เครื่องมือสำหรับตรวจวัดภาวะสมองฝ่อเชิงปริมาตรแบบอัตโนมัติโดยเอ็มอาร์ไอสำหรับการตรวจวินิจฉัยโรคอัลไซเมอร์ในเวชปฏิบัติ

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บทคัดย่อ

การฝ่อของฮิปโปแคมปัสเป็นตัวชี้วัดทางชีวภาพที่มีความสมเหตุสมผลที่สุดของโรคอัลไซเมอร์และสามารถตรวจพบได้โดยเอ็มอาร์ไอเชิงปริมาตร ซอฟต์แวร์ของเอ็มอาร์ไอเชิงปริมาตรแบบอัตโนมัติได้ถูกพัฒนาขึ้นเพื่อแก้ปัญหาในการนำไปใช้ทางเวชปฏิบัติของวิธีการวัดด้วยมือและวิธีกึ่งอัตโนมัติ อย่างไรก็ตาม ยังไม่มีข้อมูลเกี่ยวกับความไวและความจำเพาะของการนำเอ็มอาร์ไอเชิงปริมาตรไปใช้วินิจฉัยโรคอัลไซเมอร์ในเวชปฏิบัติทั่วไป นอกจากนี้ การฝ่อของฮิปโปแคมปัสยังสามารถพบได้ในภาวะทางระบบประสาทที่มีปัญหาด้านความจำที่หลากหลาย ไม่เฉพาะในโรคอัลไซเมอร์เท่านั้น การฝ่อของฮิปโปแคมปัสที่ตรวจด้วยวิธีเอ็มอาร์ไอเชิงปริมาตรแบบอัตโนมัติควรนำมาใช้สนับสนุนการประเมินทางคลินิกมากกว่านำมาใช้แปลผลแบบเดี่ยว

คำสำคัญ: เอ็มอาร์ไอเชิงปริมาตร โรคอัลไซเมอร์ การฝ่อของฮิปโปแคมปัส

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Tools for fully automated volumetric measurement of cerebral atrophy from MRI for routine clinical practice in diagnosing Alzheimer's disease

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Abstract

Hippocampal atrophy is the best validated biomarker of Alzheimer's disease (AD) and can be detected quantitatively by volumetric magnetic resonance imaging (vMRI). Fully automated vMRI software was developed to overcome many clinical translating hurdles of the manual and semi-automated methods. However, there are no data of sensitivity and specificity of vMRI to be used as a tool to diagnose AD in general clinical setting. Moreover, the hippocampal atrophy can be found in various neurological conditions with memory impairments, not only the AD. This hippocampal atrophy results from vMRI should be accompanied by/with the clinical evaluation rather than be used alone.

Keywords: Volumetric magnetic resonance imaging, Alzheimer's disease, Hippocampal atrophy

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Introduction

Neurodegenerative disease such as Alzheimer's disease (AD) is associated with a characteristic pattern of neuropathology spreading in the brain[1]. The progressive accumulations of abnormal proteins both amyloid-beta (Aβ) and hyperphosphorylated tau were found in the AD brain. This pathology occurs early in medial temporal lobe (entorhinal cortex and hippocampus) followed by progressive neocortical change[2]. These changes are accompanied with regional cerebral atrophy that can be detected noninvasively by volumetric magnetic resonance imaging (vMRI)[3]. Hippocampal atrophy is the best established and validated biomarker because it occurs in the early stage of disease and it is easy to identify and recognize the boundary on coronal MRI slices[4]. Methods of quantified hippocampal volume can be semi-quantitative visual rating scales or quantitative labor intensive manual tracing. Hippocampal volume is associated with the stages of AD and prodromal AD; otherwise known as mild cognitive impairment (MCI) and the conversion from MCI to AD[5]. Inclusion of biomarker e.g. hippocampal volume in the evaluation of the patient with memory complaint could improve the accuracy of early diagnosis of AD as in the proposed new criteria for early diagnosis of this disease[6].

Despite research supporting the value of vMRI in evaluating cognitive impairment, translation to clinical practice faces many hurdles[7]. There is no standard imaging protocol to select the appropriate clinical MRI parameters. The three-dimension output requires more scanning time and more data storage. vMRI procedures need high grey-white contrast that is not essential in general radiological practice. Spatial dimension varies across the scanners built by different manufacturers, versions, equipments and software[8]. The corrections of spatial distortion, motion or other artifacts are crucial in the volumetric procedures. Manual and semi-automated methods still require expert. Thus, inter- and intra-operator variability limits the generalizability. Application into clinical workflow which is related to images format and output system is another important issue in routine clinical practice.

