Title: The usefulness of MRI in assessing brain atrophy for people suffer from multiple sclerosis

Author: Patrycja Mazgaj, Zofia Drzazga, Aldona Giec-Lorenz

Citation style: Mazgaj Patrycja, Drzazga Zofia, Giec-Lorenz Aldona. (2020). The usefulness of MRI in assessing brain atrophy for people suffer from multiple sclerosis. "Acta Physica Polonica B Proceedings Supplement" (2020), Vol. 13, no. 4, s. 955-960. DOI: 10.5506/APhysPolBSupp.13.955

THE USEFULNESS OF MRI IN ASSESSING BRAIN ATROPHY FOR PEOPLE SUFFER FROM MULTIPLE SCLEROSIS*

Patrycja Mazgaj, Zofia Drzazga

A. Chełkowski Institute of Physics, University of Silesia, Chorzów, Poland

Aldona Giec-Lorenz

Helimed Diagnostic Imaging Sp. z o.o.
Laboratory of Magnetic Resonance Imaging, Katowice, Poland

(Received June 12, 2020)

Nowadays, volumetric and morphometric (VBM) techniques based on MRI data play a significant role in the research on neurodegenerative diseases. The aim of this work was to present the influence of age and gender on brain atrophy in patients ail to the most common demyelinating disease — multiple sclerosis (MS) — in the group of between 20–60-year-olds not treated with any disease-modifying drugs using VBM methods. MRI data of 31 patients obtained during the routine clinical work by MAGNETOM Aera 1.5T scanner were analysed. The faster decline of brain parenchymal fraction with age was observed in men than in women. VBM results showed that grey matter loss in significant regions of the brain such as visual cortex, SMA, caudate nucleus and the accumulation of damages can lead to the disability of patients.

DOI:10.5506/APhysPolBSupp.13.955

1. Introduction

The central nervous system (CNS) is an essential part of the nervous system in vertebrates and includes brains and the spinal cord. The human brain divided into two hemispheres is connected by the white matter aggregate called corpus callosum. Each of hemispheres consists of four main lobes: frontal, parietal, temporal and occipital, on which the cortical surface functional centres are corresponding to, *e.g.* for sight, movement, speech. Unfortunately, the brain undergoes atrophy. The term atrophy determines

* Presented at the 45$^{\text{th}}$ Congress of Polish Physicists, Kraków, September 13–18, 2019.

the loss of the brain tissue that occurs in every organism during the natural ageing process, but in the cases of specific diseases and disorders such as Alzheimer's diseases (AD) and Multiple Sclerosis (MS) this process is faster. The last one became one of the most common demyelinating disorders of the CNS in people between 20–40 year olds. Primary damage of myelin sheaths and their breakdown results in secondary damage to nerve fibres, which gradually reduces a patient's quality of life.

Magnetic resonance imaging (MRI) is essential in the diagnosis of MS, tracking its progress and monitoring the effects of the drugs therapies. Currently used MRI sequences allow imaging changes not only in the area of white matter (WM) but also the grey matter (GM). A significant role in research on demyelinating diseases played techniques such as volumetric or morphometric, which based on MRI data. Volumetric analyses allow for the quantitative assessment of nervous tissue loss and its expression using the brain parenchymal fraction (BPF), which is calculated as the ratio of the sum of grey and white matter volume (BPV, brain parenchyma volume) and total intracranial volume (TIV, sum of GM, WM and CSF). Voxel-based morphometry (VBM) allows to indicate local differences in brain anatomy using a statistical approach to parametric mapping. VBM results for the healthy are well-defined [1, 2], however, analyses for neurodegenerative diseases are still under discussion. The purpose of the work is to present the impact of the age and gender on brain atrophy in patients ail to multiple sclerosis between 20 and 60 years old using volumetric and morphometric analyses.

