

Classification of normal and pathological tremors using a multidimensional electromagnetic system

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Received 2 July 1998; received in revised form 22 September 1999; accepted 20 December 1999

Abstract

A new multidimensional movement analysis system was used to record limb tremor over six degrees-of-freedom, and signal processing techniques were explored to develop a suitable classification method to distinguish between different types of tremor. The specific aims were to investigate the ability of the system to screen for differences between normal subjects and a group of neurological patients, and then to differentiate between three diagnostic groups of patients.

Postural tremor at the hand was recorded in normal subjects ($n=24$) and patients with essential tremor ($n=21$), multiple sclerosis ($n=17$) and parkinsonism ($n=19$). Data were collected using a 3Space Fastrak[®] (Polhemus, Inc.) over six degrees-of-freedom (three translational directions and three rotations). Spectral estimates produced measures of tremor frequency and amplitude. Mathematical models of the data, using autoregressive modelling and K-nearest neighbour classification, produced parameters used to classify, (1) the normal subjects and 24 patients (using the three rotational movements), and (2) the three patient groups (using all six movement directions). Results were given in terms of the probability of each subject belonging to the groups being classified.

Tremor frequency and amplitude showed large overlap between the groups. The screening classification produced high probabilities of correctly classifying normal subjects ($>70\%$) and patients ($>70\%$). The diagnostic classification produced clear differences between the patient groups (60% for essential tremor, 80% for multiple sclerosis and 60% for parkinsonism).

The ability of this assessment technique to distinguish between postural tremor in normal subjects and neurological patients suggests that it could be developed as a screening tool. Classification of tremors between the patients groups, with a high degree of sensitivity, indicates the potential for further development of the system as a diagnostic aid. © 2000 IPPEM. Published by Elsevier Science Ltd. All rights reserved.

Keywords: Tremor measurement system; Normal physiological tremor; Pathological tremor; Autoregressive modelling; Classification

1. Introduction

Limited methods exist for making objective measurements of tremor in a clinical setting. The diagnosis of neurological disorders in which tremor is a symptom is generally straightforward when the condition is advanced and other confirmatory symptoms are present. In the early stages of a disease, however, there may only be one symptom, which may be shared by other disorders and thus lead to misdiagnosis [1]. For example, postural tremor is the typical presenting symptom of essential tremor but it may also be the presenting symp-

tom in parkinsonism, and can precede other symptoms by several years [2]. In the early stages of some cases of parkinsonism where postural tremor is the only symptom, patients are often diagnosed with essential tremor. Conversely, when essential tremor is misdiagnosed, the most common incorrect diagnosis is of parkinsonism [3]. The rate of misdiagnosis of idiopathic parkinsonism may be 25% or more [1].

Two tremor classification systems are in common use: one based on the state of activity of the tremulous limb and the second on the disease causing the tremor [4]. Both have faults, however, and might benefit from additional information about the likely diagnosis from a system producing recordings of limb motion. In addition, it would be beneficial if the system could be used as an

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objective assessment tool for monitoring changes over time in a clinical setting.

Tremors in the upper limb are commonly recorded using a one-dimensional accelerometer [5]. Three-dimensional accelerometers can detect acceleration in three orthogonal directions [6] but not rotational movements. It might be that different disorders exhibit different patterns of movement that would not be detected by measurement over one, as routinely assessed by accelerometry, or even three degrees-of-freedom (df). The present study examined tremor in patients over six df (in three planes and about three axes of rotation).

Commonly used data analysis techniques include spectral estimation by the Fast Fourier Transform (FFT) and amplitude measures taken from the spectral estimates [7]. Pathological tremor frequencies tend to fall into bands associated with different disorders, but the bands are wide and may overlap [8]. Frequency alone is therefore not completely reliable as a guide to the pathology producing the tremor. Measures of amplitude can indicate the progress of a disease, but they do not provide information about the pathology and require awkward calibration procedures.

Autoregressive (AR) modelling may have potential for characterising tremors as it models both frequency and damping information (the damping of a resonance gives an indication of its strength within a signal). For example, Miao and Sakamoto [9] used AR model parameters to investigate the effects of fatigue on normal finger tremor. AR modelling is effective for spectra consisting of peaks, making it particularly suited to the analysis of tremor where spectra are characterised by their peaks only. A data classification scheme based on the non-parametric K-nearest neighbour (K-nn) method, which is independent of amplitude, may be suitable for distinguishing types of tremor (explained in “Methods” section below).

The aims of the present study were to investigate the ability of a system for recording and analysing upper limb postural tremor to screen for differences between normal subjects and a group of neurological patients, and then to differentiate between patients with essential tremor, multiple sclerosis and parkinsonism. The recording equipment (3Space Fastrak[®], Polhemus, Inc., PO Box 560, Colchester, Vermont 05446, USA) uses electromagnetic technology to detect movement over six df, so all possible movements are detected. Data analysis involved measurement of tremor frequency and amplitude. Further analysis adopted AR modelling to parameterise the data and provide features for tremor classification using the Knn method. The results of the classification process were given in terms of the probability of a subject belonging to a particular group and thus differentiate between the types of tremor.

