# ELECTROENCEPHALOGRAM-BASED METHODS FOR ROUTINE DETECTION OF DEMENTIA

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***Abstract:*** **This paper is concerned with progress towards the development of an objective and affordable method for early detection of Alzheimer's disease. The aims of the work reported in this paper are to examine whether the human Electroencephalogram (EEG) is truly fractal and, if not, discover whether there is a better method which uses the same underlying signal properties that allow Fractal Dimension measures to differentiate between normal and demented subjects. Our results show that the human EEG is unlikely to be fractal and that Fractal Dimension measures are not appropriate. We found that there are underlying EEG signal properties that change during the onset of dementia - mainly in the region of the P3 and P4 (Posterior) channels. This localisation supports a recent Magnetic Resonance Imaging study, which showed that the main sites of cortical atrophy in early Alzheimer's Disease are in the medial temporal lobe (which is deep within the brain and not normally observable with surface EEG) and posterior cortex. Concentrating on EEG recordings from this posterior area of the scalp and using newly derived metrics we report early indications of a much-improved method.**

***Keywords:*** **EEG, dementia, fractal, Alzheimer's.**

## I. Early Detection Of Alzheimer's disease

Improved life expectancy [1] has led to a significant increase in the number of people in the high-risk age groups that will develop Alzheimer's disease and other dementias [2]. Efforts are being made to develop treatments such as the Acetylcholinesterase inhibitors (Tacrine, Donepezil and Exelon), which are claimed to slow the progress of the disease [3]. However, unless a sufferer is diagnosed in the early stages the treatments cannot give the maximum benefit [4]. A recent study of Cortical Atrophy in the Lancet [5] showed the period between the onset of Alzheimer's disease and meeting the current clinical criteria was between 3 and 5 years. Therefore, there is an urgent need for a practical decision support tool that will enable the earliest detection of dementia within the large population of people at risk.

Current techniques such as Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) that are used to diagnose and assess neurological disorders require specialist equipment and expert clinicians to interpret results. Such techniques, which are valuable in the diagnosis of dementia or assessment of the nature of a neurological disorder, are inappropriate as a method of detecting individual subjects with early dementia within the large at-risk population, because everyone within the at-risk group would need to be tested regularly and this would carry a high cost. Therefore, it is desirable to develop a low cost method of assessment, which can be carried out quickly by a non-specialist clinician.

Analysis of the electrical activity of the brain (the Electroencephalogram or EEG) may provide the basis of an acceptable and affordable method for early detection of dementia. The EEG has long been used for diagnosis of neurological disorders but it always required subjective interpretation. If it were possible to automate the process of interpretation this would add objectivity and provide the desired first line of screening.

It is well known that disorders of the brain are accompanied by changes in the EEG [6]. The challenge is to automate EEG analysis such that early changes due to dementia can be reliably detected before the development of clinically significant mental decline. This could provide a basis for future development of a system that may be used by a General Practitioner during routine health checks of older patients, akin to those used for driving licence renewal.

It is recognised that a great deal of effort has been expended in the pursuit of automated EEG analysis and there are few successful automated methods used in clinical practice. A notable exception is perhaps Bispectral Analysis in Anaesthesia.

## II. Non-linear methods

As the brain is a complex network of synapses and neurones that have non-linear behaviours, it has been suggested that the brain could, in a mathematical sense, be chaotic. A tutorial review of non-linear dynamical analysis of EEGs is given by Pritchard and Duke [7].

Research in EEG dimensional complexity has evolved from an early work which suggests that human EEG under some conditions may represents deterministic chaos of relatively low dimension [8], through studies measuring the dimension of the strange attractor [9], to a recent work that has questioned whether the EEG represents a chaotic signal; Pritchard [10] reported that surrogate-data testing suggests normal EEG is high

dimensional and does not represent low-dimensional chaos.

