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Letter to the Editor

Epileptic EEG activity detection for children using entropy-based biomarkers

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ABSTRACT

Seizures, which last for a while and are a symptom of epilepsy, are bouts of excessive and abnormally synchronized neuronal activity in the patient's brain. For young children, in particular, early diagnosis and treatment are essential to optimize the likelihood of the best possible child-specific result. Electroencephalogram (EEG) signals can be inspected to look for epileptic seizures. However, certain epileptic patients with severe cases show high rates of misdiagnosis or failure to notice the seizures, and they do not demonstrate any improvement in healing as a result of their inability to respond to medical treatment. The purpose of this study was to identify EEG biomarkers that may be used to distinguish between children with epilepsy and otherwise healthy and normal subjects. Savitzky-Golay (SG) filter was used to record and analyze the data from 19 EEG channels. EEG background activity was used to calculate amplitude-aware permutation entropy (AAPE) and enhanced permutation entropy (impe). The hypothesis that the irregularity and complexity in epileptic EEG were decreased in comparison with healthy control participants was tested statistically using the t-test ($p < 0{,}05$). As a method of dimensionality reduction, principle component analysis (PCA) was used. The EEG signals of the patients with epileptic seizures were then separated from those of the control individuals using decision tree (DT) and random forest (RF) classifiers. The findings indicate that the EEG of the AAPE and impe was decreased for epileptic patients. A comparison study has been done to see how well the DT and RF classifiers work with the SG filter, AAPE and impe features, and PCA dimensionality reduction technique. When identifying patients with epilepsy and control subjects, PCA with DT and RF produced accuracies of 85% and 80%, respectively, but without the PCA, DT and RF showed accuracies of 75% and 72.5%, respectively. As a result, the EEG may be a trustworthy index for looking at short-term indicators that are sensitive to epileptic identification and classification.

1. Introduction

Epilepsy is a neurological disorder disease with more than 50 million people get affected around the world, epilepsy considered the most presented brain disorder and the second most common neurological problem [1–3]. It causes abnormal neural activity changes resulting in recurrent and spontaneous seizure activity in epileptic persons including elevation of synchronization of neuronal firing, which causes an unexpected and transient electrical defect in the brain [4].

The classic example of symptoms associated with epilepsy is the creation of abnormal feelings, emotions, and sensations in addition to muscle seizures and loss of consciousness. Ongoing studies and a proper understanding of epileptic seizures have reduced the side effects of the disease based on the affected area and tissue of the brain [5–7]. Epileptic seizures often have also negative consequences for the body and mind and social effects as well as are associated with wounds, loss of consciousness, and sudden death.

The electrical field produced by brain neurons can be recorded by EEG for research purposes. This diagnostic method is considered an important tool for assessing brain function in diseases such as epilepsy because it includes many neurophysiological and obsessive data.

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Identification of the programmed seizure of epilepsy or its acknowledgment help in long-term epilepsy checking as is the case for search and recovery.

There are two types of Electroencephalogram (EEG) signals, stationary and non-stationary. EEG signal stability can be used to identify epileptic seizures by time-area highlights and recurrence space highlights.

In this way, EEG became the method of choice in both diagnosis and research of epilepsy since it can affect areas of the cortex and underlying deep-brain systems [8–10]. Tracking of seizure events is possible in epileptic persons is available by monitoring uninterrupted assessment of brain activity by using a continuous EEG. The prompt action by caregivers during monitoring of the epileptic person needs a rapid detection of seizure onset or seizure attack, however, still under development. The accurate action also needs a classification algorithm been compatible with data inputs of short-term EEG

Visual scanning and prolonged examination is the method used to detect epilepsy spikes through EEG recordings, but this method takes a long time to diagnose and is inaccurate, especially in the long recording by EEG, besides the complexity of the brain and its neural signals emanation needs a method to verify the EEG recording [11]. The mentioned defects are circumvented by using automatic methods such as linear and non-linear time-frequency analysis for example largest Lyapunov's exponent (LLE) and correlation dimension (CD).

By accepting the EEG as a non-stationary signal, strategies have been established that rely on changing wavelets and changing multiple wavelets to examine and sequence epileptic seizures [12–14].