2. Methods

2.1. Subjects

Eighty-one subjects took part in this study. Twenty-one had been diagnosed with variants of essential tremor (7 male, age range 21–80), 17 with multiple sclerosis (4 male, age range 29–76), 19 with parkinsonism (14 male, age range 28–82) and 24 were normal subjects (6 male, age range 20–68). Patients were recruited from an out-patients tremor clinic in a teaching hospital, a local Multiple Sclerosis Unit and from a rehabilitation hospital. Duration of time from diagnosis ranged from months to years and, as commonly found in neurological conditions, the actual onset of the disease was not possible to define. The patients exhibited a range of tremor severity during testing from absent to very severe and were not required to stop taking medication. The present study included atypical subjects without tremor as a symptom in order to cater for cases where tremor has not developed or may be sub-clinical and other inconclusive symptoms have emerged first.

The normal subjects were recruited from the staff and visitors at the rehabilitation hospital and were subject to the following exclusion criteria: fractures or soft tissue injury to the upper limbs or spine within the last two years severe enough to affect normal activities; neurological diseases or tremor in the subject or close family members; systemic diseases (e.g. diabetes); drugs taken that might cause tremor; alcohol taken within the previous 12 hours. All subjects gave their informed consent and the study was approved by the Riverside Research Ethics Committee.

2.2. Measurement equipment

Measurements were made using the 3Space Fastrak[®] (Polhemus, Inc.), which has a sampling rate of 120 Hz. A transmitter, containing three orthogonal coils, creates a magnetic field and the position of a sensor (also containing three coils) is monitored as it moves within the magnetic field. Measurements of sensor position are made relative to the transmitter, over six degrees-of-freedom (6-df, i.e. in three planes and about three axes of rotation, see below). The system has a static accuracy of 0.8 mm for sensor position and 0.15° for sensor orientation. The range (transmitter/sensor separation) is 0.76 m at the stated accuracy, and up to 3.05 m with a reduced accuracy. The resolution is 0.5 mm per m of transmitter/sensor separation for position and 0.025° for orientation. Recordings can be affected by metallic objects near to the transmitter. To minimise such effects large metallic objects were kept over 1 m away from the transmitter and subjects were positioned to minimise the distance between the transmitter and sensor. No interference was seen, however, during calibration tests with

metallic objects in the vicinity [10]. Briefly, the amplitude response over a range of frequencies (0–16 Hz) was determined by vibrating the sensor with a known input amplitude, and recording the output. There were no measurable effects on amplitude between recordings made with the transmitter more than one metre or within 60 cm away from large metallic objects.

2.3. Data collection

Subjects were seated in a straight-backed chair with their feet flat on the floor. The sensor (mass 17 g, dimensions $2.8 \times 2.3 \times 1.5$ cm) was secured on the dorsum of their preferred hand in an elastic pocket on a modified wrist support. Subjects maintained the following upper limb position during data collection: arm held out straight, parallel to the ground with the shoulder at 90° , the elbow and wrist extended and the hand pronated (facing downwards), in a loose fist. This arm position was determined from a pilot study and was found to be the most sensitive position to differences between normal and pathological tremors (Spyers-Ashby and Stokes, unpublished data). The transmitter was placed on a table close to, and in front of, the subject [11]. The subject was asked to raise their arm and maintain it in the position whilst data were collected for ten seconds.

Each ten second data file consisted of six time series corresponding to the six movement directions (translational movements, X, Y, Z; rotations, azimuth [Az] or pitch, elevation [El] or yaw, and roll [Ro], see Fig. 1). The subject was asked to concentrate on keeping their whole body still during data collection but no physical restraints on upper limb movement were imposed. An investigation into the reliability of the

measurements showed that they were repeatable within and between recording sessions undertaken on different days [11].

2.4. Data analysis

Data analysis was carried out using MATLAB® for Windows (version 4.2) and SPSS for Windows (version 8.0). Data were input to MATLAB functions as time series of equal length for the frequency and amplitude estimates, and as matrices of reflection coefficients (1 matrix per subject group) for the classifications. There were four stages to the data analysis: (1) estimation of tremor frequency, (2) estimation of tremor amplitude, (3) classification of data in 3 df from normal subjects and a group of patients and (4) classification of data in 6 df from patients with essential tremor, multiple sclerosis and parkinsonism. Tremor data are commonly analysed by applying the Fourier transform to produce spectral estimates [12:10–36]. In order to allow comparisons with previous studies, the present study adopted similar spectral estimation techniques for the determination of tremor frequency and amplitude.

Initial inspection of the data showed that translational (X, Y, Z) movements in normal subjects were of such low-amplitude that most time series had a “stepped” appearance and therefore contained little useful information about the nature of the normal tremor. No such effects were seen in the time series of rotational movements, so analyses involving normal subjects (stages 1, 2 and 3) were based on the Az, El and Ro rotation data. All data collected from patients were suitable for analysis, therefore stage 4 of the data analysis involved all six movement directions. Examples of the six, 10-second time series produced by a normal subject and a patient with multiple sclerosis are given in Figs. 2 and 3 respectively in the “Results” section.

