Research Article (Araştırma Makalesi)

A Simple MRI-Based Visual Guide To Differentiate Alzheimer's Disease From Mild Cognitive Impairment

Alzheimer Hastalığını Hafif Bilişsel Bozukluktan Ayırmak İçin Basit Bir MRI-Tabanlı Görsel Kılavuz

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Özet

Amaç: Bu çalışmada manyetik rezonans görüntülemede (MRI) hipokampus uzunluğunun görsel olarak değerlendirilmesi yoluyla hafif bilişsel bozukluk (HBB) ile Alzheimer hastalığı (AH) arasında ayrım yapmayı amaçladık.

Gereç ve Yöntemler: HBB ve AH tanısı alan hastalar hastane bilgi yönetim sisteminden geriye dönük olarak tarandı. Hipokampus yüksekliğinde azalma olup olmaması ile hipokampal atrofinin tanımlanması MRI ile değerlendirildi. Hipokampusta yükseklik kaybı olan hastalar klinik araştırmacı tarafından AH olarak sınıflandırıldı ve hastaların tanıları sistem üzerinden daha sonra kontrol edildi.

Bulgular: Çalışmaya AH (n=14) ve HBB (n=42) olan toplam 56 hasta dahil edildi. AH hastalarında HBB hastalarından anlamlı olarak daha fazla hipokampal atrofi vardı ($\chi 2$=6.222, SD=1, p=0.013).

Sonuç: HBB ve AH arasındaki ayırıcı tanı kompleks bir konudur. MRI'a basit bir bakış, klinik rutinde hekime kısa bir fikir verebilir.

Anahtar kelimeler: Alzheimer hastalığı, hafif bilişsel bozukluk, hipokampus, MRI

Abstract

Objective: To distinguish between mild cognitive impairment (MCI) and Alzheimer's disease (AD) by visual assessment of the length of the hippocampus in magnetic resonance imaging (MRI).

Material and Methods: Consecutive patients diagnosed with MCI and AD were retrospectively searched on the Hospital Information Management Systems. MRI was rated for hippocampal atrophy defining with and without loss of hippocampal length. Patients with loss of hippocampal height were classified as having AD by the clinical investigator, and the diagnosis of the patients was checked on the system.

Results: A total of 56 memory clinic patients with AD (n=14) and MCI (n=42) were included in the study. AD patients had significantly more hippocampal atrophy than MCI patients ($\chi 2$=6.222, df=0.13, p=0.013).

Conclusion: There is a complex issue in the differential diagnosis between MCI and AD. A simple glace to the MRI may give a brief opinion to the physician in the clinic routine.

Keywords: Alzheimer's disease, mild cognitive impairment, hippocampus, MRI

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INTRODUCTION

Alzheimer's disease (AD) is the most common progressive neurodegenerative disease and cause of dementia (1). In contrast, mild cognitive impairment (MCI) is a grey area of cognitive dysfunction that is difficult to diagnose, even among educated medical professionals. For instance, despite existing positive clinical findings, it is usually difficult to make a pinpoint diagnosis of whether the patient is diagnosed with AD or MCI at the time of the diagnosis (2). For instance, whether AD represents an increasing cognitive impairment and worse prognosis compared to a more stable MCI progress often provides insufficient clues to make a clear distinction. Similarly, while dementia represents a clinically relevant step toward increasing impairment and worse prognosis, there are many similarities in diagnosing and recognising MCI and mild dementia (3). These findings suggest the importance of advanced imaging (FDG-PET, fMRI, MR spectroscopy) and biological parameters (genetic tests, CSF amyloid examination) to overcome this hurdle in the differential diagnosis of dementia conditions. However, these diagnostic methods are expensive and time-consuming, making their usage difficult in everyday clinical practice.

Structural magnetic resonance imaging (MRI) focusing on specific disease-relevant brain regions is widely used as a prognostic and predictive tool in routine clinical neurology. Herein, a hippocampal volume measurement is one of the most studied methods used as a structural MRI biomarker of AD (4), even though it requires some automatized processes to come to a definite conclusion.

In light of these new approaches, the researchers use different approaches to evaluate of the hippocampi by combining the structural data with the clinical data obtained from the patient. Hence, a number of studies have suggested that the shape and texture of the hippocampi provide valuable diagnostic information irrespective of the volume of the hippocampus (5,6).

Here, we aimed to assess how accurately hippocampus length can suggest our diagnosis of dementia (Alzheimer's disease or MCI), which is easy to apply under everyday outpatient clinical conditions.

MATERIALS AND METHODS

A total of 56 patients (42 MCI and 14 AD) with memory problems applied to Alanya Research and Training Hospital, Department of Neurology, in the period 2020 and 2022 were included in this retrospective study. The inclusion criteria for the study as (1) a completed Mini-Mental Status Examination (MMSE), (2) MRI available, (3) a diagnosis of AD, MCI with a follow-up period with the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) by a neurologist. Excluded patients with (1) traumatic brain injuries and a history of severe psychiatric disorders or somatic diseases significantly affecting cognitive performance, and (2) dementia, except of AD and MCI.