There are two aspects of EEG given a clinical practice widely used in research a diagnosis of epilepsy [4]. These two methods to detect EEG-based seizures are explained as; a) subjects have been screened to distinguish between healthy and epileptic children that's means ictal and interictal EEG distinguished from normal EEG; b) detect a seizure in children with epilepsy and which means ictal is distinguish from interictal EEG.

Nonlinear has been received more attention compared to linear methods in EEG characterization since the latter believed to affected by a physiological process controlled inherently, which leads to an increase in the importance of EEG signals and emphasizes its ability to analyze epilepsy by recognizing epileptic seizures, the determination of the proximity of epileptic seizures is the presence of the spikes, the impending seizure can be predicted using the EEG signal [15–17].

Due to its ability to record intrinsic and physiologically key features [18], entropy measures received attention in the biomedical field, especially those that assess signals' complexity, that is why many entropy measures were been a method of choice for their ability to estimate the complexity as a nonlinear healthy physiology dynamical biomarker to detect epilepsy by short-term EEG [19]. These methods include approximate entropy (ApEn) [20], sample entropy (SampEn) [21], permutation entropy [20], symbolic dynamics-based entropy [22], and fuzzy entropy (FuzzyEn) [23], such as the use of entropy such as sample entropy, approximate entropy (AE), Kolmogorov entropy, and multiscale entropy (MSE) analysis.

Recently a measure of complexity has been introduced, which is Permutation Entropy (PE), which is used for different types of time series [15]. This method calculates different symbols' relative frequency and relies on time series mapping by symbolic sequence. These features make the PE an increasingly important tool in the analysis activity of EEG (for example see [24]), due to its ability to track the dynamics of brain activity the PE consider a feature for automated, where it was recently used to describe brain activity during epilepsy as in [25]. To achieve useful discriminations, several research efforts have been made in the stages of feature extraction, dimensionality reduction, and classification. To prevent overloading the classifier, shorten the calculation time, and improve classification accuracy, feature vectors must be carefully examined before being applied to the classifier. A common technique to prevent potential redundancy in high-dimensional data is feature dimensionality reduction. By using the dimensionality-reduced features as an input to the classifiers, the categorization of epileptic patients from control individuals by EEG signal analysis was made more accurate. The use of principle component analysis (PCA) dimensionality reduction was made possible by its quick and easy real-time implementation. Finding a hyper-plane that divides the data points representing several classes and minimizes the variance within the class under the supposition of normal data distribution is their goal in order to produce a new variable that combines the original predictors. To improve classification accuracy, this work is the first to employ PCA as a dimensionality reduction technique. Finally, classification staging is required to distinguish epileptic patients from healthy individuals. Due to their high accuracy and superior performance, decision tree (DT) and random forest (RF) classifiers are utilized at this step to classify biological signals like dementia and brain disorders. Therefore, both classifiers are used in this investigation.

The main focus of this research is the investigation of epileptic seizures in children. AAPE and impe were computed to automatically detect seizures using a Discion Tree and Random Forest classifiers. The taken issues of classification in the present study were presented by classifying both epileptic and normal EEG subjects. Depending on the entropy, accurate calculations can be made to detect seizures through scalp EEG signals [26,27]. We examine the performance of EEG data by applying entropy analysis in the detection of epilepsy based on short-term EEG, where the aim was to introduce a short-term analysis protocol that can detect an optimal seizure.

The computed performance was suggested for applied AAPE and impe, however, we achieved the best performance when (Principle Component Analysis) PCA was applied as a dimensionality reduction technique.

Therefore, in the present study, AAPE and impe were computed to expand the knowledge about the epilepsy process and classify children as epilepsy and healthy. The significant differences between the brains of healthy children and those with epilepsy were statistically confirmed using a T-test at the level of significance $p < 0.05$.

2. Materials and methods

Fig. 1 shows a proposed block diagram to show the difference between the gender in brain regions in emotional states.

