Title: Assessing the Effects of Alzheimer’s Disease on EEG Signals Using the Entropy Measure: A Meta-Analysis

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Abstract
Introduction and Aims
Alzheimer’s disease is the most prevalent neurodegenerative disorder and a type of dementia. 80% of dementia in older adults is because of Alzheimer’s disease. According to multiple research articles, Alzheimer's has several changes in EEG signals such as slowing of rhythms, reduction in complexity and reduction in functional associations, and disordered functional communication between different areas of the brain. This research focuses on the entropy parameter.

Materials and Methods
In this study, the keywords Entropy, EEG, and Alzheimer's were used. In the initial search, 102 research articles were found. In the first stage, after investigating the abstract of articles, the number of them was reduced to 62, and upon further review of the remaining articles, the number of articles was reduced to 18. Some papers have used more than one entropy of EEG signals for comparing and some of them have used more than one database. So 25 entropy measures were considered in this Meta-Analysis. We used the standardized mean difference (SMD) for finding the effect size to compare the effects of Alzheimer’s disease on the entropy of the EEG signal with healthy people. Funnel plots were used to investigate the bias of Meta-Analysis.

Conclusion
According to the articles, results and funnel plots of this Meta-Analysis, entropy seems to be a good benchmark for comparing the EEG signals in healthy people and people who have Alzheimer’s disease. It can be concluded that Alzheimer’s disease can significantly affect EEG signals and reduce the entropy of EEG signals.

Keywords: EEG signal, Entropy, Alzheimer's disease, Meta-analysis
1. Introduction and Aims

Alzheimer’s disease is a common neurodegenerative disease that more than 10% of Americans over age 65 years and nearly 50% of people older than 85 years suffer from it [1]. This disease was discovered in 1907 by a German psychiatrist and neurologist, Alois Alzheimer. The prevalence of this disease has been much higher in people older than 65 years [2]. Several physiology changes take place in Alzheimer’s disease such as the degeneration of neurons, the formation of neurofibrillary tangles (tau protein masses) and senile plaques (hypercellular masses of beta-amyloid protein) in the hippocampus, outer cortex of the brain and other areas, reduction in brain mass, degeneration of the cortex and enlargement of the ventricles. Alzheimer’s disease is categorized into four stages: 1- The first stage is Mild Cognitive Impairment (MCI) where there is no reliable sign of the disease [3]. 2- In the “early stage” the patients will be faced with difficulty in forming words, remembering names and daily events, and they also will experiment short-term memory impairment. 3- In the “middle stage” the patients will miss some of their abilities such as speech, appropriate words use, judgment, logical thought, planning, organizing, visual cognition and focused. 4- In the “advanced (severe) stage” all cognitive activities and motor functions are affected, such as mastication (chewing) and swallowing [4].

Unfortunately, no definitive treatment options have been identified for Alzheimer's disease so far. Thus the usual treatment plans are purely palliative (aimed at reducing the rate of progression), and drugs are only effective at certain stages of the disease [5]. However, early diagnosis of the disease is invaluable to reduce the rate of its progression. In this regard, Electroencephalography (EEG) abnormalities of Alzheimer’s disease (AD) patients have been extensively studied for several decades [6]. One of the most critical issues of EEG studies on AD is the improvement of the accuracy of differential diagnosis of AD and early detection in the pre-clinical stage by examining EEG alterations in subjects having risk factors for AD. Although Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and Single Photon Emission Computed Tomography (SPECT) are currently the most commonly used neuroimaging modalities in Mild Cognitive Impairment (MCI) studies, quantitative EEGs also have the potential to become a valuable and cheap tool in the early diagnosis of AD [7]. Also, the time resolution of the EEG is better than other tools.

Several studies have investigated the effect on Alzheimer’s disease on brain activity by comparing the EEG signals between healthy individuals and Alzheimer’s patients. They have revealed several number of changes in the brain activity in Alzheimer’s disease patients compared to healthy subjects, such as slowing of rhythms, reduction in complexity and functional associations, and disordering functional communication between different brain areas. There are also different methods for assessing signal complexity in articles such as sample entropy [6], auto-manual information [8], Lampel-Ziv complexity [9], measuring complexity in recurrence plots Recurrence Quantification Analysis (RQA) [10], Multi Scale Entropy (MSE) [4], Permutation Entropy (PE) [11], Tsallis entropy [12], largest Lyapunov exponent [7], correlation dimension [13], fractal dimension [14], simplicity dimension and relative energy of frequency bonds [15].
There are numerous articles on the changing complexity of EEG signals in Alzheimer's disease patients compared to healthy individuals. These changes can be decreasing or increasing. We want to do a Meta-Analysis to obtain a general conclusion on this topic. A Meta-Analysis is a precise method for collection, integration, and evaluation of scientific evidence. In the complexity of the EEG signal debate, we have focused on the specificity of different entropies. Accordingly, this article aims to find the answer to the question, “Can Alzheimer’s disease significantly affect EEG signals or not?”