An alternative to dimensional complexity measures is the Fractal Dimension, which was introduced as a practical measure of EEG signal complexity [11]. Development of this method has continued at Plymouth [12]. One of the most important realisations was that the EEG exists in an affine space. In an affine space the axes have incompatible units and there is no natural scaling between them (distance along the time axis cannot be compared with distance along the voltage axis) and as such diagonal distances are not meaningful [13]. To demonstrate this effect the normal measure of Fractal Dimension, the Divider Dimension, was repeated on a single Alzheimer's subject and a single normal subject and it was found that the arbitrary voltage/time scaling affected the results. A scaling of 0.6nV/s, for example, gave Fractal Dimensions similar to those normally reported with a Normal subject exhibiting a higher complexity than an Alzheimer's subject but a higher scaling of 2.5nV/s gave very different results (Normal subject had a lower Fractal dimension than the Alzheimer's subject). This problem is a direct consequence of applying the divider dimension to the EEG, which exists in an affine space.

The best Fractal Dimension technique, which is suitable for use in affine space, is known as the Fractal Dimension of the Zero-set of the Autocorrelation function [14].

An aim of our work is to find a reliable and appropriate measure or index that allows the differentiation between normal and demented subjects.

## III. Data

Data for this study were obtained using the traditional 10-20 system in conjunction with a strict protocol [15]. The common average montage (using the average of all channels as the reference) was used in all recordings and the sampling rate was 256Hz.

EEGs were collected from 7 patients (3 Alzheimer's patients, 3 mixed type (Alzheimer's and multi-infarct dementia) patients and 1 multi-infarct dementia patient) and 8 age matched controls (over 65 years of age). All of the age-matched controls had normal EEGs (confirmed by a Consultant Clinical Neurophysiologist). One age matched control (known as 'vol1') has subsequently developed Alzheimer's disease; this record is of particular interest because it is potentially of a subject early in transition from 'normal' to Alzheimer's diseased.

The EEG recordings encompass various states: awake, and drowsy with periods of eyes closed and open. The analysis described in this paper takes the whole recording including artefacts and has no *à priori* selection of elements 'suitable for analysis'. This approach leads to a prediction of the usefulness of the techniques, as they would most conveniently be used in practice.

## IV. Evaluation Metric

As, this research is aimed at analysing an EEG recording to derive an index which is significantly different for normal and demented subjects it is important to have a measure that describes how well the index performs this task. We have chosen to measure the performance of a candidate index using, what we have termed, a "Method Evaluation Metric". To evaluate this we begin by calculating the candidate index for all demented and control subjects, then the mean and estimated population standard deviation ($\sigma$) of the index for the control subjects is recorded (excluding Vol1 who went on to develop Alzheimer's). Finally, the difference between the mean of the index from the controls and the closest index from any of the demented subjects (i.e. closest to normal) is divided by $\sigma$. Thus calculated, the Method Evaluation Metric describes how many standard deviations the "most normal" demented subject is from the mean of the control subjects. As a guide a 3 is good and 6 is excellent. A similar figure may be produced for Vol1 to see whether there was a significant, previously undetected decline. An illustrative example is given in Table 1 where the index under evaluation is the Fractal Dimension of the Zero-set of the Autocorrelation function.

The example in Figure 1 shows that it is unlikely that the most normal of the demented subjects could have come from the population of normals and that Vol1 is hardly distinguishable.

## V. A new approach

The above results are encouraging but their specificity and sensitivity are not adequate to give the reliable, automated method we seek. The technique also lacks credibility because there is no apparent reason why the Zero-set dimension of the autocorrelation of an EEG should be a good indicator of dementia. This lack of credibility is important because without it the technique will not be used and nobody will benefit. For these reasons we set out to determine what it is about the EEG signal that makes the method work. The expectation was that this would improve performance and build credibility.

The first step was to determine whether the fractal nature of the signal contributes to the performance of the technique. To do this we took the Fourier transform of the signal before the Fractal Dimension was measured, randomised the phase and reconstructed the signal. Surprisingly, the performance of the technique improved with the Method Evaluation Metric rising for the most normal demented subject to 29.6 $\sigma$ and for Vol1 6.8 $\sigma$.

We concluded that all the information necessary for the operation of this method must lie in the power spectral density (not the phase) and therefore any fractal nature of autocorrelation of the EEG cannot be a contributory factor.