2.1. EEG data acquisition and recording procedure

The EEG data sets were obtained using a Micromed Brain Spy Plus Embia via Giotto 2, 31021 Mogliano Veneto, Treviso, Italy, EEG recording headset. Data analysis, spike, and seizure detection are all done with it. 19 electrodes were employed, including 2 reference electrodes and 1 ground electrode. It utilized the 10-20 international standards, therefore the layout of the EEG electrodes is (FP1, FP2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T5, P3, Pz, P4, T6, O1, and O2). Filters with low pass, high pass, and notch functionality were built into the Micromed EEG. The sampling frequency was 256 Hz, while the upper cutoff and notch filters removed frequencies of 220 Hz and 50 Hz, respectively. The low pass filter suppressed a frequency value of 0.15 Hz. A limit of fewer than 5 kilo-Ohms was set for the electrode impedance. The participants in the current study, 20 primary school youngsters between the

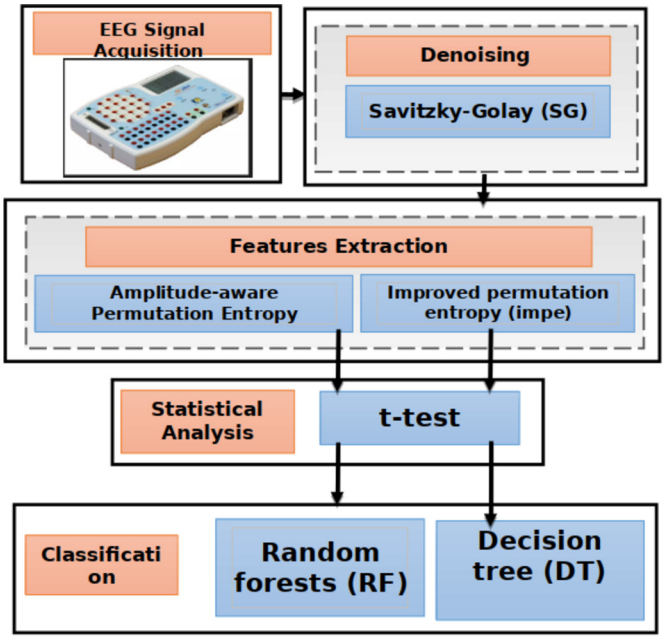

Fig. 1. Block diagram of the ongoing study.

ages of 6 and 12 (ten healthy, normal students, and ten abnormal, epileptic students) had their EEG datasets analyzed. None of the healthy control youngsters had any neurological or mental disorders. The Human Ethics Committee of the Ibn-Rushd Training Hospital in Baghdad, Iraq, gave its approval to each experimental protocol. Each epileptic child was chosen from the Neurology Clinic at the Ibn-Rushd Training Hospital, and each research participant signed an informed consent form (ICF).

2.2. Denoising stage

To get the best results, external noise sources and internal ones (patient's body noise) must be eliminated. Therefore, a butter worth notch filter has been used to remove the power line interference noise and a second-order bandpass filter ranging from 0.1 to 60 Hz has been used in the first stage.

Savitzky–Golay (SG) sift with unique qualities was used next to smooth through the sign with the least demolition. This method adopts the post-moving effect of screening the signal in contrast to the wavelet. The highlights in the order of periods are protected by using the SG channel as they include relative minimums and maximums which speak profoundly concern for them with a marker division, for example, EEG [28–31].

There are two main parameters in running an SG Filter frame size and polynomial arrangement. Therefore, the constants of an SG filter were set as in equation (1); points of the EEG signal, where N is a window size, N_r and Nl represent right and left signal points of a current signal point respectively. The test is installed with SG channel specification in polynomial order and envelope size of 51 samples to remove noise and smooth out the EEG dataset.

$$N = N_r + Nl + 1 \tag{1}$$

2.3. Features extraction

The AAPE and impe types of entropy have been estimated in this study to distinguish between epileptic EEG signals and those from normal, healthy control participants. In this work, features from the original EEG time series for each of the 19 channels were extracted using 60 seconds, N=15360 samples, and 6 windows of 10 seconds each (2560 samples). Entropies have been utilized to find anomalies in the EEGs of pediatric epilepsy patients. AAPE is adapted from permutation entropy (PE) of Bandt-Pompe. The AAPE system overcomes the problems of normal PE which are ignoring the amplitudes mean value and the adjacent samples' differences. This system also helps in solving the problem of recorded identical values of amplitude samples (which is applicable for digitized time series). In contrast, the is a sensitivity to changes in frequency and amplitude of the signals with AAPE methods because it has high reliability in determining the signal motifs. In contrast to PE, AAPE has the ability to reduce noise effect, and well detection of spikes well; even samples have single spikes. The change was larger in multi-sample spikes recorded with AAPE compared to PE.

