Analysis of fMRI Time Series: Neutrosophic-Entropy Based Clustering Algorithm

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***Abstract*—Analysis of Functional Magnetic Resonance imaging (fMRI) time series plays a vital role in identifying the activation behaviour of neurons in the human brain. However, due to the complexity of the fMRI data, its analysis is challenging. Some studies show that the clustering methods can be beneficial in this respect. We apply a Neutrosophic Set-Based Clustering Algorithm (NEBCA) to fMRI time series datasets by this motivation. For the experimental purpose, we consider fMRI time series related to working memory tasks and resting-state. The clusters with different densities for the two analyzed cases are determined and compared. The identified differences indicate brain regions involved with the processing of the short-memory tasks. The corresponding brain areas are denoted according to Automated Anatomical Labeling (AAL) atlas. The statistical reliability of the findings is verified through various statistical tests. The presented results demonstrate the utility of the neutrosophic set based algorithm in brain neural data analysis.**

***Index Terms*—neutrosophic set, entropy, clustering, functional Magnetic Resonance Imaging (fMRI) time series**

I. Introduction

Many research contributions have been made related to the time series analysis of functional Magnetic Resonance Imaging (fMRI) in recent years [1]-[4]. In the last decade, fuzzy set theory [5] has also been increasingly used in fMRI time series analysis [6]-[8] due to its robustness in dealing with inherent uncertainties. However, fuzzy set-based methods [6]-[8] applied to the fMRI data are not sufficiently effective to fully determine patterns in different brain areas. This indicates that a more robust method is needed to deal with the uncertain behaviour of fMRI data. Recently, a study by Singh and Rabadiya [9] demonstrated the effectiveness of Neutrosophic Set (NS) theory [10] over fuzzy set methodology. Based on NS, Singh [11] proposes a clustering algorithm called Neutrosophic-Entropy Based Clustering Algorithm (NEBCA) [11]. They demonstrate the application of NEBCA in clustering various Magnetic Resonance Imaging (MRI) of Parkinson's Disease (PD) patients. The application of this algorithm has not yet been studied in other domains. So, this motivates us to apply NEBCA to the analysis of the fMRI time series. For study purposes, we choose fMRI time series related to working memory task Global processing task (GLO) and Resting State (RES) data. By applying NEBCA, clusters with different densities are generated. Finally, these clusters are analyzed to identify the differences between GLO and RES in terms of their activation patterns of neurons in the human brain.

This article is structured as follows. In Section II, the background for NS theory is presented. In Section III, the clustering method NEBCA is explained. Description of fMRI time series datasets is provided in Section IV. Experimental results are presented in Section V. In Section VI, Conclusions and future directions are illustrated.

II. Background for NS Theory

This section provides background for NS.

Definition 1: (NS) [10]. Assume that X is a universe of discourse. A NS $\mathbb{N}$ for $x \in X$ can be represented by three degrees of membership functions, viz., true (T_N), indeterministic (I_N) and false (F_N); where, T_N, I_N and F_N for the $x \in X$ can be expressed as: $T_N, I_N, F_N : X \rightarrow {}^{-}0, 1^{+}[$, $x \equiv x(T_N(x), I_N(x), F_N(x)) \in \mathbb{N}$, and ${}^{-}0 \leq T_N(x) + I_N(x) + F_N(x) \leq 3^{+}$.

The three membership functions, namely T_N, I_N and F_N, are called *neutrosophic membership functions (NMFs)*.

Wang *et al.* [12] defined an instance of the NS as a *Single Valued Neutrosophic Set (SVNS)*. When the universe of discourse X is discrete and finite, then the SVNS can be defined as follows:

$$\mathbb{N} = \left\{ \frac{\langle T_N(x_1), I_N(x_1), F_N(x_1) \rangle}{x_1} + \frac{\langle T_N(x_2), I_N(x_2), F_N(x_2) \rangle}{x_2} + \ldots \right\} = \left\{ \sum_{i=1} \frac{\langle T_N(x_i), I_N(x_i), F_N(x_i) \rangle}{x_i} \right\}, \forall x_i \in X \quad (1)$$

When the universe of discourse X is continuous and infinite, then the SVNS can be defined as follows:

$$\mathbb{N} = \left\{ \int_X \frac{\langle T_N(x_i), I_N(x_i), F_N(x_i) \rangle}{x_i} \right\}, \forall x_i \in X \quad (2)$$

In Eqs. (1) and (2), the horizontal bar denotes a delimiter. The numerator in each term represents the

Manuscript received November 2, 2021; revised April 19, 2022.

