EFFECT OF MINICOLUMNAR DISTURBANCE ON DYSLEXIC BRAINS: AN MRI STUDY

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ABSTRACT

The minicolumn is generally considered the basic unit of the neocortex in all the mammalian brains. Enlargement of the cortical surface is believed to occur through the addition of minicolumns rather than a single neuron. This study aims at testing the hypothesis that brain developmental disorders can be diagnosed and analyzed in terms of the minicolumnar disturbance. To do this, we propose to correlate the pathological findings in terms of the minicolumnar structure to the MRI findings in terms of volumetric analysis.

1. INTRODUCTION

Brain function research suggests that the minicolumn, not individual neuronal cells, are the basic unit of operation in the brain. For example, Mountcastle[1] reported “The effective unit of operation in such a distributed system is not the single neuron and its axon, but groups of cells with similar functional properties and anatomical connections”. The most highly respected textbooks of neurobiology consider the vertical organization of the cortex a basic concept of neurobiology, commonly referring to it as the columnar hypothesis.[2] Minicolumns are defined as vertical organization of neurons arranged in the neocortex. Minicolumns, rather than the neurons, are believed to be the basic unit of the brain, i.e., the enlargement of the neocortex, in the phase of the development of human brain, occurs through the addition of minicolumns rather than single neurons. And, on the contrary, in the aging phase, the neocortex loses whole minicolumns not some randomly scattered neurons. Thus, any disturbance in the number, structure or organization of minicolumns will affect the development of the brain and, as a result, its functionality. According to this, we hypothesize that the brain developmental disorders and aging disorders can be diagnosed and analyzed in terms of the analysis of the number as well as the organization of the minicolumns in the neocortex.

This project aims to find a link between the pathological studies or the microscopic domain work and a macroscopic framework represented by a non-invasive imaging technique. Therefore, the major objective of this paper is to correlate the pathological findings vis-a-vis the minicolumns to the MRI findings represented by the volumetric analysis of the neocortex.

The paper will be organized as follows; Section 2 will explain the problem, the data set, MRI protocol and the hypothesis that should be proven. Section 3 will explain the methodologies used for brain extraction, segmentation and white matter parcellation. Section 4 will show the experimental results.

2. PROBLEM STATEMENT, MOTIVATION AND DATA SET DESCRIPTION

Autism and dyslexia are two of the most complex developmental disorders that affect children. Dyslexia is characterized by the failure to develop age appropriate reading skills despite normal intelligence level and adequate reading instructions [3]. However, autism is a more complex disease characterized by social interaction, language, behavior and cognitive learning.[4]

One of the major causes of developmental disorders is that some parts of the communications network of the brain fails to perform its tasks properly. Hence, most of the previous MRI studies [4, 5, 6] focused on investigating morphometric brain changes through some certain structures such as the corpus callosum, brain stem and other structures.

The basic contribution is that it analyzes the morphometric changes in the normal and dyslexic brains through investigating the minicolumnar organization rather than structures. The analysis is based on the fact that the failure to develop proper communication between the different parts of the brain can be caused by the disturbance in the minicolumns. Meanwhile, postmortem studies have shown that a common feature to both disorders is a disturbance with the minicolumns. These studies indicate that within the general population, dyslexia and autism exist as opposite tail ends within the normal distribution of the minicolumnar widths [7]. This can be illustrated in Fig. 1.

![Fig. 1. Illustrating the idea of obtaining the moving the outer contour using the signed distance function](image_url)

Thus, dyslexia, the widths of the minicolumns are generally
larger than the minicolumns in normal control cases and the brain is proved, pathologically, to have less number of minicolumns. The converse is true in autism. In the normal brain, the minicolumnar interconnectivity is on the order of 1000 [8]. Therefore, the number of connections (white matter) would be highly affected by any change in the number of minicolumns. Therefore, to conclude the previous discussion, the hypothesis is: in dyslexia, the widths of the minicolumns are larger than they are in normals, and hence; the number of minicolumns in the dyslexic patients is less than its corresponding in normal control cases.

Less number of minicolumns means much less connections which implies smaller white matter volume, and the contrary occurs in autism. Therefore, the major objective of this study is two fold; first, is to try to prove this hypothesis by proving that the volume of the white matter in dyslexic cases is smaller than its corresponding in normal control cases. Second, to emphasize that the change in the volume of the white matter is resulting from the communication 1 between the minicolumns, thus, the white matter will be parcellated into inner and outer compartments to prove that the increment or decrement in white matter volume should occur in the outer compartment.

