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Self-Organizing Maps as a Tool for Segmentation of Magnetic Resonance Imaging (MRI) of Relapsing-Remitting Multiple Sclerosis

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***Abstract* - Multiple Sclerosis (MS) is the most prevalent demyelinating disease of the Central Nervous System, being the Relapsing-Remitting (RRMS) its most common subtype. We explored here the viability of use of Self Organizing Maps (SOM) to perform automatic segmentation of MS lesions apart from CNS normal tissue. SOM were able, in most cases, to successfully segment MRIs of patients with RRMS, with the correct separation of normal versus pathological tissue especially in supratentorial acquisitions, although it could not differentiate older from newer lesions.**

Index Terms - Self Organizing Maps, SOM, Magnetic Resonance Imaging, Demyelination, Multiple Sclerosis

I. INTRODUCTION

Being one of the most concerning illnesses at present, constant and fast changing on its protocols and medications available, demyelinating diseases, such as multiple sclerosis (MS), are among the leading causes of medical help being sought both in the inpatient and outpatient environment, either due to acute situations, such as the need ofemergency care in case of a relapse of recent onset, as well as prompt neurological consultation for outpatients who experience troubles originating both from the disease and from the side effects medications offer.

MS can be subdivided [13], in accordance to the disease course, between Relapsing-Remitting, Secondary Progressive and Primary Progressive, the first being most prevalent. The use of tools to assure better quality of imaging, in this scenario, is highly desirable and should always be improved.

Currently, Magnetic Resonance Imaging (MRI) plays a key role not only for diagnosis, but also for the evaluation of rate of disease progression. Lesion load on MRI is correlated with disability outcome in MS. In both cases, the examiner needs to gather information from distinct acquisitions, that must be seen separately, one at a time, then ponder which will be the next steps taken, including maintenance or modification of the pharmacological treatment.

In this paper, the use of SOM Self-Organizing Maps (SOM), a neural network multivariate pattern recognition technique is proposed. The computational analysis can aid on the identification of neurological lesions, making diagnosis more robust and therapeutic decisions more precise, providing a better characterization of the geometry and extension of the injury, hence facilitating the identification of compromised regions.

According to Kohonen [4], the biggest advantages of SOM are being a non-supervised technique of segmentation, and being widely used in many fields, such as geology [11, 15], mathematics [16], finances [17] and engineering [18]. Besides, the better performance of SOM among other unsupervised techniques, as principal component analysis (PCA) and independent component analysis (ICA), was demonstrated by Coléou et al. [22], which motivated the choice of this tool.

In medicine, its use is still to become more frequent. SOM has already been validated for segmentation of human tissue in previous works [9, 10]. In neuroradiology, it is more frequently used with functional images (fMRI) [6,7,8], but not so much with conventional images for anatomic interpretation.

Mei et al [1], as Vijayakumar et al [2], have shown that SOM can be successfully used to separate neoplasm from normal tissue in the brain, as well, it can segment different areas of the lesion.

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MS automatic segmentation could play an important role, as one could be more assured of following the rate of increase of the lesion burden for the same patient, in a more precise way [12]. Abdullah et al, on an article in 2011[3], have shown a supervised training method of segmentation that could predict possible lesions of MS in MRI. However, to our knowledge, no indexed paper so far has further explored the segmentation of MS lesions based on an unsupervised learning technique, as with SOM, among others.

This present study aims to investigate the capability of the assisted segmentation of MS lesions by SOM, as well as to contribute to data on the yet-not-frequent use of SOM in medical research.

II. Materials and Methods

We collected FLAIR, T1 and T1 with Gadolinium (Gd) – with enhancement present in half of the cases – which in this context represents lesions of newer nature brain 1,5 Tesla MRI acquisitions that represented, for the same patient, the same topographic level of the lesion in 10 patients with confirmed diagnosis of Relapsing-Remitting MS, 2 males and 8 females, with ages from 21 to 69 years, as described in Table I. The topography chosen for each patient represented the area with the highest lesion burden. Half had Gd enhancement at the time of the acquisition. MS patients characteristically have lesions of different times of onset, and the enhancement by Gd demonstrates that new lesions have appeared roughly within the last 3 months, and are useful information regarding treatment decision. All patients were under immunomodulating regimen and being regularly followed at our institution on the moment the MRIs used in this research was performed.

