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A CASE STUDY OF BRAIN VOLUME REDUCTION IN MULTIPLE SCLEROSIS

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ABSTRACT

The development of sophisticated magnetic resonance imaging techniques and software for medical imaging processing and analysis has led to a significant progress in multiple sclerosis research and clinical care. The measurement of brain volumes provides a quantitative representation of damage, thus facilitating the objective follow-up process. The parameters obtained, though not being used routinely in clinical practice, are more and more often applied in clinical studies. The amount of whole brain and regional atrophy, estimated from serial scans, is considered important not only for disease progression, but also for cognitive dysfunction which is common in multiple sclerosis. In this paper we describe a volumetric study of two magnetic resonance scans of a patient with relapsing-remitting multiple sclerosis, performed 16 months one after the other, and analyzed using FSL SIENA software. Analysis demonstrated brain volume reduction of 1.7% between the two scans. We discuss the advantages of the method and its possible clinical applications.

Keywords: Brain Volume, Brain Atrophy, Magnetic Resonance Imaging (MRI), Multiple Sclerosis

INTRODUCTION

The conceptions about the nature of multiple sclerosis (MS) and the implicated pathological processes have evolved significantly from the classical era of Charcot to present day. The initial conception of an inflammatory and demyelinating disease with exclusive damage to the white brain matter has been replaced by more recent ones. They not only consider the lesions of the gray matter, but discuss their possible leading role for the irreversible disability and cognitive impairment that develop in the course of the disease [1].

Since the introduction of magnetic resonance imaging (MRI) in research and in the diagnostic process and follow-up of patients with MS, new techniques for quantitative assessment have been sought. This would not have been possible without the development of information technology and the creation of powerful specialized software products. The measurement of brain volume, white and gray matter, and lesions, is able to provide a quantitative representation of the impairment [2]. The pathological process can thus be followed-up using serial measurements at specified time intervals. Such option could be very important in terms of assessing the efficacy of treatment. Though these measurements are not currently used in routine clinical practice, they play an important role in clinical trials of potential new drugs [2, 3].

The pathological process in MS leads to the formation of focal alterations of the central nervous system which can be visualized on routine structural MRI [4]. However, if some areas of white and gray brain matter appear normal on conventional magnetic resonance imaging, they may also be affected by the pathological process. They are described as "normal appearing white matter, NAWM" and "normal-appearing grey matter, NAGM", respectively. These areas are subject to alterations which are "invisible" through routine assessments, but are of great importance for the development of brain atrophy in MS. The quantitative measurement of general and regional brain atrophy in MS is an essential addition to the assessment of cognition which is becoming more and more important in research and practice [5]. In fact, a certain degree of brain atrophy, demonstrated as a reduction of brain volume by computerized analysis of structural magnetic resonance images, may be present in healthy persons. Giorgio et al. have described a progressive decrease of gray matter volume after middle age, as well as a decrease of white matter volume beginning in younger adulthood [6]. But while in healthy individuals the loss of brain volume reaches 0.3% per year, in patients with MS it is between 0.6% and 1% [4]. Atrophy begins early in the course of the disease. Its development has even been described in patients with clinically isolated syndrome, followed up for a one-year period, at the end of which they have conformed to the diagnostic criteria for multiple sclerosis [7].

Current methods used to assess whole-brain atrophy in patients with MS can be classified into 2 groups based on their reliance on segmentation and registration algorithms. Segmentation-based methods employed to measure whole-brain atrophy in MS include the brain parenchymal fraction, the index of brain atrophy, the whole-brain ratio, the brain

to intracranial capacity ratio, and SIENAX, among others. Current registration-based methods used to measure whole-brain atrophy in MS include the brain boundary shift integral, SIENA, statistical parametric mapping, template-driven segmentation, and voxel-based morphometry [8]. Methods for measuring brain atrophy can also be divided into manual, semi-automatic and automatic, based on their level of independence of human intervention during image processing. Among the automatic methods which may prove useful not only in research but in clinical practice is SIENA [9], part of FSL [10]. FSL is a comprehensive library of analysis tools for MRI, functional MRI, and diffusion tensor imaging data, written mainly by members of the Analysis Group, FMRIB, Oxford, UK. Most of its tools can be run both from the command line and as "point-and-click" graphical user interfaces. SIENA is the routine which estimates percentage brain volume change (PBVC) between two input images, taken of the same subject, at different points in time. It calls a series of FSL programs to strip the non-brain tissue from the two images, register the two brains (under the constraint that the skulls are used to hold the scaling constant during the registration) and analyse the brain change between the two time points. It is also possible to project the voxelwise atrophy measures into standard space in a way that allows for multi-subject voxelwise statistical testing [9, 10].

CASE REPORT

We describe a volumetric study of two 3D T1 MRI scans of a patient with relapsing-remitting multiple sclerosis, performed 16 months one after the other, and analyzed using SIENA. The patient is a 34-year-old female, E.K. Her first symptoms had appeared 2 years before the first presentation to the clinic: numbness of the extremities, mild weakness, and imbalance. Two relapses had been described thus far. The initial clinical exam was normal. Neurological exam showed mild paraparesis, hyperreflexia, bilateral Babinski's sign, mild locomotor and dynamic ataxia. Expanded disability status scale (EDSS) score was 2.0. The patient conformed to the clinical diagnostic criteria for relapsing-remitting multiple sclerosis [11]. MRI was performed, showing multiple subcortical white matter lesions, hypointense on T1 and hyperintense on T2, in line with the diagnosis of MS (Fig. 1A). The patient was scheduled for clinical and MRI follow-up, and 16 months later she presented to the clinic for a second time. No relapses had been documented since the previous visit. Clinical and neurological exams showed no dynamics. A second MRI scan was performed (Fig. 1B). 3D T1 series from both scans were processed through SIENA in order to calculate the difference in brain volume between the two time points. After processing by the different routines, a final brain edge movement image was produced (Fig. 2) and estimated PBVC was output. Results showed brain volume reduction of 1.7% between the two MRI scans.