2. Materials and methods

The studied group consisted of 31 patients with diagnosed MS (ICD-10, G35) before starting therapy. The average patients age was 40.23 ± 9.6 years. The group consisted of 23 females and 8 males and their mean age was 38.96 ± 7.6 and 43.9 ± 11.9 years, respectively. The control group consisted of 6 neurologically healthy volunteers and their mean age was 24.5 ± 2.2 years. Unfortunately, due to the profile of the medical facility, it was not possible to gather a large control group sufficiently varied in age. Hence, the decision to choose a control group that matches the age of MS patients from literature [3]. Brain MRI was performed on a Siemens 1.5T MAGNETOM Aera scanner using a 20-channel head-neck coil in Helimed Diagnostic Imaging Center as a part of routine clinical work. FLAIR (TR = 5000 ms, TE = 334 ms, TI = 1800 ms, ST = 1.1 mm) and T1 MPRAGE before and after gadolinium-based contrast injection (TR = 1900 ms, TE = 2.97 ms, TI = 1100 ms, ST = 1.0 mm) sequences were acquired.

The VBM procedure was performed in the SPM12 in MATLAB. All raw T1 brain images were segmented into GM, WM and CSF volumes using tissue probability maps. Subsequently, GM volumes were normalised to the standard MNI (Montreal Neurological Institute) space using the DARTEL toolbox. The study-specific group brain template was created for analysis. The individual volumes were modulated by the total brain volume and smoothed using 8 mm FWHM Gaussian kernel. To analyse global changes in GM across the whole brain, the statistical tests were performed. The multiple regression test was used to check which regions had proportionally less grey matter depending on age and the two-sample t-test was utilized to check the impact of sex and to find statistically significant differences between brain regions. Subsequently, the dependent one-sample t-test was performed in Statistica 13 to estimate results against age. The Shapiro–Wilk test was used to check the normality of the distributions and the homogeneity of the variance. The significant results were regarded for differences for $p < 0.05$.

3. Results

Figure 1 presents BPF values of MS patients as a function of age with a linear fit of data. Calculated mean BPF value (0.87 ± 0.01) is similar to results reported for other MS patients groups [3, 4] (for example, BPF $= 0.85 \pm 0.01$ was reported by Vågberg *et al.* [3]) and lower than in healthy adults *e.g.* 0.89 ± 0.01 [3]. It is interesting that in our study, values of BPF in young MS patients (at the beginning of the disease) were comparable with results of our control group consisted of young people. It was also noticeable that brain tissue loss in our middle age patients group is comparably fast to that in healthy elderly [5].

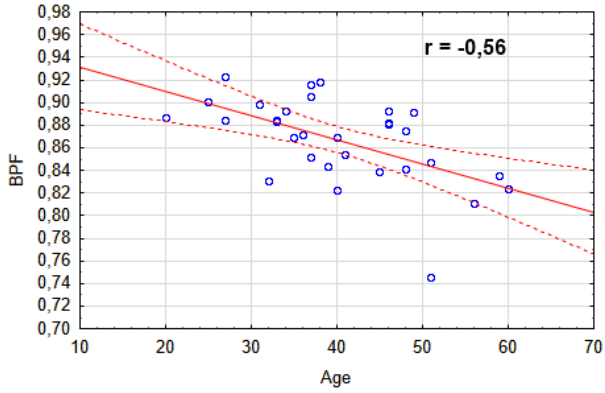

Fig. 1. BPF values of MS patients.

Calculated Pearson's correlation coefficient of BPF with age in MS patients showed value $r = -0.56$ which is slightly lower than mean population BPF parameter ($r = -0.41$) for healthy adults [2]. Additionally calculated correlations between BPF and age separately for females and males, respectively -0.42 and -0.66, showed a decline BPF with age in each group. Therefore, it seems that the atrophy process is faster in men than in women suffer from MS and there are differences between gender, which were observed in healthy adults [1, 5]. Nevertheless, due to small patients group our study has limitations that should be considered when interpreting our results.