Guided by the performance metric and mathematical intuition we discovered that there were observable differences in the spectra of the normal and demented subjects' EEG. This was surprising because the spectrum of the EEG has been studies for many years without, we believe, these differences being reported. A simple metric was constructed to measure these differences based on the zero crossing intervals in the raw EEG data. This method is not described in detail in this paper but the results are presented below. The evaluation metric for the most normal demented subject was 21.2 σ and for Vol1 was 13.0 σ.

The next step in the development of this method was to review whether any of the EEG channels was better at determining the presence of dementia. This was done by computing the Method Evaluation Metric for each channel (Fig. 1). From Fig. 1 it may be seen that the most affected channels are P3 and P4. This is an important result because it concurs with a recent Magnetic Resonance Imaging study [5], which showed that the main sites of cortical atrophy in early Alzheimer's disease are in the medial temporal lobe (which is deep within the brain and not normally observable with surface EEG) and posterior cortex where we have observed the maximum effect.

Using the new method on just P3 and P4, the Method Evaluation Metric for the most normal demented subject was 12.8 σ and for Vol1 was 9.1 σ. It should be noted that the reason why just using P3 and P4 appears to be less effective than using all channels is because there is significantly less data and therefore the standard deviation of the results from normal subjects appears larger. However, these results are adequate for good differentiation between demented and control subjects and they require only 2 channels to be monitored.

## VI. Conclusions and Future Work

The results indicate that the new technique which requires only 2 channels to be monitored for a short period of time (2 to 4 minutes) gives good separation between demented and control subjects. It would also appear from Vol1 that a subject who has a normal EEG (as judged by a clinician) could be detected as abnormal by this technique years before the onset of clinically significant symptoms. This is a very important result because, if it is confirmed in a larger trial, it may show that the method would enable clinicians to administer drugs that slow the progression of dementia earlier and therefore prolong the symptom free state.

The next step will be to evaluate the method by using it to analyse a library of previously recorded EEG data (probably at Deriford Hospital, Plymouth).

Table 1 Illustrative example

| Comment | Subject | Index |
|---|---|---|
| Measured index from normal Subjects. | Vol2 | 0.590 |
| | Vol3 | 0.648 |
| | Vol4 | 0.622 |
| | Vol5 | 0.562 |
| | Vol6 | 0.627 |
| | Vol7 | 0.539 |
| | Vol8 | 0.670 |
| Mean | Mean | 0.6083 |
| Estimated population Std Dev | SD | 0.0469 |
| Measured index from demented subjects. | AD1 | 0.323 |
| | AD2 | 0.368 |
| | AD3 | 0.331 |
| | MID1 | 0.384 |
| | MIX1 | 0.324 |
| | MIX2 | 0.270 |
| | MIX3 | 0.438 |
| Most normal demented | MIX3 | 0.438 |
| Difference from mean normal to most normal demented | Mean-MIX3 | 0.170 |
| Method evaluation metric. i.e. the difference of mean normal to most normal demented | $\frac{\text{Mean-MIX3}}{\text{SD}}$ | 3.63 σ |
| Control who went on to develop Alzheimer's | Vol1 | 0.516 |
| Difference from mean normal to Vol1 | Mean-Vol1 | 0.092 |
| Method evaluation metric. i.e. the difference of mean normal to Vol1 | $\frac{\text{Mean-Vol1}}{\text{SD}}$ | 1.97 σ |

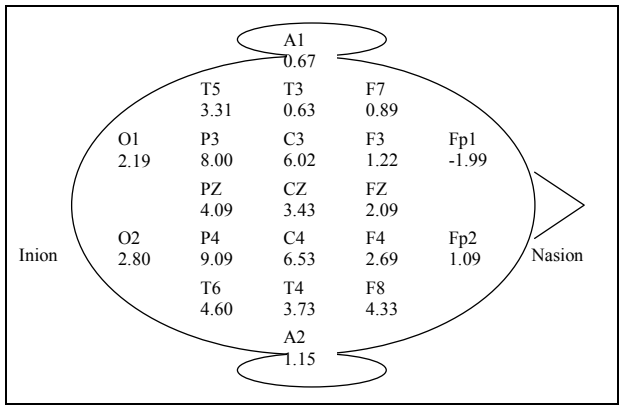


Figure 1, Variation between channels

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