2. METHODS

The proposed approach to accomplish the objective consists mainly of four steps; first, brain extraction algorithm is applied to remove all the non brain tissues from the images. Second, brain segmentation is performed to isolate the white matter. Third, white matter parcellation is performed to parcel the white matter into inner and outer compartments and finally, volumetric measures for the whole white matter, as well as, the outer compartment are recorded, and then tests of hypothesis are performed to investigate if there exists a significant difference between the groups or not. The following subsections will provide a brief description to each of the previously mentioned steps.

3.1. Brain extraction and segmentation

Brain extraction is being applied to remove all the non brain tissues such as skull and fat. The MRIcro software has been utilized to perform skull stripping and extract the brain. Having extracted the brain, Level sets segmentation approach has been utilized for the segmentation. Segmentation partitions the image into regions [9] each belonging to a certain class. In our approach a separate level set function is defined for each class and automatic seed initialization is used. The probability density functions of classes are embedded into the velocity term of each level set equation. The parameters of each one of these density functions are re-estimated at each iteration. The competition between level sets based on the probability density functions stops the evolution of each level set at the boundary of its class region.

Let \( \Omega \subseteq \mathbb{R}^n \) be open and bounded \( n \)-dimensional volume. Let \( I : \Omega \rightarrow \mathbb{R} \) be the observed \( p \)-dimensional image data. We assume that the number of classes \( K \) is known. Let \( p_i(I) \) be the intensity probability density function of class \( i \) (assumed to be Gaussian). In this work we associate the mean \( \mu_i \), variance \( \sigma_i^2 \), and prior probability \( \pi_i \) with each class \( i \). In accord to the estimation methods in [9, 10], the model parameters are updated at each iteration.

The classification decision is based on Bayes' decision [10] at point \( x \) as follows:

\[
i^*(x) = \arg \max_{i=1,...,K} \{ \pi_i p_i(I(x)) \}.
\]

(1)

The term \( (\nu) \) (the moving front directional term) for each point \( x \) is replaced by the function \( \nu_i(x) \) ([9]) so the velocity function is defined as:

\[
F_i(x) = \nu_i(x) - \epsilon \kappa(x), \forall i = 1..K.
\]

(2)

where \( \nu_i(x) = -1 \) if \( i = i^*(x) \) and it is 1 elsewhere. If the pixel \( x \) belongs to the front of the class \( i = i^*(x) \) associated to the level set function, the front will expand, otherwise it will contract. Now, we put the level set equation in the general form using the derivative of the Heaviside step function \( \delta_\alpha(z) \) as follows:

\[
\frac{\partial \phi_i(x,t)}{\partial t} = \delta_\alpha(\phi_i(x,t)) (\epsilon \kappa(x) - \nu_i(x)) |\nabla \phi_i(x)|.
\]

(3)

The function \( \delta_\alpha(z) \) selects the narrow band points around the front \( \kappa \) is the curvature. The proposed approach has been used to classify between the white matter, gray matter and cerebrospinal fluid. The approach has proved to be promising in extracting the white matter.

3.2. White matter parcellation

White matter parcellation aims at dividing the white matter into inner compartment and outer compartment: the outer compartment is a strip of the white matter where the connectivity between the minicolumns occurs. This area is extracted by detecting the outer contour of the white matter and moving this contour inwards 2 to obtain a boundary between the inner and outer compartments. The way we see the outer compartment

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1 Communication between minicolumns is represented by the U fibers that connects the different parts of the neocortex, since the minicolumns exist in the gray matter and connects through the white matter, then these U fibers exist in the white matter layer that is very close to the gray matter “Outer Compartment of the White matter”

2 By an arbitrary distance that is sufficiently large to include all the U fibers that connects between the minicolumns
of the white matter or the region of interest that we are looking for is the region of the white matter where the minicolumns communicate to each other, i.e. the region where the axon ends and the synapses communicate to different dendrites to transfer information. Therefore, we have two choices to determine such a region; either to ask a neuroscientist to draw this boundary (between the inner and outer compartments) manually which is very effort and time consuming. Or, to choose a distance that will be sufficiently large so that it is guaranteed that the communications between the minicolumns occur through it. Bearing in mind that if the chosen distance is larger than the actual one "that could be determined by a neuroscientist", this will just add a bias to the volumes but the differential comparison will still be valid. For this purpose, level set methods are used to detect the outer contour of the white matter, and then the signed distance function, intersection with plane \( Z=0 \) represents the outer compartments.