2.4.1. Estimation of tremor frequency

To estimate frequency, the time series were analysed using one of MATLAB’s in-built functions (psd.m) which estimates the power spectral density of a signal. Preliminary estimates of tremor frequency for all movement directions were found to be the same within subjects. The rotational movements produced the clearest spectral peaks, however, so subsequent frequency estimation was based on the roll rotation time series. The data were high-pass filtered at 1 Hz to reduce the effects of low frequency drifting motion of the upper limb. Frequency spectra of the filtered time series were produced using Fourier analysis and the peak frequency determined. The median and range of values for the four groups were found.

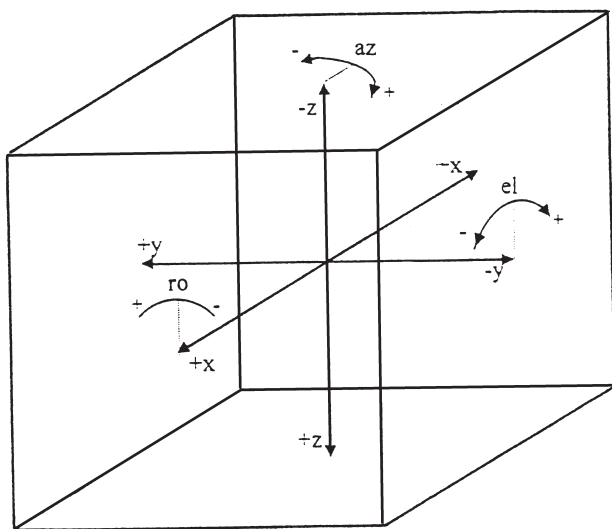


Fig. 1. Directions of translational movements and rotations of the sensor with respect to the transmitter in six degrees-of-freedom. Translational movements: x, y and z. Rotations: az = azimuth or pitch; el = elevation or yaw; ro = roll.

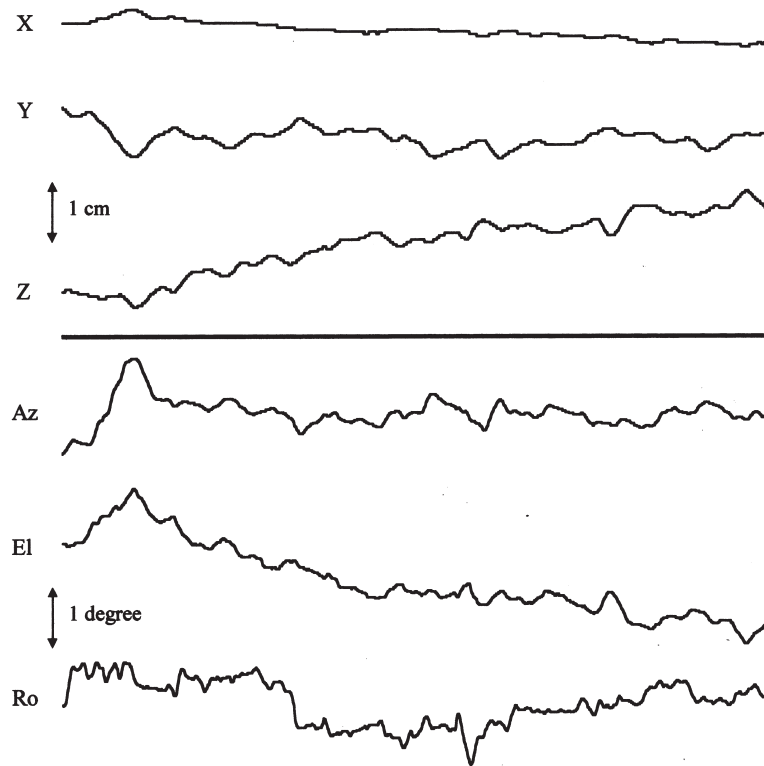


Fig. 2. Example of raw tremor signals detected over six degrees-of-freedom, for ten seconds, in one normal subject.

2.4.2. Estimation of tremor amplitude

An estimate of the tremor amplitude was made by finding the spectral power between 2 and 25 Hz for the three rotational movements (amp_Az, amp_El, amp_Ro for the azimuth, elevation and roll rotations respectively). The total amplitude was then estimated as the vector sum of the three values, i.e.

$$\text{Amplitude} = \sqrt{\text{amp_Az}^2 + \text{amp_El}^2 + \text{amp_Ro}^2}$$

The contribution of the translational movement data to the overall amplitude in patients was negligible. The median and range of values of amplitude in the four groups were then found.