2. Materials and Methods

Different sources must be considered, and there should not be a focus on a specific source or language. This Meta-Analysis using online search engines were done in four scientific databases: IEEE, Science Direct, Google Scholar, Medline (PubMed). To find appropriate articles, suitable keywords must be used in the search. Our keywords are Entropy, EEG and Alzheimer’s. Meta-Analysis needs the definition of inclusion criteria that are derived from the PICO (Population, Intervention, Comparison, Outcome) model [8].

Inclusion criteria for this Meta-Analysis are:

- A physician has already diagnosed Alzheimer’s disease in the patient’s group.
- The effect of Alzheimer’s disease on the entropy of the EEG signal is reported.
- The reported feature of the EEG signal is entropy.
- Results of the amount of entropy on both groups of healthy and patients have been reported.

After titles and abstracts evaluation of found articles, those who passed the mentioned filters were chosen. In our initial search, 102 articles were found on this subject. Upon investigating their abstracts, the number of relevant articles appropriate to this Meta-Analysis was reduced to 62. Finally, after reviewing the research articles and making sure that they have satisfied the inclusion criteria, this number was reduced to 18. Three papers have used more than one entropy measure of the EEG signal; (Hereafter for discussion on each of entropy measures used in an article, we create a record in Meta-Analysis and we call it a study. Two of them have used two entropy measure (2 × 2 = 4 studies) and another one has used four entropy measure (1 × 4 = 4 studies) also two articles have used two different databases (2 × 2 = 4 studies) and the rest of the papers used only one entropy measure and one database, 13 studies are in total. So, this Meta-Analysis was included 25 studies (4+4+4+13=25 studies). Figure 1 is PRISMA (Preferred Reporting Items for Meta-Analysis) flow diagram [9]. The selected articles were investigated, and two types of data were extracted from them, including general data information and the statistical parameters, which are shown in Table1.

3. Meta-Analysis

As mentioned in section two, 25 studies can be extracted from the 18 selected articles. The Meta-Analysis of these studies is discussed in section 3-1 which is called “General Meta-Analysis”. Some articles have used more than one entropy measure or the same author has written more than one article. This causes a problem of dependence that is discussed in section 3-2.
3.1. The General Meta-Analysis

A forest plot as the most important output of a Meta-Analysis demonstrates the composition of the effect size of each research in the form of fixed or random-effect size models. This plot also displays the standard deviation and error of each study obtained from the combined value. The forest plot is depicted in Figure 2-(a) using Comprehensive Meta-Analysis (CMA) software [10] and is calculated for the 25 mentioned studies. The method of calculating the parameters used in the forest plot is given in Appendix A.

As described in Appendix A, the statistical significance shows whether the observed relationship between variables or differences between groups is justified by chance or not. This probability is represented by the probability value (P-value). The level of p-value is between 0 and 1. The statistical problems express a p-value of $10^{-6}$ which means the value is very low. So the smallness of this probability value ($P \text{ value} < 10^{-6}$) represents that the observed difference or relationship between the variables is inherent and not based on chance. Therefore, the null hypothesis is rejected, which indicates that the entropy of the EEG signals in the patient group is significantly different from the entropy of the EEG signals in healthy counterparts.

Here, to study the heterogeneity, which is described in Appendix B, the Q index is used. As seen in Table 2-(a), Q has a small value ($Q = 42.174$), and the P-value is higher than 0.01. Therefore, the null hypothesis based on the fact that the studies were homogeneous is not rejected. Additionally, another index to test the homogeneity is $I^2$. As mentioned, this index measures the ratio of the variance between studies to the total variance. This index is smaller than 50% that also exhibits the homogeneity of studies.

