EVALUATION OF BRAIN COMPLEXITY IN PSYCHIATRIC PATIENTS USING FRACTAL GEOMETRY

Letizia Squarcina[1], Alberto De Luca[2], Marcella Bellani[1], Paolo Brambilla[3,4], Federico E Turkheimer[5], and Alessandra Bertoldo[2]

[1]Section of Psychiatry, AOUI Verona, Verona, VR, Italy, [2]Department of Information Engineering, University of Padova, Padova, PD, Italy, [3]University of Udine, Udine, UD, Italy, [4]Dept. of Psychiatry and Behavioral Sciences, University of Texas Medical School, Houston, TX, United States, [5]King's College London, London, United Kingdom

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TARGET AUDIENCE

This work is addressed to MRI scientists and clinicians who are interested in non-standard analysis of structural MRI images

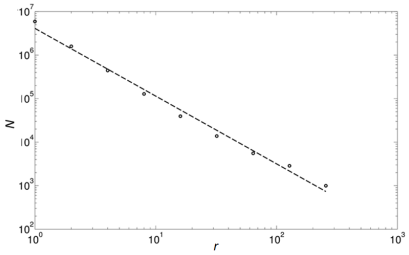

Fig. 1 – Linear regression of N on r (slice 55, subject 1 (HC))

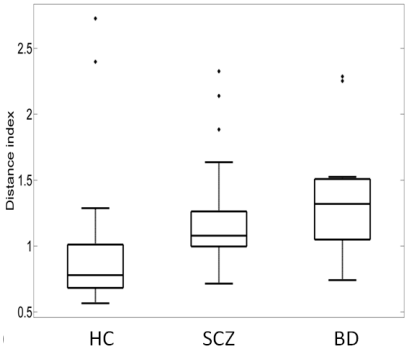

Fig. 2 - box plots of the distance indexes of the three groups in respect to the healthy average FD

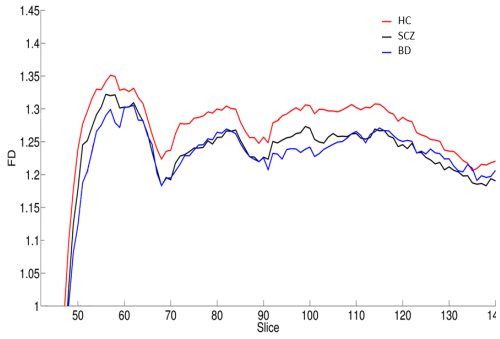

Fig 3 - FD values slice by slice on the frontal lobe. Lines represents the group average values.

PURPOSE

With this study we use fractal geometry to analyze T1 data of patients affected by schizophrenia (SCZ) or bipolar disorder (BD), with the aim of distinguishing between healthy and pathological brains using the complexity of brain structure, in particular of gray matter (GM) as a marker of disease.

METHODS

Dataset: 39 healthy volunteers (HV, all Caucasians, 28,36 +/- 5,43 years old), 25 subjects affected by schizophrenia (SCZ, all Caucasians, 34,96 +/- 7,69 years old) and 11 patients affected by bipolar disorder (BD, all Caucasians 41 +/- 8,91 y.o.) participated to the study. MRI data were obtained using a Siemens 3.0 Tesla Magnetom Allegra MRI scanner (Siemens Ag). T1 data (matrix 256× 256x150; voxel size 0.94x0.94x1 mm^3; TR = 2.3 ms; TE = 3.93 ms) were acquired.

Analysis: T1 images were skull-stripped, segmented into GM and aligned to the MNI 1 mm template using FSL[1]. Frontal Lobe, Occipital Lobe, Parietal Lobe and Temporal Lobe were derived from the MNI structural atlas[2] and superimposed on patients data. The computation of fractal dimension (FD) of the brain cortex and its substructures was based on the box-count algorithm[3], which consists in covering the binarized (i.e. segmented) image with boxes of increasing size and calculating then the linear regression of the logarithm of the count of non-empty boxes N on that of the size of the box r. We modified this algorithm, with the aim of avoiding the segmentation processing step, weighting the count of every non-empty box with the maximum grey level inside the considered box. Moreover, to increase sensitivity to local structural changes, instead of considering a single FD value for each slice, we considered 5x5 blocks and computed their FD taking into account the surrounding $n \times n$ voxels, with $n \in [15,20,25,30,35,40,50,65]$. The final FD value of the slice is computed by averaging the FD values of the blocks. We verified that the regression of N on r resulted in a straight line and considered the residuals of the linear fit. The parameter n is a key value for the global performance of the algorithm. To assess the best value to be used in in our study, we decided to use the value that maximized the distance between a subset of 5 healthy subjects and 5 schizophrenia affected subjects. To quantify the difference in FD between subjects and groups, we defined a distance index d as in:

$$d(x,y) = \sum_s |x(s) - y(s)|$$

where x and y are the vectors containing the FD values of the slices of the two subjects; and s is the slice level. To have reference values in comparing healthy with pathological brains, we built a template by averaging FD values of the healthy volunteers data. Standard deviation (SD) was evaluated and used to create a confidence interval of 2SD. We also performed a slice by slice t-test to assess the difference at slice level between the three groups.

RESULTS

As can be seen in Fig. 1, the behavior of N in respect to r can be approximated with a straight line. Residuals of the linear fit have a mean and standard deviation close to 0 (order fo 10^{-15}). A similar procedure was applied to the sub-structures, leading to the same result. The value of n strongly influences the differences in FD between and within the groups. We chose to adopt n=35 through all the study, as this value, in most structures, lead to the highest separation between the groups and reduced internal differences of the healthy group. Consistent average FD values were found across all the structures in HC, ranging from 1.41 (± 0.05, temporal lobe) to 1,45 (± 05, occipital lobe). Whole brain FD was 1,63 (± 0.08). FD on the whole brain resulted in d increased of 27% for the SCZ group and 53% for the BD subjects in respect to the HC whithin-group d. FD values resulted lower in pathological subject in respect to HCs, especially in frontal lobe (Fig. 3). The t-test comparing the average FD values slice by slice resulted in 94 different slices out of 140 for the HC versus SCZ, and 75 different slices for the HC versus BD, both with an average p-value of 0.005.

CONCLUSION AND DISCUSSION

In this work, we evaluated a new method for the characterization of pathological brains. We avoid segmentation, which is time consuming and can introduce errors and artifacts, and manual checking of results. Most publications on fractals use a global approach to compute FD, hence resulting in a single value for each considered structure. Many neurological pathologies can produce modifications at local level, which are discernible with our method. We found noticeable differences in FD values between healthy and pathological subjects: Both pathological groups showed statistically smaller FD values than healthy subjects. Frontal lobe resulted to be markedly affected by structural modifications: this confirms previous literature findings[4]. This method also allows considering every patient individually, thus not limiting the study to group level, as it happens in VBM or TBSS.

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