TABLE I
Patients Enrolled

PATIENT	AGE	SEX	Gd ENHANCEMENT	LOCATION OF SLICE STUDIED
1	46	M	-	Supratentorial
2	33	F	-	Supratentorial
3	33	F	+	Supratentorial
4	39	F	-	Supratentorial
5	25	M	+	Supratentorial
6	39	F	+	Supratentorial
7	46	F	-	Supratentorial
8	21	F	+	Infratentorial
9	44	F	+	Supratentorial
10	69	F	-	Infratentorial

Gd = Gadolinium

The acquisitions, for each patient, were then pre-processed and registered, in a fashion that their boundaries were mostly coincident. The images were then transformed from raster into points by ArcMap software [21], data was gathered and the absolute black (regions of the pictures that had no brain tissue, with gray scale value of 0 in all acquisitions) suppressed, in a worksheet, with values of gray of T1, T1 Gd and FLAIR for each pixel. Subsequently, the generated matrix ran through SOM, first for training neurons, and then segmenting the neurons in clusters by k-means, using for both tasks SiroSOM, a Matlab-based SOM implementation available from CSIRO, Australia, idealized by Fraser and Dikson [5]. The parameters used for training neurons are displayed in Table II.

SOM is a neural network tool formed by two layers: the input data samples, and the map of nodes, called neurons, that can learn, in a simplified model of brain processing by a iterative method. Let be $x = [x_1, x_2, x_3, \ldots, x_n]$ the sample of n dimensions to be classified, and N the number of samples. The two map dimensions of SOM are heuristic determined by two close numbers whose multiplication is closest to $5 * \sqrt{N}$, and whose ratio is equal to the ratio of the two biggest eigenvalues of the covariance matrix of input data. Each node is associated to a weight (w), with n dimensions, randomly distributed. The target of the algorithm is to adjust the values of weights to better classify the input samples, in this case by Euclidian distance parameter. The vector between the closest node and the sample is called Best Matching Unit (BMU) and is used to update the weighs as follows:

$$w_i(t+1) = w_i(t) + \alpha(t) \cdot h_{BMU}^i(T) \cdot [x_k - w_i(t)] \qquad (1)$$

in which t is the iteration, h_{BMU}^i is the radius of neuron neighborhood with hexagonal lattice, which was defined as a Gaussian equation, and determines the neurons to be updated, and α is the learn radius, defined as:

$$\alpha(t) = \alpha_0 / \left(1 + 100\frac{t}{T}\right) \qquad (2)$$

in which T is the training length. In this study, the training was done in two parts: an initial one with rough values, and a refined one, with lower values, all shown in table II.

The distance map between the nodes, called U-Matrix, enables the visualization of the clustering results. Once the technique preserves topography, it is possible to visualize closer groups of nodes (in cold colors) representing similar patterns, while more distant ones are associated with disparate patterns.

In order to evaluate SOM performance, two errors are calculated: topographic (Te) that computes the occurrences in which the samples is associated to a BMU that is not adjacent in map structure, and quantization (Qe) that measures how close the input data is to the BMUs.

Because the number of map nodes are big, they are usually clustered by k-means method, in which k is defined by the David-Bouldin index.

III. Results

The most important variables and results of SOM are summarized in table II.

TABLE II
PARAMETERS USED IN NEURON TRAINING BY SIROSOM

Patient	Map Size	Rough Training			Fine Training			Final Qe	Final Te
		Initial Radius	Final Radius	Training Length	Initial Radius	Final Radius	Training Length		
1	64 × 62	90	23	20	23	1	400	0.0114	0,257
2	52 × 50	73	19	20	19	1	400	0,0825	0,083
3	70 × 68	98	25	20	25	1	400	0.0228	0.025
4	68 × 66	95	24	20	24	1	400	0.0048	0.126
5	66 × 64	92	23	20	23	1	400	0.0056	0.153
6	66 × 64	92	23	20	23	1	400	0.0261	0.026
7	68 × 66	95	24	20	24	1	400	0.0171	0.027
8	44 × 42	61	16	20	16	1	400	0.0717	0.087
9	68 ×66	95	24	20	24	1	400	0.0055	0.122
10	44 × 42	61	16	20	16	1	400	0.0232	0.319

On Fig. 1a one can see an example of component plots and the U-Matrix generated in patient 2. The number of clusters c to be created, being $c \in \mathbb{N} \mid 2 \leq c \leq 25$, was defined based on the internal clustering of the Davies Bouldin Index (DBI), provided in SiroSOM, where the lowest value for each analysis indicated the possible best result. Fig. 1b shows an example of plot of the values of DBI for each possible value of c. SiroSOM results were than transformed back from points to raster, including cluster number for each pixel. This transformation allowed the composition, by ArcMap, of one single image, segmented on basis of similarity as explained above.