3.2. The same data and The same author Meta-Analysis

In the Meta-Analyses, the reviewers collect the extensive information of initial studies. When they have two or more initial studies that have been written by the same author or they have more than two studies that have used the same database, these issues cause "same author" or "same data" problem in Meta-Analysis that leads to the dependence between studies. We used one of the method suggested in [11] to eliminate this dependence. Among the articles with the same data, articles that are more general and comprehensive than the rest of the articles with similar data are chosen; if analysts choose a study from several studies to report in order to get rid of the dependency between studies, they will lose some of the information, which is the disadvantage of this method.

4.2.1 The same data Meta-Analysis

In this section, we investigate the case in which the most comprehensive paper was selected from articles with the same data. Between [5, 12-15] we chose [12] because that is the most recent one [14] has four entropy measures, and its database is the same as the database of [4, 12, 13, 15]. So we omitted all of those studies. [16] used Multiscale Permutation Entropy (MPE) and Multivariate Multiscale Permutation Entropy (MMPE), so we omitted study with MMPE measure entropy. [17, 18] use two similar databases in two investigated studies in each of them. Therefore, we chose the study with database 2 in [17] and database 1 in [18]. So we performed the Meta-Analysis with 14 studies in this section.

The forest plot is shown in Figure 2-(b). The amount of Standardized Mean Difference (SMD) of effect size is calculated for various studies. In addition, the weights of each study are shown. The reported P-value in Table...
2-(b) is very small ($P - value < 10^{-6}$). As mentioned before, in this case, the null hypothesis is rejected. The null hypothesis indicates that the entropy of the EEG signals in the patient group is not significantly different from the entropy of the EEG signals in healthy counterparts. About heterogeneity, as it is seen in Table 2-(b), $Q$ has a small value ($Q = 25.794$), and the P-value is higher than 0.01. Therefore, the null hypothesis is not rejected. The null hypothesis indicates that the studies were homogeneous. $I^2$ value is smaller than 50%, which indicates that the studies are homogeneous.

4.2.2 The same author Meta-Analysis

In this section, we investigate the case in which the most comprehensive paper was selected from articles with the same authors. Between [5, 12, 13, 15, 19, 20] that Abásolo wrote them we chose [12] because that is the most recent one. Among four entropy measures used in [14] and written by Azami and two entropy measures used in [16] and written by Morabito, we chose $MSE_\mu$ and MPE respectively because those are more similar to other entropy measures in other studies. [17, 18] use two similar databases in two investigated studies, which are written by Al-nuaimi and Zhao respectively. Therefore, we chose the study with database 2 in [17, 18] because the number of participants in this database is more than database 1. So we performed the Meta-Analysis with 13 studies in this section.

The forest plot, the SMD value of the effect size for the various studies, and the weight of each study in this Meta-Analysis are shown in Figure 2-(c). The reported P-value in Table 2-(c) is very small ($P - value < 10^{-6}$). It means the null hypothesis saying that the entropy of the EEG signals in the patient group is not significantly different from the entropy of the EEG signals in the healthy counterparts is rejected. So the alternative hypothesis is confirmed which indicates that the two mentioned groups have a significant difference. As was seen, $Q$ has a small value ($Q = 22.332$) and a P-value is greater than 0.01. Therefore, the null hypothesis based on the fact that the studies were homogeneous was not rejected. According to $I^2$ value, this index is smaller than 50%. Therefore, it seems that the studies are homogeneous.

4. Funnel plot

Funnel plots (for more information see Appendix C) were first proposed as a means of detecting a specific form of publication bias. The exaggeration of treatment effects in small studies of low quality provides a plausible alternative mechanism for funnel-plot asymmetry. In this situation, the effect calculated in a Meta-Analysis will tend to overestimate the intervention effect. Greater asymmetry indicates greater bias.

Figures 3 shows the funnel plots of the Meta-Analyses; In section (A) funnel plot of General Meta-Analysis is shown, in section (B) we can see the funnel plot of the same data Meta-Analysis and in section (C) funnel plot of the same author is depicted. According to this figure, the studies with the low sample size are at the bottom of the funnel plot, and conversely studies with the larger sample size are at the top of this plot. It is seen that there is no asymmetry in shape in any of the plots. Thus, the possibility of bias in this regard is canceled.

5. Discussion and Conclusion
In this Meta-Analysis, the effect of Alzheimer's disease on the EEG signal was studied using the entropy measure. Twenty-five studies were included in this paper. According to the results and funnel plots of this Meta-Analysis, entropy seems to be a proper index for comparing the EEG signals in patients with Alzheimer's disease with healthy controls. It can be concluded that Alzheimer's disease can significantly affect EEG signals and reduce the EEG signal's entropy. The null hypothesis in this Meta-Analysis is that there is no significant difference between the two groups. According to the very small obtained p-value (near zero), this hypothesis is rejected, and two groups have a significant difference.

