Research Article

Multiple sclerosis and eye: Geometric complexity of the optic nerve head microvascularity—a pilot study

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Abstract

Multiple Sclerosis (MS) is a progressive neurodegenerative disease of the central nervous system characterized by focal demyelinating lesions in the white matter of the brain or spinal cord. When MS affects the nerves in a person’s eyes, it can cause Optic Neuritis (ON). We have investigated the microvascular pattern of the nerve head performing the evaluation of its fractal dimension (geometric complexity). Mean geometric complexity of the optic nerve head microvascularity in the affected eye in patients with multiple sclerosis resulted higher than in control normal subjects (p<0.01), and, moreover, the unaffected eye in patients with multiple sclerosis showed a geometric complexity that was not significantly different from that of the affected eye and higher than in control normal subjects (p<0.01). These data, if confirmed in a higher number of patients, could show a characteristic microvascular pattern of the optic nerve head in subjects affected by multiple sclerosis, giving us a possible tool to identify earlier subjects that can develop multiple sclerosis.

Introduction

Multiple Sclerosis (MS) is a progressive neurodegenerative disease of the central nervous system characterized by focal demyelinating lesions in the white matter of the brain or spinal cord. Lesions cause a range of varying symptoms depending on the location of lesions, and can include changes in autonomic, motor or sensory functions [1,2]. In particular, for the purpose of this article, MS often presents early ocular manifestations secondary to inflammatory demyelination of the visual pathway, also causing optic neuritis [3]. We can recall that a majority of patients experience at least one episode of ocular involvement in the course of their disease [4,5].

Fractal analysis is emerging as a powerful tool to perform differential diagnosis and prognosis of the patients in pathology as well to improve the effectiveness and safety of patient care [6–8]. A lot of papers focused the usefulness of fractal analysis in the study of the retinal vessels [9–14]. In this paper we present a study of the microvascular pattern of eyes in MS patients, studying by fluorangiography and fractal analysis the optic nerve head microvascularity.

Materials and methods

Patients

Patients with unilateral optic neuritis without optic disc oedema (ON) affected by MS (n=6) were recruited from the Department of Medicine, Surgery and Neuroscience at the University of Siena. Three patients were female and three were male (mean age=32.3 years). In the control group, six patients were female and seven were male (mean age=48.7 years).

Each patient underwent a complete neuro-ophthalmic examination, including assessment of visual acuity, colour vision, papillary reaction, slit-lamp examination, applanation tonometry, Goldman visual field testing, visual evoked potentials, dilated fundoscopy and fluorescein angiogram. All patients were examined using a fluorescein angiogram within the first two weeks after they reported the first symptoms and before treatments; all patients gave informed consent. Fluorescein angiogram of normal subjects (n=13) were used as controls. The protocol for this research project was approved by the Ethics Committee of the University of Siena and it conforms to the provisions of the Declaration of Helsinki, 1955 (as revised, Edinburgh, 2000).
**Image analysis**

Static fluorescein angiogram was performed (IMAGEnet 2000, v.2.0, Topcon). The early, intermediate and late phases of the angiogram were studied. Images of the early venous phase of the angiogram (around 20 seconds) gave the best visualization of the optic disc vessels and were saved (Figure 1). The same magnification was used for each subject.

A manual outline of the trajectories of the two-dimensional microvascular network was performed down to microvessels of 20 micron of diameter, processed to threshold the vessel network without background interference and converted into an outline of one pixel (Figure 2) by means of Jmicrovision, http://www.jmicrovision.com and Image Analyzer softwares http://www.fosshub.com/Image-Analyzer.html.

**Geometric complexity, D0**

Briefly, the skeletonized image is covered by nets of square boxes, from 10 pixel to 130 pixels wide and the amount of boxes containing any part of the outline is counted. A log-log graph is plotted on the side length of the square against the number of outline-containing squares. If our image is fractal, a logarithmic linear segment appears: the slope of the linear segment of the graph represents the local fractal dimension [15] of the image (Figure 3). The correlation coefficient of the straight line was always above a value equal or greater than 0.99, thus justifying our fractal approach. The methodology was implemented using Benoit 1.3 software (TruSoft Int’l Inc, http://trusoft-international.com/html) and validated measuring computer generated Euclidean and fractal shapes of known geometric complexity. Inter- and intra-observers errors were <3%.

**Statistical analysis**

Mann–Whitney’s U test was used in order to compare the fractal indexes between the groups and to ascertain the statistical significance; regression analysis was used to ascertain the log-log plot linearity.

**Results**

Geometric complexity of the optic nerve head microvasculartiy (affected eye) in MS patients showed a higher value than in normal subjects (Figure 4, Table 1).

Geometric complexity in unaffected eyes of the MS patients was not significantly different from that of the affected eye (Figure 5, Table 2). Both the eyes, affected and unaffected one, revealing a geometric complexity higher than in normal control subjects, \( p<0.01 \) (Tables 1,2).

**Discussion**

Fractal approaches grow in importance, year by year. Fractality, the geometric concept related to highly irregular shapes that originates from simple iterated function with non-integer, or fractional, dimensions and a property known as...
ON patients, being the risk of progression to multiple sclerosis within two years of an acute attack of ON. It is important to establish differential diagnosis among the different causes of ON [3], in order to treat patients earlier.

Our results show that the mean geometric complexity of the microvascular pattern of the optic nerve head is higher in the eye affected by ON than in the eye of control subjects, according to our previous results [16,17]. Moreover, in these MS patients the eye not affected by ON, also, showed a higher geometric complexity of optic nerve head microvasculature than in the normal subjects, overlapping the data of the eye affected by ON. These data show a characteristic microvascular pattern of the optic nerve head in subjects affected by multiple sclerosis: if confirmed in a higher number of patients it can give us a tool to identify earlier subjects that can develop multiple sclerosis.

### References


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