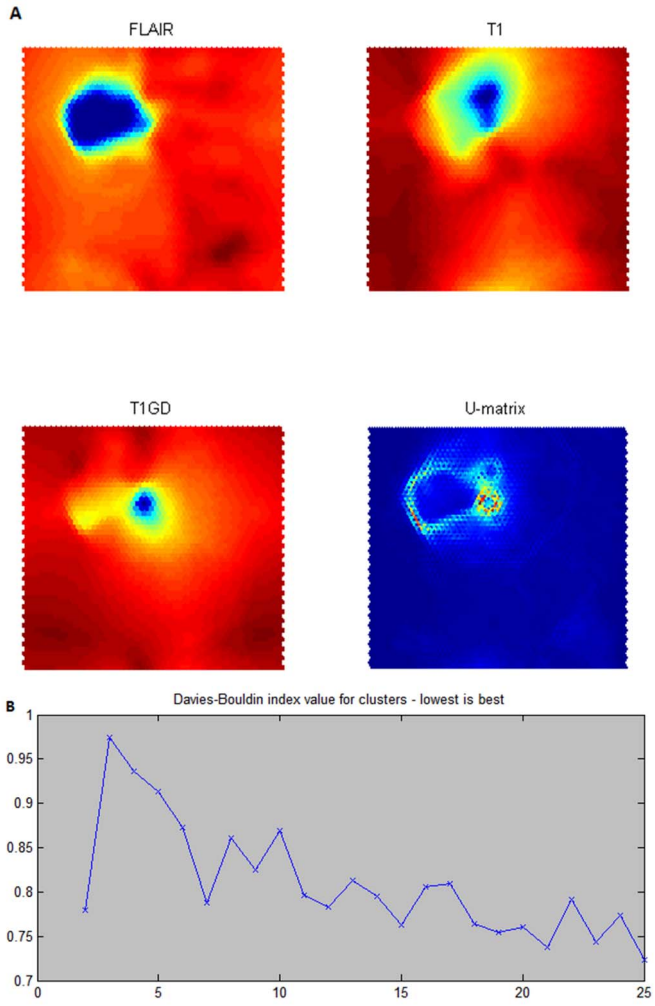

Fig 1 – A. Maps of Components, plotted separately; B. Davies-Bouldin Index values for c clusters, being $c \in \mathbb{N} \mid 2 \leq c \leq 25$

Images obtained by SOM can be seen in Figure 2, alongside with FLAIR and T1-Gd acquisitions of each patient. Each SOM generated image is segmented in colors which represents different clusters.

In all supratentorial images, we are able to notice a complete separation of the lesions in one or two specific clusters, usually with the most hyperintense part of the lesion being put in one cluster, and the lesser bright in another, but both different from the adjacent healthy/healthier tissue. However, for the same patient, lesions with and without Gd enhancement were classified as the same cluster.

In some patients (more prominent on patients 5 and 6), a part of the cortex/juxtacortical area is classified as the same cluster as the lesions.