As mentioned, there are many articles on the effects of Alzheimer's disease on the EEG signal. However, this article has advantages such as specificity and comprehensiveness compared to previously published articles with a close topic. For example, in [29], the effect of Alzheimer's disease on only sample entropy and fuzzy entropy of the EEG signal has been studied, but in this article, we use all kinds of entropy methods to find it by Meta-Analysis. So this article is more comprehensive than [29]. Also, for example, in [30, 31], the authors have studied and done Meta-Analysis for the effect of Alzheimer's disease on the EEG signal using all methods such as slowing of rhythms, reduction in complexity and functional associations, while in this article we have tried to discuss signal complexity and specifically entropy of EEG signal. In our Meta-Analysis, one single writer had written several of the found articles, and some articles have used a similar database. So there are dependencies between studies, which were solved with one of the approaches used in [19]. However, the disadvantage of this method is that parts of data would be omitted. The small amount of Q in the various Meta-Analyses examined indicates homogeneity of the Meta-Analysis. Statistical significance was used to determine whether the two groups were significantly different and not by chance. Despite the importance of these methods, their use in determining this difference is limited. For example, a statistically significant result (p-value) will improve by increasing the number of samples despite the clinical explanation of the effect size. Also, the P-value is greater than 0.01 in the heterogeneity test, which means that the null hypothesis suggesting that studies are homogeneous is not rejected and there is no heterogeneity between studies. We applied a funnel plot for the publication bias, which indicates there is no asymmetry in this plot; therefore, this Meta-Analysis has no publication bias.

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Conflict of Interest: The authors have no financial or any other kind of personal conflict of interest with this article.

Author contribution: Farnaz Ghassemi: Instructed the concepts, performed analysis and discussion, contributed to the design of tables and figures, reviewed and edited the manuscript. Hajar Ahmadieh: Performed literature search, data extraction and analysis, wrote the article, performed the design of tables and figures.

We have no conflicts or Funding to report.
Figure 1-PRISMA flow diagram (Preferred Reporting Items for Meta-Analyses) shows the number of identified records, excluded, and included studies. Article*= Primary searched the paper  
Study**= entropy measures used in an article which may be more than one in a paper
Figure 2: Forest plot for entered studies into CMA Software (General Meta-Analysis)
### Statistics for each study

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<th>Variance</th>
<th>Std diff in means</th>
<th>Mean limit</th>
<th>Upper limit</th>
<th>Z Value</th>
<th>p-Value</th>
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### Model

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### Figure 3 - Forest plot for entered studies into CMA Software (The same data Meta-Analysis)
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<th>Relative weight</th>
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*Figure 4- Forest plot for entered studies into CMA Software (The same author Meta-Analysis)*
Figure 5- Funnel graph of Meta-Analyses. (a) General Meta-Analysis. (b) The same data Meta-Analysis. (c) The same author Meta-Analysis.

Lozenges showed in this figure illustrate the fixed-effect model, which is explained in Section 4
Table 1—Information extracted from studies entered into the Meta-Analysis