Many clinical translating hurdles have been overcome by using the large-scale, multicenter longitudinal neuroimaging biomarker study. One such example is the Alzheimer's Disease Neuroimaging Initiative (ADNI) which had included 800 elderly subjects comprising 200 elderly controls, 400 amnestic mild cognitive impairment (aMCI) patients and 200 patients with early-onset AD[9]. This study has tried to develop the standardized and optimized imaging procedures aimed at bringing them to clinical practice. NeuroQuant (Cortechs, Inc., CA, USA), a US FDA-approved image analysis software provides fully automated volumetric measurements of several brain structures[10]. This fully automated vMRI software has provided standardization of image acquisition, correction of spatial distortions, improved data throughput, the possibility of generating normative database of brain structures volumes, reduced reliance on high-level expertise and decreased inter-operator variability. Moreover, these measures have been validated against the manual segmentation method[11].

However, translation of such tools to routine clinical practice still faces some critical issues. The most important problem is that there are no data of sensitivity and specificity using these tools for diagnosing dementia such as AD in general clinical setting. Furthermore, the processes using these vMRI procedures still require qualitative visual review by an expert to detect significant artifact and gross brain abnormalities in segmentation errors[12]. Concerns

about extra expense and time consumption for additional processes of the software are the other issues to be considered as well[13].

Recently, there was a clinical practice-based study using fully automated vMRI for diagnosing dementia of Alzheimer's type[14]. One hundred and twenty-two elderly patients referred to the memory clinic at Oslo University Hospital were analyzed using NeuroQuant to quantify the volumes of various brain structures. Two doctors separately made clinical diagnosis of dementia types using ICD-10 criterion with blindness of the MRI results. The receiver operating characteristic (ROC) analysis and area under the curve (AUC) calculation were performed. The results showed that the mean age was 67.2 years, and 60 percent were men.

Sixty-three patients were diagnosed with dementia of Alzheimer's type, 24 patients were dementia with other types, 25 patients had MCI and 10 patients had subjective cognitive impairment (SCI). This volumetric MRI method could distinguish patients with Alzheimer's dementia from those without dementia, but could not distinguish from those with other types of dementia. Brain structures in which volumes were significantly different between patients with Alzheimer's dementia and those without dementia included the hippocampus, amygdala, putamen, anterior cortex, cortical gray matter, lateral ventricles and inferior lateral ventricles. The best threshold proportional volume of the hippocampus per intracranial cavity which could be used to distinguish patients with AD from those without dementia was 0.48 percent with 74 percent sensitivity and 71 percent specificity. Because the vMRI procedure cannot distinguish the AD patients from those with other types of dementia, it should support the result of clinical evaluation rather than using its result alone. This result has been correlated with the knowledge that the hippocampal atrophy can be found in various neurological conditions with memory problems. These include frontotemporal dementia (FTD)[15], epilepsy[16], schizophrenia[17], traumatic brain injury[18] and depression[19]. This study has given the valuable information for consideration in routine clinical use because the research was conducted in real clinical setting. The diversity of patients are seen and the pretest probability of clinical criteria is low as compared with the laboratory-based research[7].

Even though the fully automated vMRI tools have been still facing some problems in translation to routine clinical practice, there has been a guidance for using these tools supporting the clinical diagnosis of patients with memory problems[7]. Firstly, if the clinical impression is neurodegenerative disease, volumetric data should be used as supportive evidence. Secondly, if the clinical impression is the absence of neurodegenerative disease, normal values from vMRI should be used to reassure the patients who worry about their health. Finally, if the clinical impression is early-onset AD but the vMRI values show normal or minimal neurodegeneration of memory structures, the less common or reversible causes of memory impairment should be investigated thoroughly e.g. medication side effects and depressive pseudodementia.

Conclusion

It would seem that the tools for fully automated vMRI are still not ready for routine clinical use in diagnosing the Alzheimer's disease. However, these tools could be used as supporting information for clinical diagnosis. More researches with these measures in relatively unselected patients seen in clinical practice are needed to translate such scientific knowledge into routine clinical practice.

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