AAPE is obtained, which has a value of $ln\, d!$, where $d!$ potential ordinal patterns $d = 3$, and scale of $l = 1$. In contrast, $N = 15360$ samples, 6 windows of 10-second length (2560 samples) were extracted from the original EEG time series for each one of the 19th channels. Mathematically, in normal PE (Bandt-Pompe method) and the case of conformity with the specification of i set, one is added to increase the group frequency and in the case of AAPE, 0 to 1 is added to the probability of that set as follows.

$$\frac{A}{d}\sum_{k=1}^{d}|Y_{t+(k-1)l} - Y_{t+(k-2)l}| \tag{2}$$

Improved multiscale permutation entropy (impe) is also essentially based on PE, where PE is theoretically simple and it has fewer parameters, it is relatively robust to artifacts and noise, and is computationally fast, which makes it better than other functions [32]. Yet the conventional MPE has two main obstacles. The first one, the MPE shows no simitry. We can explain the second one that when using MPE with long temporal scales of the signal, it shows comparably a variance in the results. Computing MPE for the coarse-graining process leads to such many samples of the resulting coarse-grained sequence equal to $\lfloor \frac{N}{\tau} \rfloor$, when the scale factor τ is high, the number of samples in the coarse-grained sequence decreases. This may yield an unstable measure of entropy.

To get rid of these problems, an Improved multiscale permutation entropy (impe) has been introduced, impe is a promising method to assess physiological changes affecting various temporal scales since it increases the accuracy of entropy calculations, producing more accurate and stable results, which has a value of embedded dimension $m = 3$, and a scale of $\tau = 1$. In contrast, which illustrates a completely regular signal, the smallest value of impe is obtained as much as 0 for 60 seconds, $N = 15360$ samples, 6 windows of 10-second length (2560 samples) were extracted from the original EEG time series for each 19 channels where it can be calculated in two steps [32]

1. We will rearrange the time series data as follows:

$$Z_i^{(\tau)} = Y_{i,1}^{(\tau)}, Y_{i,2}^{(\tau)}, \ldots \tag{3}$$

Where $Y_{i,j}^{(\tau)}$ is:

$$Y_{i,j}^{(\tau)} = \frac{\sum_{f=0}^{\tau-1} X_{f+i+\tau(j-1)}}{\tau} \tag{4}$$

in the MPE method, only $Z_1(\tau)$ is considered.

2. PE of each of $z_1(\tau) \mid (i = 1, \ldots, \pi)$ is separately calculated. Then, the average of PE values is computed as follows:

$$impe(x, \tau, d) = \frac{1}{\tau}\sum_{i=1}^{\tau} PE(z1(\tau)) \tag{5}$$

d determines the number of accessible states d!.

2.4. Statistical analysis

Nineteenth denoised channels of EEG dataset from 10 solid typical and 10 epileptic children for cerebral cortex starters were assembled according to scalp area to 5 recording regions. Seven front channels were merged with the aforementioned regions and these channels are (Fp1,2,3,4,7,8 and Fz) with two- time channels (T3 and T5) and three wall channels (P3,4 and Pz) in addition to the occipital channels (O1 and 2) and the 3 central channels (C3,4 and Cz). Typicality in the current research was examined by Kolmogorov–Smirnov test, while homoscedasticity was examined by Levene's test. In this study, a t-test was used as a factual instrument by utilizing SPSS 23. Right now, the test was applied to AAPE and impe highlights. For each part, the independent variables (IV) were gatherings the subjects (control solid typical and kids with epilepsy) as the subsequent IV, though mentioned highlights were the dependent variable (DV). In the current study, all statistical tests were set to a $p < 0.05$.