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<th>Duration (min)</th>
<th>Number of participants</th>
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<th>MMSE&lt;sup&gt;3&lt;/sup&gt; (AD/HIC)</th>
<th>Artifact Filtering Band Pass Filter with cut off frequency (Hz)</th>
<th>Type of entropy measure</th>
<th>Sampling frequency (Hz)</th>
<th>Mean AD/HIC</th>
<th>SD AD/HIC</th>
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<td>11/11</td>
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<td>13.1 ± 5.9 / &gt;30</td>
<td>0.5-40 SpecEn&lt;sup&gt;4&lt;/sup&gt;</td>
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<td>0.656 / 0.702</td>
<td>0.104 / 0.096</td>
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</tr>
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<td>13.1 ± 5.9 / &gt;30</td>
<td>0.5-40 SampEn&lt;sup&gt;1&lt;/sup&gt;</td>
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<td>0.646 / 0.763</td>
<td>0.179 / 0.178</td>
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<tr>
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<td>15/18</td>
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<td>15.9±4.5 / -</td>
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<td>1.783 / 1.773</td>
<td>0.055 / 0.036</td>
<td>m=2 r=0.2 N=1200 T=7</td>
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<tr>
<td>4</td>
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<td>&gt;5</td>
<td>11/11</td>
<td>72.5 ± 8.3 /72.8 ± 6.1</td>
<td>13.1 ± 5.9 / &gt;30</td>
<td>0.5-40 MSE</td>
<td>256</td>
<td>1.477 / 1.554</td>
<td>0.087 / 0.101</td>
<td>m=1 r=0.25 T=6</td>
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<tr>
<td>5</td>
<td>[20]</td>
<td>&gt;5</td>
<td>1/10/8</td>
<td>74.8 ± 8.3/74.9 ± 5.9</td>
<td>12.6 ± 5.9 / &gt;30</td>
<td>0.5-40 ApEn&lt;sup&gt;7&lt;/sup&gt;</td>
<td>256</td>
<td>0.856 / 0.996</td>
<td>0.213 / 0.214</td>
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<td>6</td>
<td>[15]</td>
<td>1.6 min</td>
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<td>200</td>
<td>1.888 / 1.898</td>
<td>0.025 / 0.018</td>
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<td>7</td>
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<td>11/11</td>
<td>72.5 ± 8.3 /72.8 ± 6.1</td>
<td>13.1 ± 5.9 / &gt;30</td>
<td>0.5-45 ApEn</td>
<td>256</td>
<td>0.706 / 0.839</td>
<td>0.196 / 0.194</td>
<td>m=1, r=0.25, N=1280</td>
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</tr>
<tr>
<td>8</td>
<td>[17]</td>
<td>4</td>
<td>Data1 3/8</td>
<td>Data1 &gt;60 / &gt;60</td>
<td>-</td>
<td>-</td>
<td>Tsallis Entropy</td>
<td>128</td>
<td>0.150 / 0.490</td>
<td>0.051 / 0.173</td>
<td>DATA1 N=5120, q=0.5</td>
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<tr>
<td>10</td>
<td>[22]</td>
<td>-</td>
<td>15/20</td>
<td>80.8 ± 9.0 /62.1± 10.4</td>
<td>-</td>
<td>-</td>
<td>ASE&lt;sup&gt;3&lt;/sup&gt;</td>
<td>200</td>
<td>53.400 / 61.780</td>
<td>8.257 / 4.684</td>
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<tr>
<td>11</td>
<td>[19]</td>
<td>&gt;5</td>
<td>7/7</td>
<td>75.6 ± 6 / 58.7±3.5</td>
<td>-</td>
<td>0.4-70 Nth order filter</td>
<td>50</td>
<td>0.780 / 0.930</td>
<td>0.100 / 0.110</td>
<td>m=2, r=0.25, N=1280</td>
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<td>72.5 ± 8.3 /72.8 ± 6.1</td>
<td>13.1 ± 5.9 / &gt;30</td>
<td>1-40 MSE&lt;sub&gt;μ&lt;/sub&gt;</td>
<td>256</td>
<td>1.596 / 1.707</td>
<td>0.147 / 0.184</td>
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<td>11/11</td>
<td>72.5 ± 8.3 /72.8 ± 6.1</td>
<td>13.1 ± 5.9 / &gt;30</td>
<td>1-40 mv MSE&lt;sub&gt;μ&lt;/sub&gt;</td>
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<td>0.102 / 0.109</td>
<td>0.013 / 0.012</td>
<td>T=3</td>
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<td>14</td>
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<td>11/11</td>
<td>72.5 ± 8.3 /72.8 ± 6.1</td>
<td>13.1 ± 5.9 / &gt;30</td>
<td>1-40 MSE&lt;sub&gt;μ&lt;/sub&gt;</td>
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<td>0.950 / 1.119</td>
<td>0.181 / 0.181</td>
<td>T=9</td>
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<td>11/11</td>
<td>72.5 ± 8.3 /72.8 ± 6.1</td>
<td>13.1 ± 5.9 / &gt;30</td>