2.4.3. Screening classification between normal subjects and patients

The signal classification process involves four steps: data collection, feature extraction (or parameterisation), feature selection and classification. Eight subjects were randomly selected from each of the patient categories to form a single group with 24 members. The three time series for rotational movements from each member of the patient and normal groups were filtered as before and then split into 60-point (0.5 s) segments, overlapping by 30 points to reduce the effects of signal non-stationarity. Each data segment underwent feature extraction by autoregressive (AR) modelling using Burg's algorithm and a model order of six. Previous studies [13,14] have shown that AR modelling is a suitable method for

describing tremor data and further details of model-based data analysis techniques are given by Cohen [15: 81–108]. The reflection coefficients (RCs or partial correlation coefficients) are one of the parameters produced by the AR modelling process and were selected as “features” for describing the tremor data. Reflection coefficients do not encode information about signal amplitude so the classification did not consider differences in tremor amplitude. Each data segment was subsequently replaced by 18 reflection coefficients (six for each rotation).

Although the classification could have been carried out with all 18 features this would have resulted in a high computational load and possibly a reduction in the reliability of the results. A process of feature selection [16] was therefore carried out with the aim of reducing the number of features to those containing the most information. The 18 features were subsequently reduced to a subset of four, which included features from all three rotational movements. Each data segment was represented by a “feature vector” with four elements or a point in a 4-dimensional “feature space”.

K-nearest neighbour classification, a K-nearest neighbour (K-nn) classification was carried out to discriminate between the two subject groups using the four features identified in the above feature selection process. Full details of the K-nn classification method can be found elsewhere [17: 85–129]. The aim of the K-nn classification was to find the probability of each subject

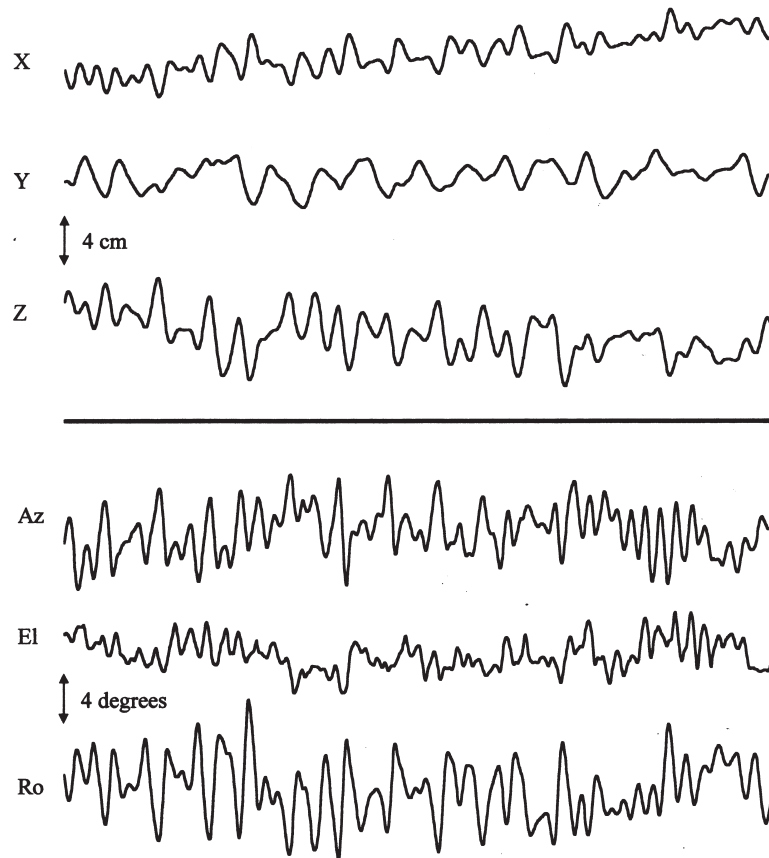


Fig. 3. Example of raw tremor signals detected over six degrees-of-freedom, for ten seconds, in a patient with multiple sclerosis.

belonging to a particular class based on the position of the features in the feature space. For the classification of normal subjects and patients, each subject had a probability of belonging to the normal group and a probability of belonging to the patient group (the sum of the two probabilities was one). These probabilities were then compared to the known class of the subject to see how effective the classifier was at estimating the class. For perfect classification of a normal subject, for example, the probability of belonging to the normal class would be one and the probability of belonging to the patient class zero. The presentation of results in terms of probability means that decisions in which there can be little confidence (i.e. where the two probabilities are near 0.5) are clearly displayed. Differences between groups were not assessed using hypothesis testing (and quotation of *P* values to determine significance or non-significance) as it conveys little meaningful information about the size of differences in sample data groups and is therefore not recommended [18].

2.4.4. Classification between the three patient groups

This classification involved the 21 patients with essential tremor, the 17 patients with multiple sclerosis and the 19 patients with parkinsonism. Data for the six movement directions from each patient were filtered and

split into segments before undergoing AR modelling as before. Each data segment was replaced by 36 reflection coefficients (six for each movement direction) and the feature selection process reduced this number to eight, including features from all six movement directions.