2.5. Classification

There is a classification for unpruned groups or regression trees called random forest [33], this classification depends on the samples collected during the training and relies on select data on a random base. Cases were predicted by predictions of the ensemble where the rating or average regression was voted by a majority. The choice of the random forest was appropriate, and this is evident from the significant improvement in performance over the single tree classifier such as CART and C4. This system is preferred when compared to Adaboost in terms of producing error rates despite the robust noise produced. The random forest algorithm was used for feature categorization. Random forests are characterized by high accuracy in classification in addition to resistance to overtraining and the efficiency of working with large data and do not require normalization of features besides required a few parameters optimizations. These advantages are particularly important in the application of the closed-loop when early detection of epileptic seizures. Dividing is used in the tree ensemble to create a random forest. The bagging technique and random selection feature have both been combined within the same classifier (24 and 25). The randomness of the trees is performed by selecting sub-groups and including $\frac{2}{3}$ training data and each node subset of features (26–28). Other training parts, $\frac{1}{3}$, calibrate the performance of each tree and calculate the error out-of-bag. To determine the development of each decision tree in a random forest, a Gini index was used as a branched index (29 and 30). The Gini index is also used in calculating the importance of features, which gives the ability to choose the desired feature. Although the feature selection is important in optimizing the detection algorithm before loading it for each patient in the implantable device, in the current research this feature has been overridden to examine the patient for the same set of features. In the present study, binary decision trees were assigned to 100. The increase in the number of trees did not significantly affect the improvement in classification accuracy. According to what Liaw and Wiener confirmed, the square root of N is the optimal number of randomly selected features (N represents the number of features). Based on that, the selected number was closest to the square root of the features and the number was four features randomly in each node. The "leave one out" cross-validation method was used for effect comparison of big versus small training data sets. Firstly, data for training only one-hour segments of EEG containing at least one epileptic seizure were compared with data for one-hour sections that did not contain epilepsy. Subclinical seizures of iEEG were used in test data tests and left out of the training data set. Subclinical seizures have been excluded in a recent study, in order to avoid the suspicion that occurs in the reading of the signs, due to their similarity with epilepsy to a large extent. Although they are similar from an electrophysiological point of view to clinical seizures, subclinical seizures are not considered real seizures from a medical point of view. Another reason to exclude these seizures is that they somehow fall between the abnormal electrical activity and the clinical seizure, and their use in the training data set causes the detection algorithm to malfunction. For detection, more than one channel was selected all selected channels were checked for performance and features and the result was presented from the electrodes as the following standards: the delay in seizure detection obtainable channel is the shortest one or the false detection rate (FDR) is lesser on the obtainable channel. The test used to assess changes in sensitivity between the use of one-hour shift slices and all available training data was Mann–Whitney's U-test.

The intracranial early seizure detection algorithm based on EEG was first invented by Bremann in addition to forest classification references [34]. The growth rules of a forest consisting of *T-tree* structure a random classifier are summarized as follows [20]. First, assume that the number of cases in the training group is N, after which random samples are taken from them and replaced in each processed sample and N training samples acquired. It should be noted that not all training data is used, while the data can be used more than once, or some data may not be used at all. Second, if M is the input features dimension, m ($m < M$) represents arbitrarily nominated sub-features specified dimension from the original feature vectors. Then the feature of the variable m is determined randomly from the features of the M, and the best split of the node is used for this purpose. Third, trees are left to grow without pruning until all training samples are completely separated. The error rate in the forest depends on two things. First, the trees are connected within the forest. In general, the more correlation between trees increases the error rate, while the lower the error the lower the correlation. The second is the power of one tree in the forest. Error rate decreases in the forest as the power increases. The number of features specified is the only parameter that is adjustable and sensitive to the random forest. The correlation and strength can be reduced by reducing their value. Based on the foregoing, a trade-off can be found between connection and strength. In the current study, we investigated the effects of different groups of trees on classification accuracy to find out the best performance in random forests.

3. Results and discussion

The effect of the SG channel is shown in Fig. 2, where the EEG data-set recording smoothed as a result of its effect. Channel No. 2 (Ch2) shows that all the commotion parts of the disturbance were stifled, and it is illustrated in the mentioned figure with a blue line, while the red line represents the recording EEG of the first boisterous.