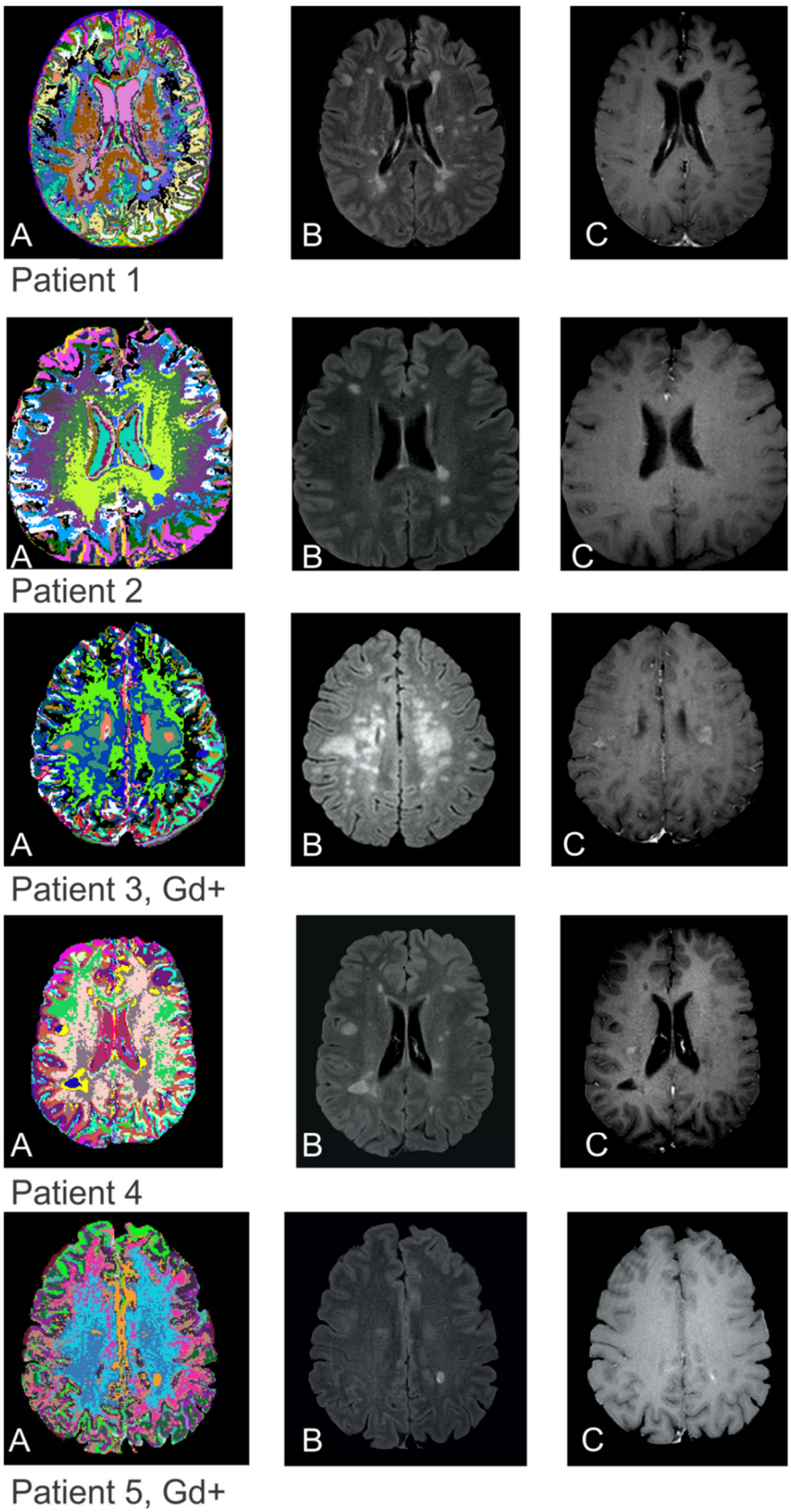

Fig. 2 – For each patient, A – SOM generated image, B – FLAIR, and C – Gadolinium T1 acquisitions. Gd+ = Patient with Gd enhancement.

