



Intercontinental validation of brain volume measurements using MSmetrix

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Abstract

Background: Brain volume assessment has become an important outcome within research and treatment of multiple sclerosis (MS). MSmetrix (Icometrix) has been developed specifically for patients with MS. The original healthy, 'normal' population used for determination of the acceptable brain volume data consisted mainly of Europeans.

Methods: In the present study, results from 295 completely normal magnetic resonance imaging scans from Brazilian subjects were plotted against the original results in MSmetrix.

Results: With regard to whole brain volume, only 2% of the healthy adult subjects from Brazil were below the 5th percentile of the graph, and for grey matter volume, only 3% of the subjects were below the 5th percentile of MSmetrix standards.

Conclusion: MSmetrix may be used across different populations.

Keywords

Multiple sclerosis, brain volume, brain atrophy, magnetic resonance image

Introduction

MSmetrix is an automated method for measuring whole-brain and grey matter volumes and atrophy based on anatomical magnetic resonance imaging (MRI). MSmetrix has been specifically designed to measure atrophy in patients with MS, using a database of MRIs on normal, healthy subjects as controls.¹ MSmetrix is currently approved by the US Food and Drug Administration for the purpose of assessing the volumes of the whole brain, grey matter and demyelinating lesions, as seen on MRI. The tool was developed in Belgium and the normal population used for the database was mostly European and North American, thus providing standard acceptable volumes for the whole brain and for the grey matter for healthy subjects over their life spans.²⁻⁵ Against this 'normal' data, brain volumes of patients with multiple sclerosis (MS) can be analyzed in order to make volumetric assessments (both on a cross-sectional and on a longitudinal basis) of brains with MS disease. Thus, brain atrophy among these patients can be assessed at any stage of the disease and plotted against the volume that would be considered normal for that particular age, sex and head size.⁶

The aim of the present paper was to analyze data from normal, healthy subjects on another continent, in order to assess whether the values obtained in the 'normal' MSmetrix population can also be considered

to be standard for a Latin American group of control subjects.

Methods

This project was approved by the Ethics Committee of Universidade Metropolitana de Santos, under the registration CAAE 59870516.3.0000.5509. Data from subjects undergoing MRI for a variety of reasons and without specific structural neurological diseases (headache, insomnia, dizziness, etc.) were used in the present study. All subjects were Brazilian and the MRI report, given by an expert in neuroradiology was that of a completely normal examination. Whole brain volume and grey matter volume from each of these subjects were plotted against the standard, normal values already included in the MSmetrix population graphs.

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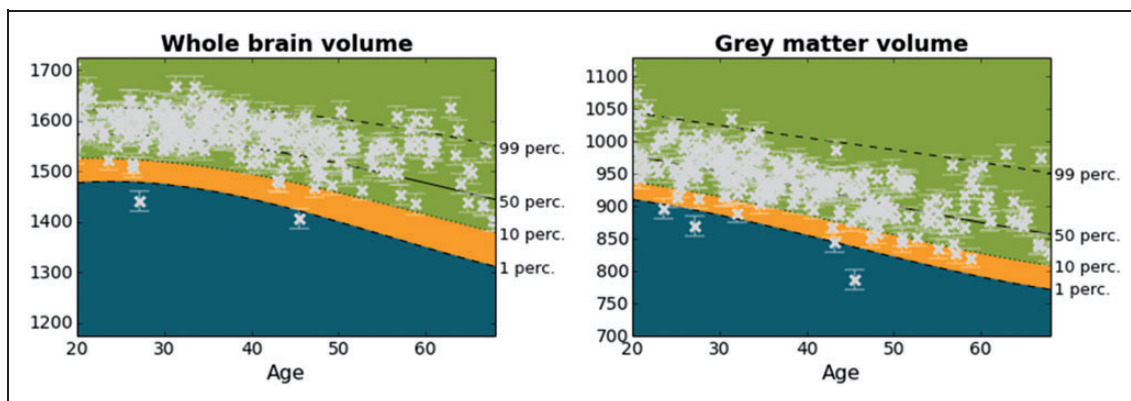


Figure 1. Results from normal Brazilian subjects (individually plotted as white crosses) against the database of control subjects from MSmetrix. Results are presented and volume (mg) of total brain and of grey matter.

No signed consent was required for the project and confidentiality of all data was guaranteed to the Ethics Committee.

The reported brain volumes for whole brain and for grey matter were normalized for head size to compensate for the physiological differences within the population. The normalization is based on a factor obtained from affine registration to standard brain atlases. Tissue class segmentation into white matter, grey matter and cerebrospinal fluid was performed on the skull stripped T1-weighted image using an expectation maximization algorithm.⁷ The algorithm optimizes a Gaussian mixture model on the image intensities that is guided by the probabilistic tissue priors. A spatial consistency model based on a Markov Random Field (MRF) is also included in the algorithm. Finally, the volume for whole brain plus grey matter volumes was extracted from these segmentations.

Results

A total of 295 Brazilian MRI scans were included in the study. The group consisted of 92 men and 203 women, with a median age of 35 years (range: 5–78 years). All reports were completely normal. Data from two subjects could not be used due to technical issues and, therefore, the final population consisted of 293 individuals. The plotted results for whole brain volume and grey matter volume for each subject are shown in Figure 1. All volumes were considered after normalization for head size, in accordance with the MSmetrix program specifications.

The whole brain volumes from these Brazilian subjects had an overall trend towards larger, higher results than those in the original MSmetrix healthy population graph. Only 2% of the adult subjects were below the 5th percentile of the graph, 77% of the subjects were above the median and 23% of the subjects were above the 95th percentile of the graph.

Regarding grey matter volume, the Brazilian subjects were not significantly different from the MSmetrix population graph, and the trend was still

towards slightly larger values: 3% of the subjects were below the 5th percentile of MSmetrix grey matter volumes, 60% of the subjects were above the median value and 6% were above the 95th percentile.

In order to investigate whether there was any dependency on age or sex for the trends noticed above, the subjects were divided according to sex and age (younger or older than 40 years). For each subgroup, the percentiles of whole volume and grey matter volume were established. The Kolmogorov–Smirnov two-sample statistical test for comparison of sample distributions showed that there were no significant differences between the percentiles obtained in these various subgroups (i.e. in comparisons of males versus females; younger versus older adults; younger females versus older females; and younger males versus older males).

Discussion

There was no overall tendency towards lower brain volumes in the Brazilian population. This result is reassuring, since a general trend towards or significant findings of smaller volumes in a different population might mean that it would not be possible to use MSmetrix worldwide. This does not seem to be the case, irrespectively of age or sex. However, the study was performed in a Brazilian population and extrapolating the results to all other populations requires caution.

Conclusion

The MSmetrix database of normal subjects can be used in different populations. The plotted results from MSmetrix reports do not need to be adjusted for different countries, given that the ‘normal’ database seems to be acceptable in at least two very different populations.

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Conflict of interest

The authors have no conflicts of interest to declare. MSMetrix is a trademark registered from June 2015 under the number IRDI-3115170 as software and equipment for the processing of biomedical images, meta data and patient data for research and diagnosis.

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