K-nearest neighbour classification, the K-nearest neighbour classification method was simply adapted to deal with three groups instead of two. The result for each subject was three values, namely the probabilities of belonging to the essential tremor, multiple sclerosis and parkinsonism groups (the three probabilities had a sum of one). By comparing the probabilities with the known class of subjects, the effectiveness of the classifier at estimating the class could be established. The output of three probability values also meant that the classes of data most likely to be confused were highlighted.

3. Results

The raw tremor signals indicated differences between the translational and rotational movements in normal subjects. Fig. 2 shows the six time series produced from a 10 s recording of tremor in a normal subject. Note the stepped appearance of the X, Y and Z direction time series and compare with the smoother time series for the three rotational movements.

Fig. 3 gives an example of the time series produced from a patient with multiple sclerosis. Note that tremor occurs in all six movement directions and is clearest in recordings of rotational movement.

3.1. Frequency and amplitude

The median and range values of tremor frequency in normal subjects are shown in Table 1. The differences between median values are clear, but the ranges overlap making discrimination between different groups difficult on the basis of frequency alone. There was also a wide range of tremor amplitudes encountered in the three patient groups (Table 1). Patients with very low amplitude tremors within the normal range were included in the sample in order to provide the K-nn method with patient data that would be more difficult to estimate, thus producing a more robust classifier.

3.2. Screening classification of normal subjects and patients

The results for the classification of normal and patient data were given in terms of probability. Each subject produced two probabilities: the probability of being a normal subject and the probability of being a patient and Fig. 4 shows plots of the probabilities of a correct classification.

Fig. 4a shows, for each normal subject, the probability of being classified as normal. There was a high probability (>70%) of normal subjects being given the correct classification. Fig. 4b shows, for each patient, the probability of being classified as a patient. The patients with essential tremor, multiple sclerosis and parkinsonism are distinguished by different symbols and, under this analysis, they could not be differentiated. Most patients were likely to be correctly classified, however, there were three that were more likely to be misclassified as being normal.

Table 1
Results for tremor frequency and amplitude in the four subject groups

	Frequency (Hz)		Amplitude (cm ² .s log scale)	
	Median	Range	Median	Range
Normal subjects	9.4	7.4–10.8	0.4	0.2–2.5
Essential tremor	6.7	5.6–9.7	7.9	0.5–60 627
Multiple sclerosis	2.9	1.8–6.0	7.8	0.2–7471
Parkinsonism	5.6	4.0–9.8	3.1	0.5–155 123

3.3. Diagnostic classification of patients

For this classification, each subject produced three probabilities: the probability of having essential tremor, multiple sclerosis and parkinsonism (Fig. 5a–c).

The results for patients with essential tremor in Fig. 5a show that there was generally a 60–70% chance of correctly classifying this type of data. Patients given the wrong classification were most likely to be misclassified as having parkinsonism (30% chance) and there was a small probability (approximately 10%) of misclassification as having multiple sclerosis.

Patients with multiple sclerosis (Fig. 5b) had a 70–90% chance of being correctly classified. The probabilities of misclassifying subjects as having essential tremor and parkinsonism were similar (approximately 10%).

Patients with parkinsonism (Fig. 5c) show a 60–70% chance of a correct classification. These results echo those presented in Fig. 5a and show patients with parkinsonism more likely to be misclassified as having essential tremor than multiple sclerosis.

4. Discussion

The tremor measurement system described in this paper can distinguish between normal subjects and patients for screening purposes, and act as a diagnostic tool to distinguish between patients with different neurological disorders. The analysis techniques used are more sensitive to differences between groups than measures of tremor frequency or amplitude. The present study also demonstrated that rotational movements offer important information about tremor characteristics as well as the translational movements traditionally examined.

4.1. Multi-dimensional measurement

The activity shown in the time series plots (Figs. 2 and 3) highlights the potential importance of measuring movement in more than one direction. These plots illustrate the multi-dimensional nature of tremor and it is therefore reasonable to suppose that data analyses involving a combination of these movements might prove more effective at discriminating between different types of tremor than using only one movement direction. This supposition was supported by the present results from the feature selection process, which showed that a combination of data from all six movement directions produced the best discrimination between patients with essential tremor, multiple sclerosis and parkinsonism.

4.2. Tremor frequency and amplitude

The results for frequency showed median values in line with published values [19,20]. Although median dif-

ferences between the groups were apparent, the overlap of ranges meant that frequency alone could not distinguish the groups, particularly between essential tremor and parkinsonism.

A pilot study demonstrated that fatigue-induced tremor in normal subjects did not influence tremor frequency during the test used but changes were seen in the classification analysis results (Spyers-Ashby and Stokes, unpublished data).