By using the five electrodes on the scalp, the age match of healthy children and those with epilepsy was controlled, and the impe entropy and AAPE values were measured, as showed in Table 1. The EEG for normal children is higher than that recorded for epileptics regarding the impe entropy and the AAPE over the temporal and occipital regions of the brain according to equations ($AAPE_{Epilepsy} < AAPE_{Normal}$) and ($impe_{Epilepsy} < impe_{Normal}$). This higher recording could be explained by an increase in mental activity and the EEG is more regular and less complex during an epileptic seizure compared to healthy people. The reduced electrical complexity of the brain in people with epilepsy is recorded by dynamic processes which the reason that causes the detection of electrical regulation of the brain. The reduced complexity of

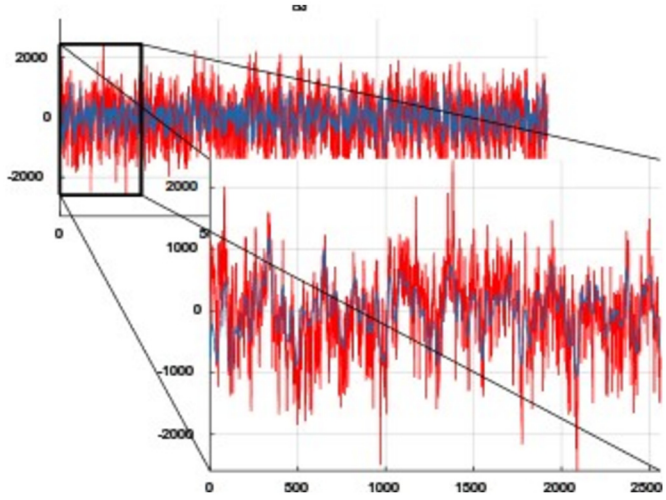

Fig. 2. The denoising results after using SG filter for Ch2 which represent Fp2.

Table 1
The EEG values for epilepsy patients are presented as (Mean SD) for all five areas of the scalp. An asterisk was placed to distinguish between the groups that contain a significant difference.

Features	Brain regions	Normal	Abnormal	P-value
AAPE	Frontal	1.053±0.017	17.058±0.044	0.05*
	Temporal	1.059±0.008	1.031±0.044	0.05*
	Central	1.053±0.017	1.071±0.087	0.05*
	Parietal	063±0.026	1063±0.09	0.05*
	Occipital	1.058±0.007	1.013±0.05	0.05*
impe	Frontal	1.058±0.044	1.549±0.085	0.05*
	Temporal	1.031±0.044	1.489±0.09	0.05*
	Central	1.071±0.087	1.583±0.211	0.01*
	Parietal	1.063±0.09	1.559±0.217	0.01*
	Occipital	1.013±0.05	1.447±0.1	0.05*

the EEG, as indicated by some studies, may be due to the death of some neurons, which leads to loss of connectivity and/or deficiency of the neurotransmitter [35]. The results proved that impe more efficient than AAPE in diagnosing epilepsy. EEG signals are clinically important as a tool for early detection of a seizure, and thus differentiate between a normal person and a person with epilepsy. The current study indicated that monitoring of clinical and even portable EEG and analysis of epileptic seizures with entropy EEG signals are among the promising methods in this field. Furthermore, obtained results shows classifier (RF) provides an 85% success rate.

4. Conclusions

This study attempts to discriminate between children with epilepsy and healthy normal subjects. SG filter has been employed for denoising and smoothing the EEG dataset, and using AAPE and impe were computed. Statistical analysis using t-test ($p < 0.05$) has been conducted to characterize the features and were used to test the hypothesis that the irregularity and complexity in epileptic EEG were reduced in comparison with healthy control subjects. AAPE and impe results in reducing the complexity in epileptic patients compared to the healthy control subjects. Therefore, AAPE and impe could be the EEG biomarkers associated with epileptic detection and identification for children patients with epilepsy. Finally, EEG could be as a valuable biomarker for inspecting the background activity in the identification of children patients with epilepsy.

Human and animal rights

The authors declare that the work described has not involved experimentation on humans or animals.

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Declaration of competing interest

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

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