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doi: 10.12720/jait.13.3.224-229

membership values in the NS $\mathbb{N}$ associated with the observation of the universe of discourse X indicated in the denominator. In Eq. (1), the summation symbol indicates the aggregation of each observation; hence, the "+" signs denote an aggregation operator. In Eq. (2), the integral sign denotes a continuous function-theoretic aggregation operator for continuous variables [11].

The NMFs can be defined as follows for the SVNS [11]:

Definition 2: (NMFs). For an SVNS $\mathbb{N}$ in X, the three NMFs T_N, I_N and F_N for $x \in X$ can be formulated as:

$$T_N(x) = \frac{x\text{-}\min(X)}{\max(X)\text{-}\min(X)} \quad (3)$$

$$F_N(x) = 1 - T_N(x) \quad (4)$$

$$I_N(x) = \sqrt{T_N(x)^2 + F_N(x)^2} \quad (5)$$

In Eq. (3), "min" and "max" represent the minimum and maximum functions, respectively.

Entropy can be used to quantify the inherent uncertainties in any feature. Such measurement of uncertainties with respect to NS is called Neutrosophic Entropy (NE), which can be defined below.

Definition 3: (NE) [11]. The NE of an SVNS $\mathbb{N}$ at $x \in X$ is represented as a measure $H(\mathbb{N},x)$, where $\mathbb{N}: \{\langle x, T_N(x), I_N(x), F_N(x)\rangle \mid x \in X\}$ which can be defined as follows:

$$H(\mathbb{N},x) = 1 - \tfrac{1}{3}(T_N(x) + I_N(x) + F_N(x)) \times E_1 E_2 E_3 \quad (6)$$

here, $E_1 = |T_N(x) - T_N^c(x)|$, $E_2 = |I_N(x) - I_N^c(x)|$, and $E_3 = |F_N(x) - F_N^c(x)|$.

III. Detailed Description of NEBCA

This section introduces the NS theory-based clustering algorithm called NEBCA. Each step of the algorithm is illustrated in terms of its application in the clustering of an fMRI time series dataset.

Step 1. Input fMRI time series dataset: Select the fMRI time series dataset as an input. This dataset can be represented in terms of a $m \times n$ matrix in the following way:

$$\mathbb{F}_{MR} = \begin{bmatrix} f_{11} & f_{12} & \dots & f_{1n} \\ f_{21} & f_{22} & \dots & f_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ f_{m1} & f_{m2} & \dots & f_{mn} \end{bmatrix} \quad (7)$$

here, $m \times n$ represents the size of the dataset.

Step 2. Represent fMRI time series dataset into NS: For each $f_{ij} \in \mathbb{F}_{MR}$, its respective NS is denoted as $\mathbb{N}_{ij}$, and can be expressed in the following matrix form as:

$$\mathbb{N}_{MR} = \begin{bmatrix} \mathbb{N}_{11} & \mathbb{N}_{12} & \dots & \mathbb{N}_{1n} \\ \mathbb{N}_{21} & \mathbb{N}_{22} & \dots & \mathbb{N}_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ \mathbb{N}_{m1} & \mathbb{N}_{m2} & \dots & \mathbb{N}_{mn} \end{bmatrix} \quad (8)$$

In Eq. (8), the three NMFs T_N, I_N and F_N for $f_{ij} \in \mathbb{N}_{ij}$ can be defined as:

$$T_N(f_{ij}) = \frac{f_{ij} - \min(U)}{\max(U) - \min(U)} \quad (9)$$

$$F_N(f_{ij}) = 1 - T_N(f_{ij}) \quad (10)$$

$$I_N(x) = \sqrt{T_N(f_{ij})^2 + F_N(f_{ij})^2} \quad (11)$$

In Eq. (9), U denotes the universe of discourse for the respective fMRI time series dataset.