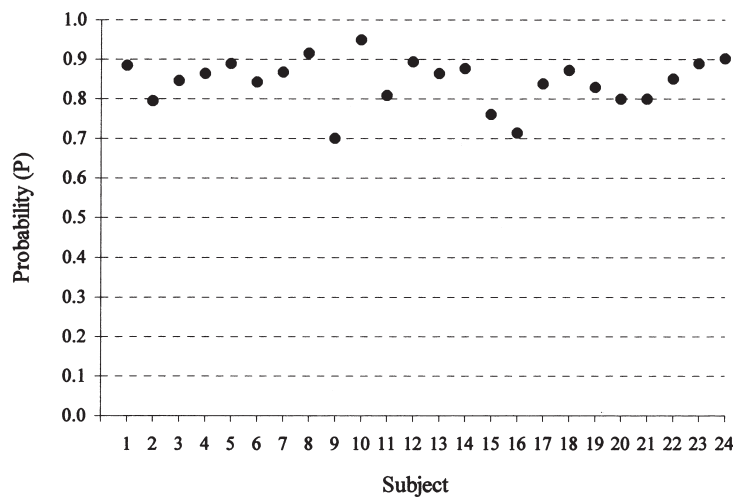
The wide ranges of tremor amplitude in the three patient groups contrasted with the relatively small range in the normal tremor group, which also had a lower median value (as expected). Subjects with a wide range of tremor severity (some within the normal range) were

included in the patient groups to produce a robust classifier with greater potential use as a diagnostic tool.

4.3. Screening classification of normal subjects and patients

Results for the classification between normal subjects and patients (Fig. 4) showed reasonable accuracy for estimating the class of normal subjects and variable accuracy for patients. In this sample, two patients with multiple sclerosis (MS) and one with parkinsonism (PD) appeared to be normal, with probabilities of being from the patient class of less than 50%. The patients who appeared to be normal did not have abnormal tremor as

a) Normal subject data



b) Patient data

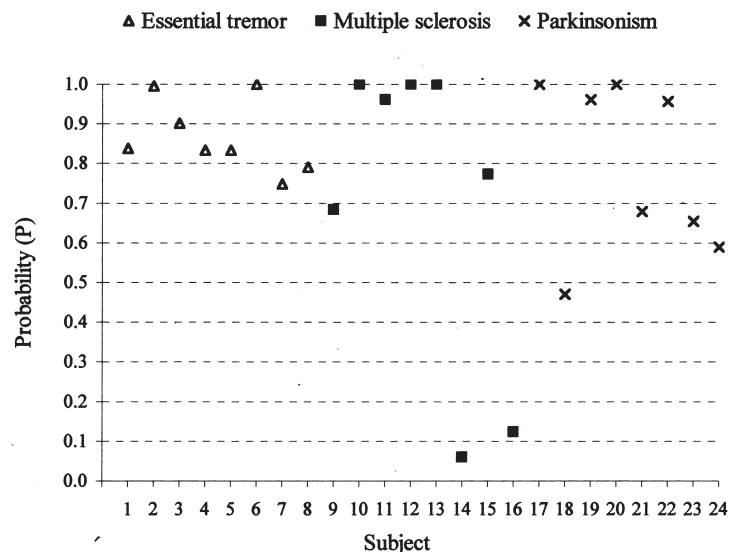


Fig. 4. Results from the K-nearest neighbour classification of data from normal subjects and patients with a neurological disorder: a) Probability that data from each normal subject ($n=24$) belongs to the correct class. b) Probability that data from each patient ($n=24$) belongs to the correct class.

a clinical symptom. Had these patients been excluded from the study, the results would have shown greater differences between the groups. There were other patients with no clinical evidence of abnormal tremor, however, whose results showed high probabilities of being in the patient group. This suggests that the reflection coefficients contain information about the nature of postural tremor that can detect sub-clinical abnormalities. Differentiation between normal and pathological tremors is generally a simple matter of comparing amplitudes [21], but in the absence of clinical tremor, such comparisons are not possible.

As reflection coefficients do not encode signal amplitude information, the difference between the two groups cannot be simply explained by differences in tremor amplitude. The differences are therefore likely to reflect a more sophisticated description of movement based on a combination of factors such as the relationship between frequency and damping which were shown to influence reflection coefficients in a pilot study [10]. The absolute

value of the reflection coefficient was reduced with increases in either frequency or damping.

4.4. Diagnostic classification of patients

Results for the classification of essential tremor (Fig. 5a) show a clear separation between the probability values for the three patient groups indicating essential tremor data were likely to be correctly classified. There was a low probability (approximately 10%) of misclassification as multiple sclerosis but the patients were more likely to be misclassified as having parkinsonism. The difficulties that can occur in the differential diagnosis of essential tremor and parkinsonism have been commented on previously [22]. Although these previous clinical findings are reflected here, the present study still shows a clear separation between the probabilities of correct classification as essential tremor and the incorrect classification as parkinsonism. Deuschl et al. [21] were able