<td>1-40 mv MSE&lt;sub&gt;μ&lt;/sub&gt;</td>
<td>256</td>
<td>0.023 / 0.029</td>
<td>0.006 / 0.008</td>
<td>T=9</td>
<td></td>
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<td>16</td>
<td>[13]</td>
<td>&gt;5</td>
<td>11/11</td>
<td>72.5 ± 8.3 /72.8 ± 6.1</td>
<td>13.1 ± 5.9 / &gt;30</td>
<td>0.5-40 ApEn</td>
<td>256</td>
<td>0.706 / 0.839</td>
<td>0.196 / 0.194</td>
<td>m=1, r=0.25, N=1280</td>
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<td>17</td>
<td>[23]</td>
<td>3/4</td>
<td>14/14</td>
<td>74.84 / 70.76</td>
<td>-</td>
<td>0.5-30 WPE&lt;sup&gt;7&lt;/sup&gt;</td>
<td>1024</td>
<td>0.690 / 0.691</td>
<td>0.009 / 0.008</td>
<td>m=6 T=1</td>
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<td>18</td>
<td>[12]</td>
<td>&gt;5</td>
<td>11/11</td>
<td>72.5 ± 8.3 /72.8 ± 6.1</td>
<td>13.1 ± 5.9 / &gt;30</td>
<td>0.5-40 ApEn</td>
<td>256</td>
<td>1.449 / 1.616</td>
<td>0.245 / 0.221</td>
<td>m=1 r=0.1, N=1280</td>
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<td>[18]</td>
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<td>Data1 3/8</td>
<td>&gt;65 / &gt;65</td>
<td>-</td>
<td>-</td>
<td>Tsallis Entropy</td>
<td>128</td>
<td>0.170 / 0.380</td>
<td>0.050 / 0.071</td>
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<td>-</td>
<td>-</td>
<td>Tsallis Entropy</td>
<td>128</td>
<td>0.230 / 0.260</td>
<td>0.048 / 0.056</td>
<td>DATA2 N=5120, q=0.5</td>
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<td>3/3</td>
<td>60-75 / 60-75</td>
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<td>0.5-32 MPE</td>
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<td>0.009 / 0.006</td>
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<tr>
<td>22</td>
<td>[16]</td>
<td>-</td>
<td>3/3</td>
<td>60-75 / 60-75</td>
<td>-</td>
<td>0.5-32 MMPE&lt;sup&gt;10&lt;/sup&gt;</td>
<td>200</td>
<td>0.867 / 0.896</td>
<td>0.014 / 0.006</td>
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<td>23</td>
<td>[24]</td>
<td>10</td>
<td>20/20</td>
<td>74.78 / 74.78</td>
<td>11.7-14.9 / 28.1-30</td>
<td>0.5-30 ApEn</td>
<td>1024</td>
<td>0.320 / 0.321</td>
<td>0.011 / 0.017</td>
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<td>24</td>
<td>[25]</td>
<td>2.16</td>
<td>14/20</td>
<td>-</td>
<td>-</td>
<td>0.5-40 ApEn</td>
<td>250</td>
<td>0.265 / 0.355</td>
<td>0.063 / 0.080</td>
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<tr>
<td>25</td>
<td>[26]</td>
<td>2006</td>
<td>63/73</td>
<td>76.7 ± 6.2 / 73.3 ± 5.9</td>
<td>23.6 ± 2.6 / 28.7 ± 1.6</td>
<td>0.1-30 MS Permutatin</td>
<td>EN</td>
<td>250</td>
<td>1.684 / 1.690</td>
<td>0.0130 / 0.011</td>
<td>T=3</td>
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Table 2 - Statistical characteristics (General Meta-Analysis)

<table>
<thead>
<tr>
<th>Model</th>
<th>Effect size and 95% confidence interval</th>
<th>Test of null [2-Tail]</th>
<th>Heterogeneity</th>
<th>Tau-squared</th>
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<tbody>
<tr>
<td></td>
<td>Number Studies</td>
<td>Point estimate</td>
<td>Standard error</td>
<td>Variance</td>
</tr>
<tr>
<td>Fixed</td>
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<td>-0.646</td>
<td>0.081</td>
<td>0.007</td>
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Table 3 - Statistical characteristics (The same data Meta-Analysis)

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<th>Model</th>
<th>Effect size and 95% confidence interval</th>
<th>Test of null [2-Tail]</th>
<th>Heterogeneity</th>
<th>Tau-squared</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number Studies</td>
<td>Point estimate</td>
<td>Standard error</td>
<td>Variance</td>
</tr>
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<td>Fixed</td>
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Table 4 - Statistical characteristics (The same author Meta-Analysis)

<table>
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<th>Test of null [2-Tail]</th>
<th>Heterogeneity</th>
<th>Tau-squared</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number Studies</td>
<td>Point estimate</td>
<td>Standard error</td>
<td>Variance</td>
</tr>
<tr>
<td>Fixed</td>
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Reference