In addition, BPF checked the distribution of brains fractions normalised by TIV as a function of age. A slight change in WM volume was observed ($r = -0.09$) unlike to GM and CSF (respectively -0.52 and 0.56) (Fig. 2). The marked decrease of GM volume and increase of CSF volume with age is in agreement with results reported by Smith *et al.* [5]. Moreover, decrease of BPV lead to the widening of the subarachnoid cranial space and brain reservoirs [5], which increases CSF volume [1].

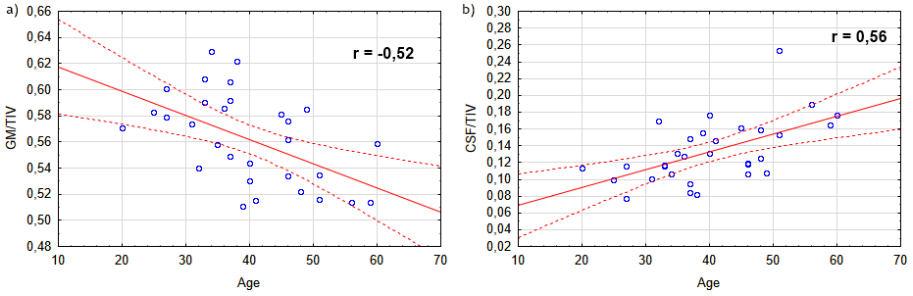

Fig. 2. Distribution of GM/TIV (a) and CSF/TIV (b) for MS patients in relations to age with a linear fit of data.

In this paper, we focused on the regional effects of the brain atrophy in MS patients. Figure 3 presents regions of the cerebral cortex with increased atrophy. Accelerated GM loss was observed bilaterally in frontal gyrus (superior and middle), right superior parietal gyrus, and supplementary motor area (SMA) like in healthy adults [1]. In MS patients, atrophy in deep GM structures such as the insula and caudate nucleus was also observed. In the studied group, GM loss in the thalamus was not observed.

Moreover, extracted regional grey matter loss differs between genders. Compared to females, in males GM loss in the cerebellum, middle cingulate gyrus and precuneus was observed what was also reported earlier for healthy men [6]. Additionally, accelerated grey matter atrophy in areas such as lingual gyrus, occipital pole and middle occipital gyrus, parahippocampal gyrus, frontal gyrus (middle), and deep grey matter structures as caudate nucleus and hippocampus was detected similarly as was mentioned by [7].

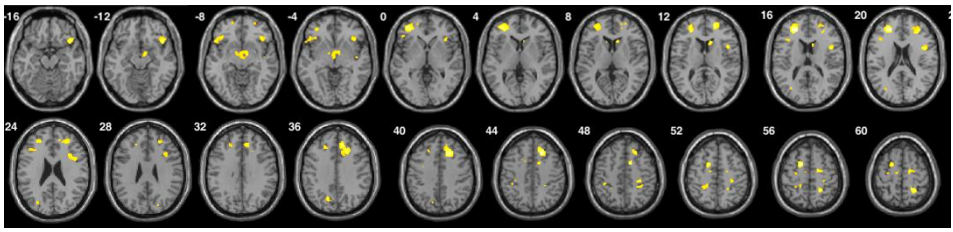

Fig. 3. VBM results. Regions with reduced grey matter in patients with SM with age presented on the average template of the studied group. The axial plane, significant voxels ($p < 0.001$).

