, agnosia, impairment of visuospatial skills, executive dysfunction, personality changes, and behavioral changes. The cause of AD is still unclear; however, its progression is usually accompanied by a decline in neurological function. Therefore, in clinical diagnosis, physicians attempt to evaluate subtle changes in the progression of the disease stage by evaluating the level of neurological function and recommending an appropriate treatment plan. The Psychiatric Rating Scale is one of the auxiliary evaluation methods commonly used by physicians. There are many kinds of psychiatric rating scales for Alzheimer's disease; however, these scales are not sufficiently accurate and comprehensive, which leads to the low credibility of the traditional scales. Moreover, they lack objectivity and are not a reliable basis for clinical diagnosis and treatment. Structural magnetic resonance imaging (sMRI) is another auxiliary evaluation method that allows physicians to diagnose based on the degree of brain atrophy in MRI images. However, this approach is highly dependent on the physician's subjective judgment and does not provide a detailed quantitative evaluation.

Deep learning is a powerful method that has been applied to medical images and automated accomplishing targeted tasks in an end-to-end way. There have been many published studies in recent years that have successfully applied this approach to medical image analysis tasks and generally achieved significant improvements ^{[2][3][4]}. Most previous studies focused on the prediction of disease categories, classifying patients' images into discrete categories. However, for many types of diseases, the stages may exhibit a continuous variation in severity that can change over time ^{[5][6][7]}. These different stages of a disease are often classified into ordinal levels (e.g., normal, mild, moderate, and severe), but variations within these ordinal levels are usually underappreciated, and deep learning methods have been applied to evaluate disease stages in limited cases. This may be owing to the absence of the gold standard and representative samples for determining the AD stage.

In the field of deep learning, evaluating the differences between images can be expressed as a metric learning problem. The contrastive learning strategy is commonly employed for metric learning, and it is often used to evaluate the similarity between images. This strategy trains a network using contrastive loss functions and considers the metric between the network output vectors as the evaluation criterion for the image similarity metric.

2. Evaluation of Neurological Function in Alzheimer's Disease

Due to the continuous growth of the aging population in China, the number of patients with AD is increasing, and an accurate and refined disease stage evaluation of AD has become a critical problem in clinical treatment. Clinically, AD begins with lesions on the brain. However, patients often do not notice any associated changes initially, and only after years of accumulation do patients exhibit obvious symptoms. Moreover, doctors cannot simply use medical imaging and clinical diagnostic data to diagnose the patient's real situation. Usually, physicians evaluate the neurological function of the patients to diagnose the stage of AD. Currently, one of the main methods for this purpose is neuropsychological testing, which allows physicians to measure the neurological function of patients by observing their performance in tasks involving multiple brain functions, such as movement, language, attention, memory, and thinking, and quantitatively evaluating their neurological function to obtain a score within a certain range ^{[8][9][10][11][12][13]}. The common traditional neuropsychological tests include the Mini-Mental State Examination (MMSE)^[8], Clinical Dementia Rating (CDR)^[9], Functional Activities Questionnaire (FAQ)^[10], Alzheimer's Disease Assessment Scale-Cognitive (ADAS-COG) [11], and Rey Auditory Verbal Learning Test (RAVLT) ^[12]. The MMSE primarily screens for cognitive impairment by guizzing both orientation and memory, whereas the CDR screens for mild cognitive impairment and classifies clinical dementia by quantifying life skills. Although neuropsychological tests can visually reflect different aspects of patients' brain function, each scale suffers from the problem of incomplete evaluation of neurological function due to different emphases on neurological function evaluation, which in turn affects the diagnosis of the severity of the disease. At the same time, the traditional psychiatric rating scales utilize a guestion-and-answer format with cooperation between physicians and patients, which may lead to a lack of patient cooperation during the evaluation stage, and the score is also affected by the biased subjectivity of the physician.

With the rapid development of medical imaging technology in recent years, neuroimaging has gradually become one of the main methods to evaluate the neurological function of patients, with structural MRI being the most frequently used ^{[14][15]}. Structural MRI is a mature medical imaging technique, which has become another important method for physicians to evaluate the AD stage of patients because of its safety, non-invasiveness, reproducibility, and sensitivity to morphological changes in the brain. During AD, the patient's brain atrophy gradually increases ^[16]. Based on this characteristic, physicians usually assess the patient's condition based on the degree of brain atrophy and the volume of gray and white matter in the sMRI images; however, due to the individual differences of patients, it is difficult for physicians to accurately diagnose the disease progression of patients.

3. Alzheimer's Diagnosis Based on Deep Learning

With the great popularity of deep learning, many researchers have tried to apply this approach to study the pathogenesis of AD, diagnose the stages of AD, and so on. For example, Suk et al. ^[17] combined MRI, PET, MMSE, and other data to train a classifier and reported promising experimental results in their paper; Ortiz et al. ^[18] achieved more than 90% accuracy on AD and Normal Control (NC) classification problems by training multiple classifiers followed by voting; Lian et al. ^[5] proposed a hierarchical fully convolution network to automatically identify local regions with the discriminatory ability in whole-brain sMRI, and on this basis, multi-scale feature representation was integrated to construct a hierarchical classification model for AD diagnosis.

So far, many studies have achieved good results on the classification problem of AD, but it is not enough to just solve the classification problem. The discrete label obtained by prediction lacks information on disease-stage changes. Few studies have applied deep learning methods to the problem of neurological function evaluation in AD; however, some studies use contrastive learning strategies to evaluate the severity of other diseases. For example, Li et al. ^[19] applied the contrastive learning strategy to continuous disease severity evaluation and disease change detection in retinopathy and osteoarthritis, and the output of the trained twin neural network achieved a correlation of more than 0.85 with the expert sort order on the 100-image test dataset ranked by experts; Li et al. ^[20] applied the contrastive learning strategy to the detection of psoriasis severity and located skin lesions in the image. The severity scores obtained by the trained network framework achieved better results than the severity index method commonly used in psoriasis. Contrastive learning has the potential to solve the problem of neurological function evaluation in AD. In general, deep learning has achieved better results than traditional methods in diagnosing the stage of AD; however, no deep learning method is available for the problem of neurological function evaluation in AD.

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