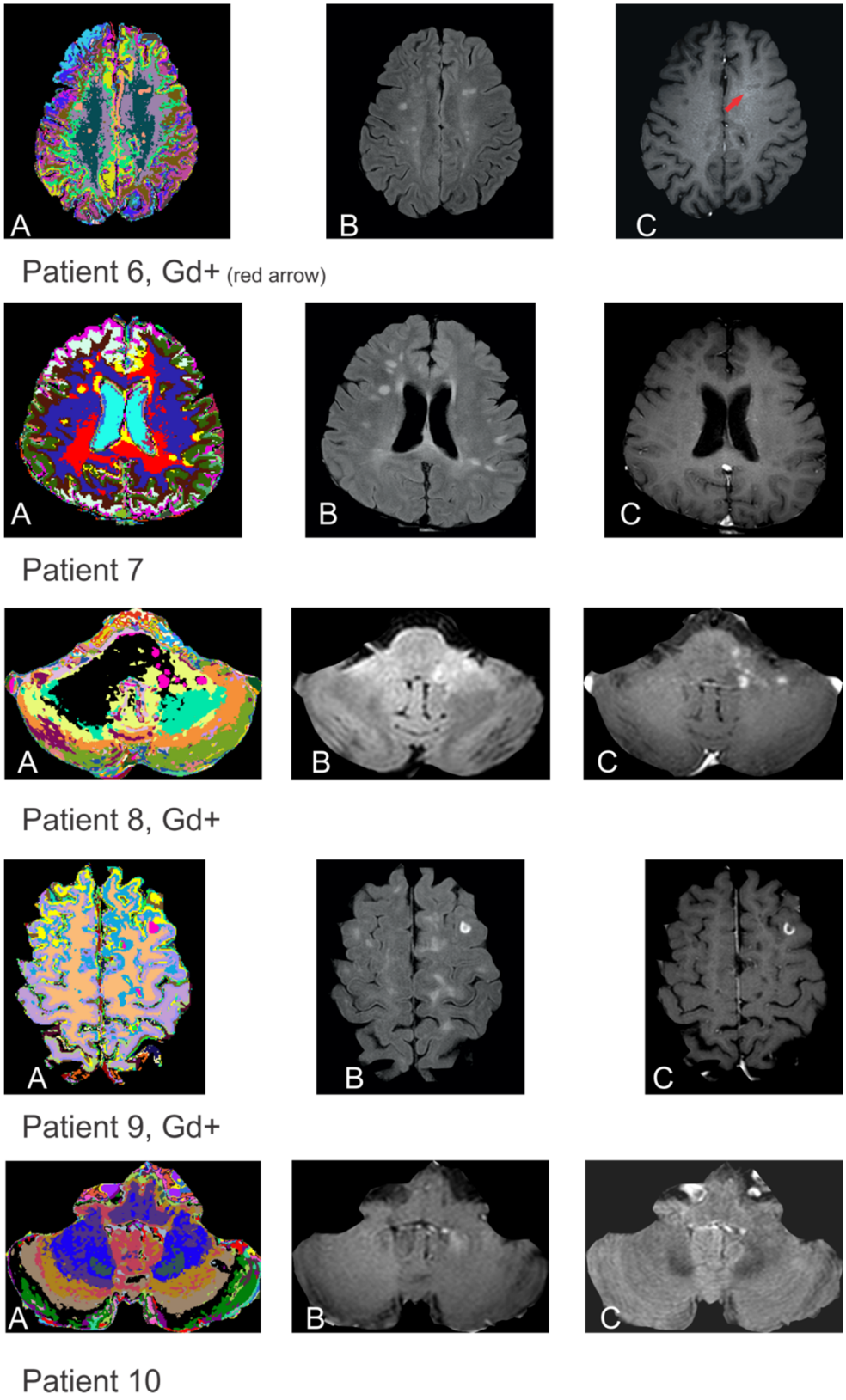

Fig. 2 (contd.) – For each patient, A – SOM generated image, B – FLAIR, and C – Gadolinium T1 acquisitions. Gd+ = Patient with Gd enhancement. On Patient 6 the area of enhancement (shown by red arrow) is better seen in other acquisitions, not displayed here

IV. Discussion

Keeping in mind that we analysed a limited number of samples and that it may carry some limitations of representation, SOM were able to successfully segment MRIs of patients with RRMS, with the correct separation of normal versus pathological tissue in general, and further research would be useful to expand the knowledge on this issue.

As mentioned above, in some patients, cortical and juxtacortical areas are classified in the same cluster as demyelinating lesions. This makes sense, as cortical areas are less myelinated, just like the lesions. However, it is not possible, only by SOM analysis, to exclude disease damage in these parts. It may be plausible, as it has now been known for some time, that MS is not only a white matter disease, and that there may be some inflammation occurring as well in a percentage of these areas cluster-similar to lesions. This is in accordance with the already proven concept of Normal-Appearing White Matter (NAWM) [19,20].

This results come in accordance with some of the previous results of SOM in brain neoplastic lesions, where SOM was able to separate lesions from healthy tissues, as well as cluster suspected areas of infiltration. These areas of suspicion (possible infiltration in neoplasms and possible inflammation/gliosis in MS) could be better accessed in upcoming research, focusing on methods of confirmation, such as biopsy/necropsy.

Though the use of Self Organizing Maps appears to be less effective on the segmentation of infratentorial lesions and also not sensitive enough to separate acute Gd enhanced lesions from lesions of older nature, it was very successful on dealing with supratentorial acquisitions.

V. Conclusions

SOM may be a useful tool for the segmentation of supratentorial lesions and for the quantification of lesion burden, being important in defining lesion load. Its use in medical imaging is yet underexploited, and novel research on neuroimaging should be encouraged, based on positive results obtained so far in the few studies already published and the fact that it is an unsupervised method, making it a diagnostic aid valid for not only people with good background of neuroimaging, but also for people of lesser knowledge (medical students and non-physician health practitioners, for example).

Our analysis suggests that demyelinated regions in MS show better lesion delineation when exploited with the aid of segmenting software, if compared to conventional acquisitions alone, such as T1 or FLAIR.

The fine definition of the geometry of the lesions is not always possible based only on individual analysis of MRI images. The use of the dimensional space defined by the analysed variables by SOM made possible not only the categorical separation of tissues, including damaged ones, but also contributed to the geometrical identification of their scope. Even though this segmentation is not binary (i.e., does not separate normal from abnormal, but rather different classes of tissues, including arranging distinct normal tissues in different clusters), it helps to distinguish lesions, grouped in one single cluster (regardless of lesion age), from other areas of the brain that do not show a clear evidence of disease activity on MRI. This learning is fundamental to the diagnosis, as well as to a more precise identification of affected regions, which may guide clinical decisions in MS.

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