Step 3. Compute NE for the NS: For each $\mathbb{N}_{ij}$, its respective NE is denoted as $H(\mathbb{N}_{ij}, f_{ij})$, and can be expressed in the following matrix as:

$$\mathbb{H}_{MR} = \begin{bmatrix} H(\mathbb{N}_{11},f_{11}) & H(\mathbb{N}_{12},f_{12}) & \dots & H(\mathbb{N}_{1n},f_{1n}) \\ H(\mathbb{N}_{21},f_{21}) & H(\mathbb{N}_{22},f_{22}) & \dots & H(\mathbb{N}_{2n},f_{2n}) \\ \vdots & \vdots & \ddots & \vdots \\ H(\mathbb{N}_{m1},f_{m1}) & H(\mathbb{N}_{m2},f_{m2}) & \dots & H(\mathbb{N}_{mn},f_{mn}) \end{bmatrix} \quad (12)$$

In Eq. (12), each $H(\mathbb{N}_{ij}, f_{ij})$ can be defined using Eq. (6).

Step 4. Select number of clusters: Select δ number of clusters as: $C=1,2,\dots,\delta$.

Step 5. Select cluster centers: Select set of randomly initialized cluster centers as:

$$C(itr) = [C_1(itr), C_2(itr), \dots, C_\delta(itr)] \quad (13)$$

here, "itr" represents the 1st iteration of the algorithm.

Step 6. Repeat:

Step 7. Compute the distance: Calculate the Euclidean distance $D[H(\mathbb{N}_{ij}, f_{ij}), C_j(itr)]$ between NE value $H(\mathbb{N}_{ij}, f_{ij}) \in \mathbb{H}_{MR}$ and the cluster center $C_j(itr) \in C(itr)$ using the formula given below as:

$$D[H(\mathbb{N}_{ij}, f_{ij}), C_j(itr)] = |H(\mathbb{N}_{ij}, f_{ij}) - C_j(itr)|^2 \quad (14)$$

If C(itr) is the closest center to $H(\mathbb{N}_{ij}, f_{ij})$, then it is assigned to the cluster G_j.

Step 8. Assign all NE values to cluster centers: Assign all $H(\mathbb{N}_{ij}, f_{ij})$ values to the nearest cluster center based on the minimum Euclidean distance.

Step 9. Update the cluster centers: Update the new cluster centers with the following formula as:

$$C_j(itr+1) = \frac{1}{S}\sum_{i=1}^{S} H(\mathbb{N}_{ij}, f_{ij}); (j=1,2,\dots,\delta) \quad (15)$$

In Eq. (15), S represents the size of the cluster G_j, where $\forall H(\mathbb{N}_{ij}, f_{ij}) \in G_j$.

Step 10. Stop the clustering process: Goto Step 6 and proceed from iteration itr = 0 to the next iteration itr = itr + 1. This process continues until the cluster centers stop changing or the algorithm reaches the maximum number of iterations Itr, i.e.; $itr = 0,1,\dots,Itr$.

The pseudocode of NEBCA is summarized in Fig. 1. The time complexity of NEBCA depends on the size of

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the matrix of an fMRI dataset, which is $m \times n$. Therefore, the total time complexity of NEBCA is $O(m \times n)$ for the maximum number of iterations Itr.

Algorithm 1: PROCEDURE NEBCA()

Input: An fMRI time series dataset as $\mathbb{F}_{MR}$ (Eq. (7)).

1. Represent each $f_{ij} \in \mathbb{F}_{MR}$ into NS denoted as $\mathbb{N}_{ij}$, and store into the matrix $\mathbb{N}_{MR}$ (Eq. (8)).
2. Compute NE of each $\mathbb{N}_{ij}$ using NE function denoted by $H(\mathbb{N}_{ij}, f_{ij})$ (Eq. (6)), and store into the matrix $\mathbb{H}_{MR}$ (Eq. (12)).
3. Select δ number of clusters as: $C=1,2,\ldots,\delta$.
4. Select set of randomly initialized cluster centers (Eq. (13)) as:

$$C(itr) = [C_1(itr), C_2(itr), \ldots, C_\delta(itr)]$$

here, "itr" represents the 1st iteration of the algorithm.

While $itr = 0$ **do**

a. Compute the Euclidean distances between NE values and the cluster centers using Eq. (14).
b. Assign all the NE values to their respective closest cluster center based on the minimum Euclidean distance.
c. Update each cluster center by employing Eq. (15).

End

$itr = itr + 1;$

Output: clustered fMRI time series dataset.

Figure 1. Pseudocode of NEBCA.