4. Discussion

In this study, we focused on the influence of age and sex on the brain atrophy in patients who have multiple sclerosis. The role of MRI in MS diagnostics is indisputable and possibilities of imaging sequences which provide demyelinating plaques imaging are not limited only to WM but also GM [8–11]. Nowadays, a significant role in research on neurodegenerative diseases play morphometric analyses which provide an opportunity to know better which regions of the brain in higher degree undergo the atrophy, but also volumetric analysis which increases diagnostics and allows monitoring of applied drugs therapies [12]. It was known that the physiological process of neural tissue loss depends on age [1] or sex [5] in healthy people as well as attendant neurodegenerative disorders like MS [13] or AD [14] which can accelerate neural tissue loss and our results confirm that. Atrophy process occurs in different brain areas and our VBM results are consistent with other results [7]. It is also worth noting that there are significant differences in regional GM loss in MS patients compared to healthy control [1, 5]. In addition to cortical changes *i.e.* in occipital pole [15], in MS patients we observed GM loss in deep grey matter structures analogously as showed [16–18] in their work, what is more interesting. Caudate nucleus, insula, parahippocampal gyrus and hippocampus the atrophy of which was observed are functionally responsible for *e.g.* sensory and motor functions, cognitive and affective processing [19, 20]. The loss of GM in these regions could give early symptoms of the disease.

Considering the impact of gender on global as well as regional effects of brain atrophy, literature shows that sex has no significant effect for GM loss for the healthy [1, 5]. However, for MS patients, the results indicated significant gender differences in early relapsing-remitting MS [21]. Our results also showed the sex differences in global and regional brain atrophy effects.

Limitation of our work was a relatively small patients group, but our results are generally consistent with other MS studies [4]. Of course, there are works whose results differ significantly from ours but this can be due to the applied methodology [2, 12, 22, 23].

5. Conclusion

Our study confirms the decline of the BPF with age which is faster in MS patients than in healthy adults. However, the volume of WM, GM and CSF changes to a different degree and is dependent on sex. Especially in the case of GM atrophy in men, this process is faster than in women. The differences we observe mainly concern GM loss and the increase of CSF with relatively small changes of WM. VBM results show that GM loss in the vital regions (visual cortex, SMA, caudate nucleus) of the brain and this accumulation of damages lead to the disability of patients.

REFERENCES

[1] C.D. Good *et al.*, *NeuroImage* **14**, 21 (2001).
[2] M. Vågberg *et al.*, *PLoS One* **12**, e0170018 (2017).
[3] M. Vågberg *et al.*, *AJNR Am. J. Neuroradiol.* **34**, 498 (2013).
[4] R. Chu *et al.*, *PLoS One* **13**, e0206939 (2018).
[5] C.D. Smith *et al.*, *Neurobiol. Aging* **28**, 1075 (2007).
[6] A.V. Witte *et al.*, *NeuroImage* **49**, 1205 (2010).
[7] M. Battaglini *et al.*, *J. Neurol. Sci.* **15**, 55 (2009).
[8] B. Bodni *et al.*, *Presse Med.* **44**, e159 (2015).
[9] P. Kolber *et al.*, *J. Neurol.* **262**, 1473 (2015).
[10] A. Klimas *et al.*, *Clin. Imaging* **37**, 637 (2013).
[11] O. Ciccarelli, J.T. Chen, *Neurology* **78**, 296 (2012).
[12] P. Mazgaj *et al.*, *Acta Phys. Pol. A* **133**, 725 (2018).
[13] R.A. Rudick *et al.*, *Neurology* **53**, 1698 (1999).
[14] B.L. Callahan *et al.*, *Alzheimers Res. Ther.* **7**, 68 (2015).
[15] X. Cao *et al.*, *Neural Regen. Res.* **12**, 787 (2017).
[16] B. Audoin *et al.*, *J. Neurol.* **253**, 1495 (2006).
[17] S. Mesaros *et al.*, *Neurology* **70**, 1107 (2008).
[18] A. Prinster *et al.*, *NeuroImage* **29**, 859 (2006).
[19] Y. Duan *et al.*, *Eur. J. Radiol.* **81**, e110 (2012).
[20] M.M. Botvinick *et al.*, *Trends Cogn. Sci.* **8**, 539 (2004).
[21] D.T. Chard *et al.*, *Brain* **125**, 327 (2002).
[22] V. Popescu *et al.*, *PLoS One* **11**, e0143942 (2016).
[23] C.C. Hemond *et al.*, *Brain Behav.* **8**, e01068 (2018).