a) Essential Tremor data

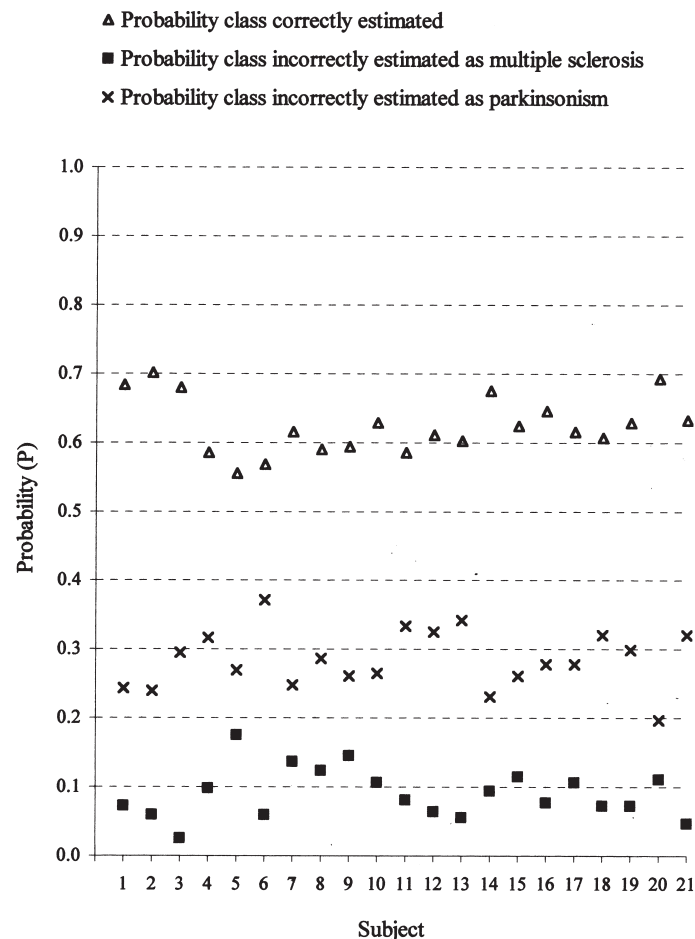


Fig. 5. Results from the K-nearest neighbour diagnostic classification of data from patients with essential tremor, multiple sclerosis and parkinsonism, showing the probabilities of each group belonging to the three classes: (a) Essential tremor ($n=21$), (b) multiple sclerosis ($n=17$), (c) parkinsonism ($n=19$).

b) Multiple Sclerosis data

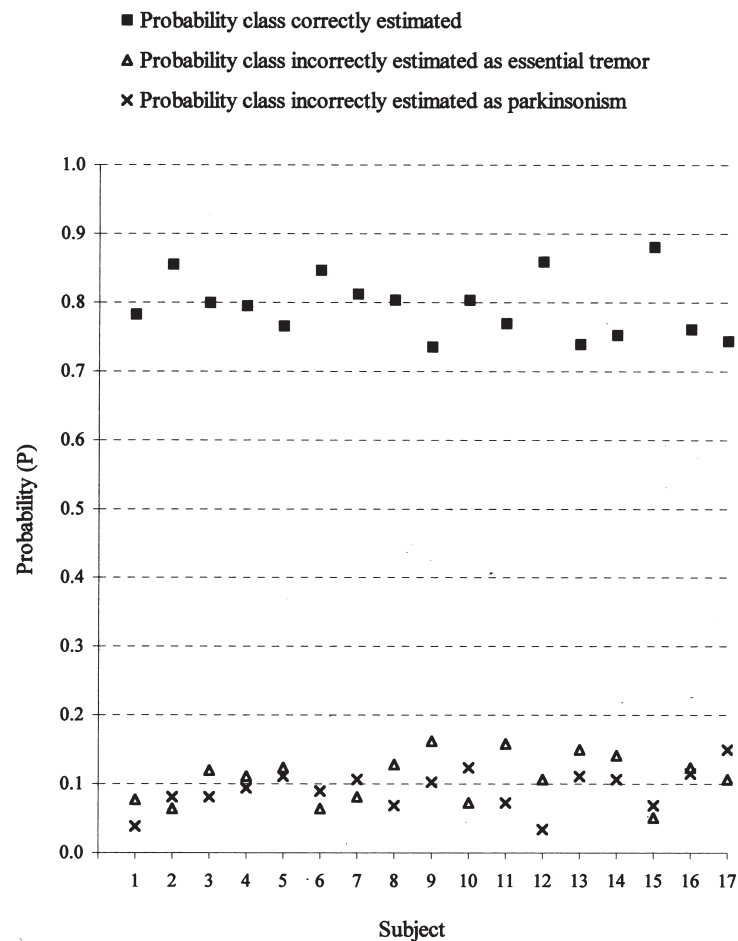


Fig. 5. (continued)

to distinguish between typical cases of essential tremor and Parkinson's disease.

Results for the classification of multiple sclerosis (Fig. 5b) show it is very unlikely that a patient with multiple sclerosis would be misdiagnosed as having essential tremor or parkinsonism using these techniques. There is no clear difference between the probabilities of incorrectly classifying a patient with multiple sclerosis as having essential tremor or parkinsonism, the probabilities of both alternatives being approximately 10%.

Results for the classification of parkinsonism (Fig. 5c) are similar to those for essential tremor, with clear separation between the probabilities. There is a small probability of misclassification as multiple sclerosis and a higher probability of misclassification as essential tremor.