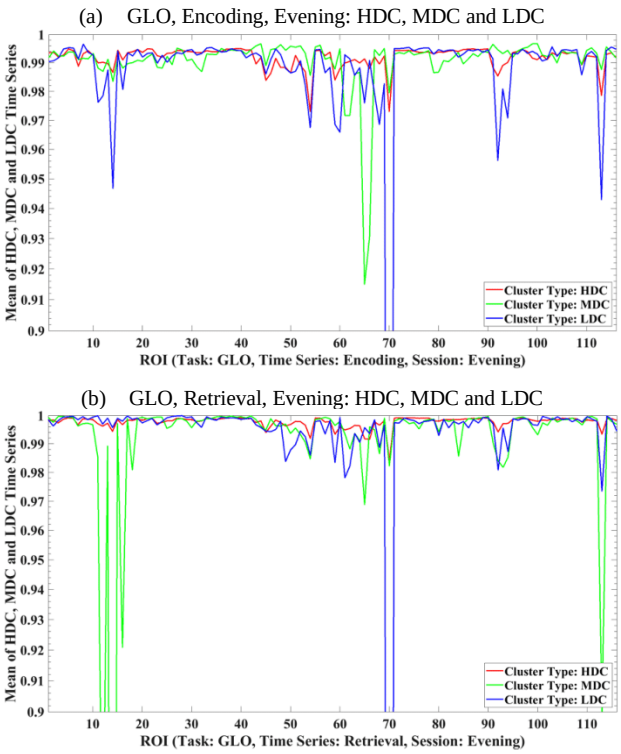

Figure 2. Differences between HDC, MDC and LDC with respect to the GLO (one typical participant).

IV. Description of Datasets

This study uses the datasets discussed in [13]. Information about the datasets is given below:

- *Experimental tasks*: The data related to two kinds of brain activation, i.e. GLO and RES, are considered. The 116 Regions of Interest (ROIs) are defined according to Automated Anatomical Labeling (AAL) brain atlas [14].
- *Sessions*: The sessions involved in the tasks are: (a) morning and (b) evening.
- *Signal types*: For the activation of signals, participants are asked to remember memory sets that are followed by simple masks. The response signals associated with this process is called encoding. Then, participants are asked to respond, and the response signals associated with this process are referred to as retrieval.
- *fMRI time series from GLO*: In GLO, participants are presented with a collection of graphics characterized by a series of overlapping similarities. The experiments' signals are recorded for both the encoding and retrieval phase in the morning and evening sessions. fMRI time series datasets of 52 participants from the GLO are selected for the experimental purpose.
- *fMRI time series from RES*: In RES, participants are not involved in any activity associated with the memorization of sets. The experiments are conducted for recording the stimuli in the morning and evening sessions. For the study, fMRI time series datasets of 48 participants are selected from this source.

V. Experimental Results

In this section, we present the experimental results based on the application of NEBCA on two different fMRI time series datasets obtained from the task GLO and RES.

A. Clustering of fMRI Time Series

NEBCA is applied to the fMRI time series of the GLO and RES to perform clustering. Labels are assigned to three different clusters obtained from NEBCA based on their densities. These three clusters with their labels are named as High Density Cluster (HDC), Medium Density Cluster (MDC) and Low Density Cluster (LDC). The mean values of their respective clustered entropy are obtained to distinguish the differences between HDC, MDC and LDC. These differences for sample participant and GLO task are presented in the form of curves shown in Fig. 2(a) and Fig. 2(b). From this Figure, one can easily notice that there are differences between HDC, MDC and LDC clusters. Moreover, these three clusters show the differences between two types of signals: encoding and retrieval. This Figure shows that fMRI time series belonging to HDC are strongly triggered, followed by MDC and LDC.

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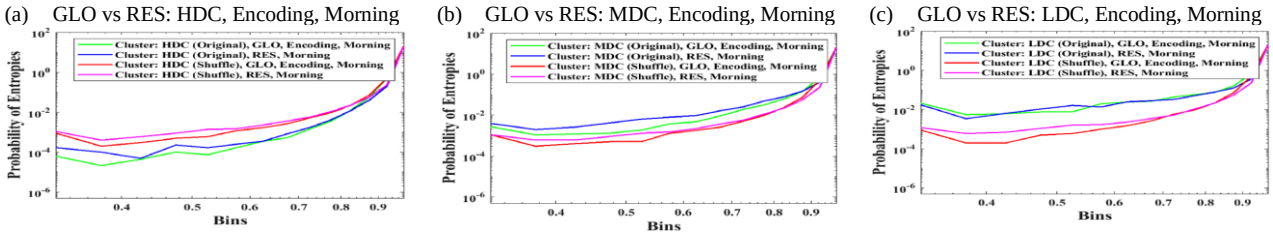

Figure 3. Comparison of probability distributions of entropies in terms of original clusters and shuffle clusters for the GLO vs RES.