The neuroradiologic investigation was performed on 1.5T MRI of the brain using coronal T1 weighted images through the medial temporal lobe, showing increasing loss of height of the hippocampal formation. Visual observations were taken on the slice that best depicted both hippocampal formations. MRI scans were assessed as loss of hippocampal loss, yes or no, by an independent clinician who was unaware of clinical information.

Statistical Analysis

The data were analysed by SPSS version 21.0 for Windows (SPSS Inc., Chicago, IL, USA). Statistical analysis of the data, as well as verification of normality, was performed using the Shapiro-Wilks test due to the small number of patients. Non-normally distributed data were analyzed with a Mann–Whitney U test and presented as median and interquartile range. The frequencies of categorical variables were compared using Pearson $\chi 2$ or Fisher's exact test, when appropriate. A value of $p < 0.05$ was considered significant.

The study was approved by the Alaaddin Keykubat University Clinic Research Ethical Committee (date: 20/07/2022, No:06-05). The study complied with the World Medical Association Declaration of Helsinki.

RESULTS

A total of 56 memory clinic patients were included in this retrospective study. 14 AD patients and 42 MCI patients who were diagnosed by a neurologist after a follow-up period were included in the investigation (**Table 1**). In respect of age, education (years), and gender, the two groups have not shown any differences ($p>0.05$). The mean MMSE scores were significantly higher in the MCI group than in AD patients (Mann-Whitney U Test, $p<0.001$). While 14 MCI patients out of 42 had hippocampal atrophy, the clinician has detected this sign in ten out of 14 AD patients. There was a significant relationship between AD and the presence of hippocampal atrophy ($\chi 2=6.222$, SD=1, $p=0.013$).

DISCUSSION

In this study, we tested the hypothesis of whether a rough evaluation of hippocampal height loss on MRI gives the clinician a brief idea of the differential

Table 1. The demographic and clinical data of the patients

Variables	MCI	AD	p
Gender, N (male/female)	19/23	5/9	0.755
Education, year, median (IQR)	11 (18)	6 (15)	0.074
Age, median (IQR)	66.60 (12.89)	64.07 (12.02)	0.522
Hippocampal atrophy (yes)/N	14/42	10/14	0.013*
MMSE, median (IQR)	25 (4)	19 (8)	<0.001**

Abbreviations: AD=Alzheimer's disease, MCI= Mild Cognitive Impairment, MMSE=Mini-mental Status Examination, N=Number of patients, SD= Standard deviation, *Pearson Chi-square test, p<0.05: Significant,**Mann-Whitney U test, p< 0.05: Significant

diagnosis between MCI and AD, which might help to tailor the diagnosis and appropriate therapeutic regimen. Herein, in contrast to various methods available to measure hippocampal atrophy, including even automatized or semi-automatized measurements such as linear measurements (7), manual volumetry (8), automated volumetry (9), and signal intensity-based scoring. We have provided reliable data for the clinical practice, which is easy to apply in neurology outpatient clinic conditions. In this respect, previous studies have consistently shown that a significant proportion of hippocampal atrophy may predict AD development in older people (10-12). However, despite their success in predicting the clinical outcomes, these methods are difficult to apply in routine clinical practice, suggesting the importance of simple visual assessment for facilitating the clinical pre-dementia and dementia diagnosis. For instance, the medial temporal lobe atrophy (MTA) score is one of the visual analysis methods for predicting AD using the Scheltens scale (7), based on visual estimation of the volume of the medial temporal lobe (13). These studies finally indicated that MTA scores showed significant predictive value for distinguishing AD from MCI and its subtypes. These studies finally concluded that critical structural changes, such as enlargement of the surrounding choroidal fissure and the temporal horn on the MRI, were important factors in defining the hippocampus height loss without errors.

The current study focuses on the hippocampal length instead of the whole temporal lobe. Herein, it is worth mentioning that a full examination of the temporal lobe requires many additional morphological parameters making it unsuitsable in the clinical routine (6,10). Since the hippocampal length is just not a specific volumetric or measurement method requiring no additional tools or education, we thought this assessment could be an easy approach to apply in neurology practice if suggested with positive findings.

Finally, we have found that hippocampal height is alone a sufficient parameter to associate with mild and severe AD patients separately. Despite this valuable data, our main limitation is that we have included only 56 patients, which should be replicated with a larger sample size in future studies. However, the strength of our research is that our approach requires no additional tools for hippocampal evaluation except for a simple visual assessment, which is of great value in neurology clinical practice in real-life hospital conditions. Additionally, our findings are important for making a precise diagnosis of MCI and AD, which might help reduce unnecessary treatment and increase the appropriate drug regimens. Additional research is needed to demonstrate the link between potentially inappropriate treatment and adverse health outcomes in MCI patients misdiagnosed as AD.

Ethical approval: The study was approved by the Alaaddin Keykubat University Clinic Research Ethical Committee (date: 20/07/2022, No:06-05). The study complied with the World Medical Association Declaration of Helsinki.

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