Fig. 1. T1 3D MRI scans: baseline (A) and after 16 months (B)

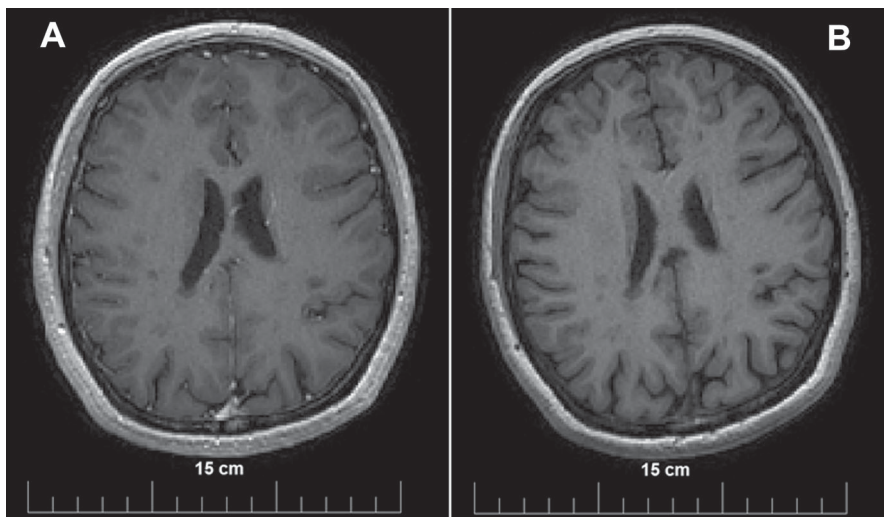
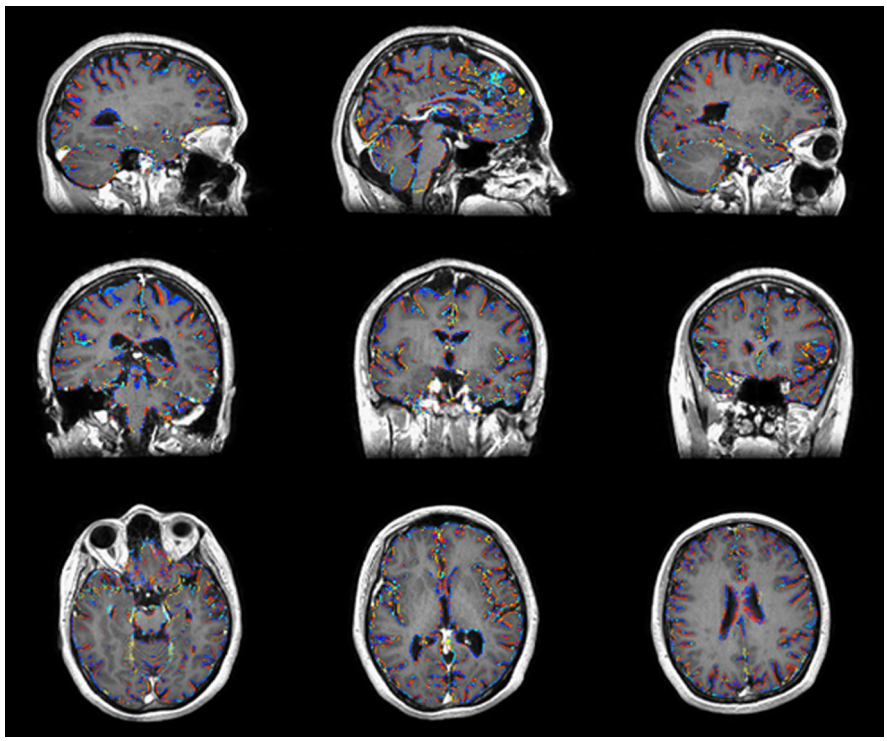


Fig. 2. Brain edge movement image (SIENA output)



DISCUSSION

For the purpose of calculating PBVC between 2 time points in our patient with MS we used SIENA, a relatively straightforward method. While currently applied in research and clinical trials, such techniques constantly improve, becoming easier and more reliable, and will most probably be included soon in routine assessment procedures. In our case we found brain volume reduction of 1.7% between the two scans (16 months). This value is slightly higher than what we expected according to published data [4]. Our findings, though limited to a single case, are in line with the conception of progressive brain tissue loss and neurodegeneration in MS. We discuss possible bias due to the lack of manual correction and to the slight discrepancy between head positions on the two MRI scans. An interesting fact is that despite the rather high PBVC, no new clinical symptoms or increase of disability were noted in our patient. This could be explained by the theory for disagreement between clinical and neuroimaging findings in MS, known as the "clinico-radiological paradox" [12], though it is usually discussed in relation with the load of demyelinating lesions rather than with atrophy. According to some authors, unlike lesion based measures, volumetric MRI assessment of brain atrophy shows a strong correlation with functional outcome, and the presence of early atrophy predicts a worse disease course [13]. Whether the brain volume reduction in our patient will prove to be a marker of further functional deterioration remains a question which will be answered after follow-up. In any case, a single clinical example is not sufficient for the purpose of establishing dependencies, and larger cohorts are needed. An interesting topic for investigation and discussion in such studies is the correlation of PBVC with changes in cognitive functions. Though at this stage automatic brain volume measurement in a single clinical case as the one presented in this paper may not be accurate for practical diagnostic or prognostic purposes, this will undoubtedly change with the constant development of technology and knowledge, and with the increasing number of studies focusing on this exciting topic.

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