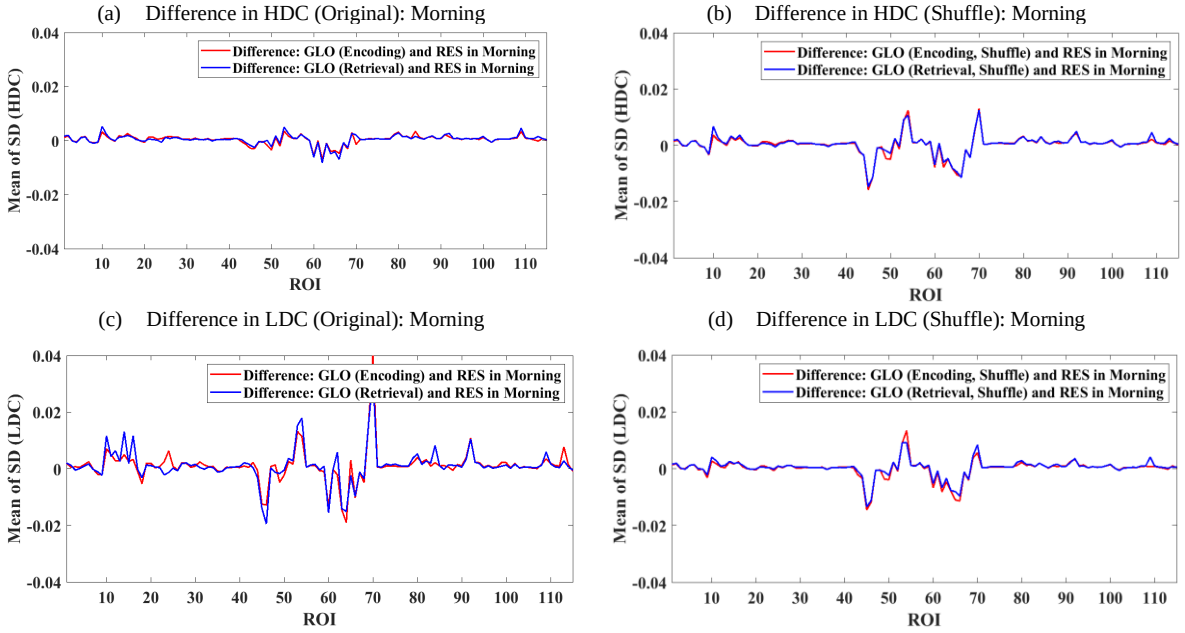

Figure 4. Comparison of differences in terms of SD for GLO (Encoding) vs RES and GLO (Retrieval) vs RES with respect to the original and shuffled clusters.

B. Distribution Analysis of Entropies

A comparison of probability distributions of fMRI time series between GLO and RES is performed with respect to three individual clusters, namely HDC, MDC and LDC. To show the algorithm's reliability, the test with randomly shuffled between the clusters time series, maintaining the original densities of the clusters, is carried out. Thus, three separate sets are prepared from the shuffled time series. These shuffled clusters are called HDC (Shuffle), MDC (Shuffle) and LDC (Shuffle). However, to distinguish the original clusters from the shuffled clusters, they are called HDC (Original), MDC (Original) and LDC (Original). A comparison of the probability distributions of the fMRI time series between original clusters and shuffle clusters with respect to the GLO and RES is shown in Fig. 3(a)-Fig. 3(c). In Fig. 3(a), it can be seen that the distribution of the fMRI time series is lower in HDC (Original) compared to HDC (Shuffle) in both GLO and RES cases. However, the distributions of fMRI time series in MDC (Original) and LDC (Original) are high compared to MDC (Shuffle) and LDC (Shuffle) in the case of GLO and RES, which is clearly shown in Fig. 3(b) and Fig. 3(c). Lower distributions of the fMRI time series in the HDC (Original) (Fig. 3(a)) indicate that NEBCA is able to perform clustering effectively and is able to accommodate the similar features of the fMRI time series in HDC (Original).