The present study included patients with atypical conditions and without clinical tremor, thus creating a greater challenge for the classification process. Had those without clinical tremor been excluded, the probability values for each group would have been higher.

However, a "failed" classification indicated that the pathological tremor did not differ sufficiently from normal tremor in the chosen parameter space and using the chosen analysis method. We cannot state that the same would be true for all parameter spaces, and there may be other analysis methods that could distinguish between the tremors that our method failed to.

4.5. Further research

These results show that there is potential for developing this technique as a clinical tool. A patient without a clear diagnosis could be tested and the resulting data classified against the databases of essential tremor, multiple sclerosis and parkinsonism. The three probability values would indicate which of the three diagnoses was most likely to be correct. The nature of the study (only one sensor, no constraint on movement, etc.) means that the equipment is quick to set up and data are easily collected. Certain procedures can sometimes be used to highlight the presence of a particular

c) Parkinsonism data

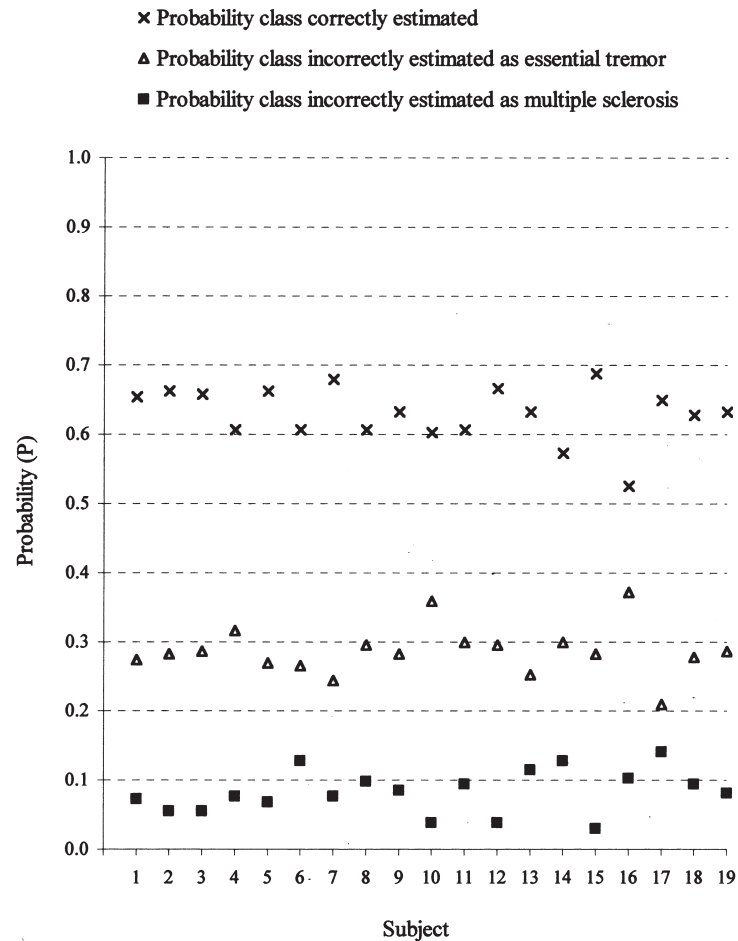


Fig. 5. (continued)

pathology. For example, Sanes and Hallett [23] found that the magnitude of tremor in patients with essential tremor was not affected by changes in upper limb posture, while other patient groups showed an exacerbation of their tremor during certain postures. In contrast, the present method appears to be able to detect the three pathologies by the application of a single test and thus provides greater standardisation.

The validity of the results could be investigated by carrying out the same analysis on data produced using other measurement techniques such as multi-dimensional optical or ultrasonic methods, but these methods tend to only make direct measurements of translational movements. The lack of translational movements seen in the time series for normal subjects suggests that the sensitivity of the system is lower than that of accelerometers. A compromise therefore needs to be made between sensitivity and the ability to measure multi-dimensional movements. The translational resolution of the system used is dependent on the sensor-transmitter separation. Placing the sensor as close to the transmitter as possible

would improve the resolution e.g. reducing the distance from 1 m to 0.5 m would increase the resolution from 0.5 mm to 0.25 mm.

The present data produce very encouraging results, showing clear differences between the three patient groups studied. Further developmental work would involve the addition of more patient groups to expand the choice of possible diagnoses. The classification results would also be improved by testing greater numbers of patients from various diagnostic groups and thus increasing the size of the databases.

In order to make the technique useful in a clinical setting, a user-friendly system has been produced which automates the data analysis. This will allow the user to carry out screening and diagnosis classifications (once more comprehensive databases are available) or produce measures of tremor amplitude and frequency for monitoring purposes.

Acknowledgements

The authors would like to thank the subjects who took part in this study, and the Neuro-disability Research Trust and the Patrick Berthoud Charitable Trust for financial support. This work was undertaken by the Royal Hospital for Neuro-disability which also received a proportion of its funding from the NHS Executive; the views expressed in this publication are those of the authors and not necessarily those of the NHS Executive.

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