3.3. Statistical analysis

The brain extraction and segmentation represent the basic preliminary work that enables us to extract the white matter from each MRI stack, and the white matter parcellation is a basic step as well to get the region of interest. Having segmented and parcellated the white matter, the statistical analysis consists of the following steps:

1. The volumes of the whole white matter of all cases have been calculated. The means \((\mu_{w1}, \mu_{w2})\) and standard deviation \((\sigma_{w1}, \sigma_{w2})\) for the normal and dyslexic groups, respectively, were calculated.

2. The volumes of the outer and inner compartments of the normal and control cases were calculated. The means \((\mu_{O1}, \mu_{I1})\) and \((\mu_{O2}, \mu_{I2})\) as well as the standard deviations \((\sigma_{O1}, \sigma_{I1})\) and \((\sigma_{O2}, \sigma_{I2})\) were calculated.

3. Three hypotheses test were performed to test the proposed concept, the first has a null hypothesis that \(\mu_{w1} > \mu_{w2}\) to compare the volumetric measures of the whole white matter. The second one has a null hypothesis \(\mu_{O1} > \mu_{O2}\) to test that the increment of volume (if proved by the first test) is resulting from the increment of the outer compartment volume. And, Finally, the third test has a null hypothesis that \(\mu_{I1} \neq \mu_{I2}\) to test if the inner compartment played any role in the volumetric changes found between the different groups.

4. EXPERIMENTAL RESULTS

The proposed algorithms were applied on both dyslexic and normal control brain images and this section presents sample results. Fig.3 shows the results of the brain extraction technique. Fig.4 shows a 3D volume of the segmented white matter for one of the dyslexic cases in the three different views: sagittal, planar and coronal.

![Fig. 2. Illustrating the idea of moving the outer contour using the signed distance function, intersection with plane \( Z=0 \) represents the original contour and the intersection with plane \( z=d1 \) represents the new boundary](image1)

![Fig. 3. Results of skull stripping(a) Original MRI slice, (b) Skull stripped MRI slice](image2)

![Fig. 4. Different views for the segmented white matter (a) Sagittal, (b) Coronal, and (c) Planar](image3)

![Fig. 5. Parcellation results for a synthetic image for a circle (a) Original contour, (b) Signed distance map, and (c) The new boundary superimposed on the original image](image4)
white matter volume in normal control cases and dyslexic patients. Table 2 shows sample results for the volumes of the outer compartment at distance d=5 pixels.

Table 1. Sample Results for the volumetric measures of the whole white matter

<table>
<thead>
<tr>
<th>Index</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normals</td>
<td>615.375</td>
<td>650.812</td>
<td>699.187</td>
<td>626.062</td>
<td>604.125</td>
</tr>
<tr>
<td>Dyslexic</td>
<td>540.562</td>
<td>546.187</td>
<td>513.562</td>
<td>529.312</td>
<td>567.562</td>
</tr>
</tbody>
</table>

Table 2. Sample Results for the volumetric measures of outer compartment of the white matter

<table>
<thead>
<tr>
<th>Index</th>
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<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normals</td>
<td>469.494</td>
<td>516.435</td>
<td>584.037</td>
<td>517.446</td>
<td>510.297</td>
</tr>
<tr>
<td>Dyslexic</td>
<td>447.555</td>
<td>446.786</td>
<td>419.589</td>
<td>441.196</td>
<td>447.663</td>
</tr>
</tbody>
</table>

Figure 7 shows a comparison between the volumetric measures of the normal cases and the dyslexic patients.

5. CONCLUSION AND DISCUSSION

From the volumetric measures and the results of the hypotheses tests, it is very clear that there is a significant difference in the white matter volumes of the normal control cases and dyslexic patients. Also, it has been verified that the decrement of volume in dyslexia occurs in the outer compartment; since the hypothesis that: there is a difference between the volumetric measures of the inner compartments of the normal and dyslexic, has been rejected with 95% which emphasizes that the inner compartment did not affect the volumetric changes between the different groups and all the changes are resulting from the outer compartment which proves the hypothesis that has been postulated at the beginning of the paper: the change in the volumes is a result of the disturbance in the minicolumns; consequently, the connections between them through the white matter.

For the future work, two directions are taken into considerations; first, analysis of the correlation between the minicolumns and other different parameters such as the gyrification index, gyral window using the deformable models will be considered. Second, diffusion tensor images are intended to be used to study the structural difference in the U fibers connecting the minicolumns to create a classifier that differentiate between two diseases.

6. REFERENCES