C. Difference Analysis between GLO and RES

This section presents the analysis indicating the differences in the fMRI time series of GLO and RES with respect to ROI. To show the variability of entropies, their Standard Deviations (SDs) are calculated for the HDC (Original), MDC (Original) and LDC (Original). Table I shows the mean values of all SDs belonging to HDC (Original), MDC (Original) and LDC (Original). This table shows that both encoding and retrieval phases in HDC (original) have low SD values of fMRI time series for GLO. Similarly, the fMRI time series of RES in HDC (Original) has low SD values for morning and evening sessions. The mean values of SD for HDC (Original), MDC (Original) and LDC (Original) also show the differences in the fMRI time series of GLO and RES.

To visualize the differences in the fMRI time series between GLO and RES, standard deviations (SDs) of the entropies with respect to the original clusters' ROI are considered together with the corresponding shuffled clusters (Fig. 4(a)-Fig. 4(d)). From Fig. 4(a) and Fig. 4(c), it can be easily seen that the fMRI time series of GLO and RES show significant differences in HDC (Original) and LDC (Original) clusters. Moreover, when comparing the curves of HDC (Original) and LDC (Original) (see Fig. 4(a) and Fig. 4(c)) with their respective shuffled cluster, i.e., HDC (Shuffle) and LDC (Shuffle) (see Fig. 4(b) and Fig. 4(d)), significant differences are also

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observed between the fMRI time series of GLO and RES. However, in the latter, the volatility of the signals is almost the same for HDC and LDC, which confirms the reliability of the used methodology. This comparative study shows that NEBCA is able to detect the differences between the stimulus patterns in GLO and RES in terms of sessions and signal types. From Fig. 4 and its representation on the brain, i.e., Fig. 5, it is possible to identify the brain areas that behave the most different between GLO and RES. According to the AAL atlas and LDC cluster, these ROIs mostly belongs to the range 45-70, which corresponds to: sensory motor, visual I and visual II regions in the Resting State Network (RSN).

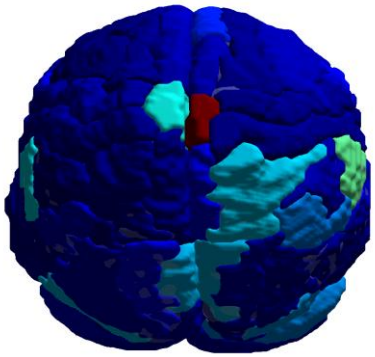

Figure 5. Absolute values of differences between GLO (Encoding, Morning) and RES for LDC (Fig. 4 bottom left panel) presented on brain heatmap with AAL atlas. Dark blue corresponds to the lowest values and dark red to the highest values.

VI. Conclusion and Future Directions

In this study, we addressed the problem of clustering fMRI time series. For this purpose, a clustering algorithm based on NS, called NEBCA, was adopted and applied to fMRI time series datasets of working memory task (i.e., GLO) and resting state (i.e., RES). NEBCA was simulated to generate three distinct clusters for the GLO and RES, which were designated as HDC, MDC and LDC. Finally, these clusters were compared to identify the differences between the fMRI time series of GLO and RES. The empirical results showed that NEBCA was able to detect the differences between them in terms of processing GLO and RES. Employing this methodology, it was possible to identify the ROIs in which the variability of these time series was significant. Finally, the visualization of the AAL atlas was used to indicate the variability in the brain areas.

NEBCA was found to be efficient in the analysis of fMRI time series datasets. However, in this study, only GLO and RES fMRI time series were considered. In the future, we will apply the algorithm to other types of the fMRI time series and compare its efficiency between verbal and non-verbal tasks related to working memory research.

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. All authors have approved the final version of the article.

Author Contributions

Pritpal Singh, Marcin Wątorek, Anna Ceglarek, Magdalena Fąfrowicz, and Paweł Oświęcimka: Conceptualization, Methodology, Validation, Reviewing and writing the article.

Acknowledgment

This study was funded by the Foundation for Polish Science Project TEAM-NET: Bio-Inspired artificial neural networks under Grant POIR.04.00-00-14DE/18-00.

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