A novel computer-based technique for the assessment of tremor in Parkinson’s disease

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Abstract

Parkinson’s disease (PD) is a common neurodegenerative disease and the diagnosis of its idiopathic form remains challenging. The diagnosis of idiopathic form is based on clinical features which can have poor sensitivity with about 25% of patients diagnosed as having the disease actually having other conditions. In this study we assess the suitability and clinical value of a low cost computer-based system as an aid to diagnosis of PD, in particular the presence of tremor. All participants (12 patients and 10 controls) performed a shape-tracing task using a graphic tablet attached to a laptop. To assess the presence of tremors in the collected data, a statistical spectral analysis of the moment-to-moment fluctuations in the position signal of the output from the digitising tablet was performed. This allowed the comparison of power spectrums obtained from the control and patient responses respectively. A peak in log power between the 5Hz & 6Hz can clearly be identified in the patient’s spectrum and is indicative of Parkinson’s related tremor and no similar peak could be seen in the control’s spectrum, suggesting this type of sequential task and automated data analysis may be useful in the diagnosis of tremor.

Keywords: Parkinson’s disease, tremor, assessment, computer-based, sequential task, elderly

Introduction

Parkinson’s disease (PD) is a slowly progressive disabling condition with a world-wide distribution. With no simple diagnostic test available to detect PD, the diagnosis depends on clinical observations. The UK Parkinson’s Disease Society Brain Bank Criteria stipulate bradykinesia to be the major feature that has to be present along with resting tremor, rigidity and disorders of posture, balance or gait. However, work by Hughes et al. suggested the predictive accuracy of this paradigm is around 82–85% [1]. In general practice, one study has shown that 103 of 402 patients had been incorrectly diagnosed as having PD or parkinsonism [2]. The commonest causes of misdiagnosis were essential tremor, Alzheimer’s disease and vascular pseudo-parkinsonism. In addition to clinical rating scales and simple timed tests of motor function, instrumental methods are employed frequently for assessment of performance or motor deficits in Parkinson’s disease. Many studies have analysed such parameters in cross-sectional patterns but shortcomings of the existing assessment methods have led to the development of continuous ambulatory multichannel accelerometry (CAMCA) [3, 4]. Using the tremor detection algorithm, ambulatory monitoring with CAMCA can also provide objective values for duration and intensity of tremor that are correlated with the clinical score for resting tremor [4]. However, the technique is not very simple and requires long periods of monitoring. Agostino et al. [5], tested the ability of patients with PD in executing repetitive motor sequences (this test implies repeating the same movement, therefore activating the same muscle groups) which involved tracing a pentagon five times repetitively and whilst tracing the pentagon, the arm movements of the patient were recorded by means of a two-joint structure with one end of this structure fixed to the table. This experiment showed that there was a potential mean of diagnosing and assessing the severity of PD and comparing it with Huntington’s chorea and dystonia [5].

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Recently, tremors have been assessed using a statistical spectral analysis of the spatial co-ordinates of the pen position during a figure-copying task. This analysis would allow the assessment of the moment-to-moment fluctuations in the position signal of the pen. Halliday et al. [6] used this type of analysis in tremor assessment where each record was divided into a number of disjointed sections of equal duration and the power spectral density function was estimated by averaging across these discrete sections.

The objectives of the present study are to assess the practicability and clinical value of low cost-computer peripherals (digitising tablet and laptop computer) in quantifying the presence of tremor in PD, using a single shape tracing task. This task uses a combination of the traditional Archimedes spiral concept widely used in tremor diagnosis [7], with the pentagon introduced in [5]. A shape tracing task with clear sequential components may increase the likelihood of detecting tremors and other core features of PD [8].

Methods

Subject populations

Twelve patients with idiopathic Parkinson’s disease (iPD) were assessed (42% female) as well as 10 controls (40% female) who did not have iPD or other neurological disorders, including stroke. Participants were enrolled from a PD specialist clinic and the Day hospital (Royal Liverpool & Broadgreen University Hospitals), after giving an informed consent approved by Liverpool Research Ethics Committee. Attendees of PD-specialist clinic, at various stages of their iPD illness, were asked—using a pragmatic random approach—to take part after having an explanation of the task. Twelve consecutive patients, who were able to give consent, took part in the study. Patients were tested while under the usual treatment regimen. The average age of iPD patients enrolled was 74.1 ± 8.4 years, and the exclusion criteria included drug-induced Parkinsonism, Parkinson-plus and multi-system atrophy syndromes, Alzheimer’s disease and significant cognitive impairment. Ten consecutive controls were enrolled and the majority were relatives attending with patients at the Day hospital, but a few were patients attending the Day hospital for general rehabilitation, and the average age was 73.2 ± 5.3 years. In order to assess the performance of the system under conditions normally found in out-patient clinics, patients were not given any specific instructions regarding medication, and were tested as under their normal medication regime.

Assessment

Conventional assessment

Participants with iPD had clinical quantitative assessment of clinical features of the illness using Unified Parkinson’s Disease Rating Scale (UPDRS) motor sections and modified Hoehn and Yahr Scale beside detailed drug history, including the dosage and timing of PD medications. Please see clinical characteristics table, Appendix 1, in the supplementary data on the journal website (http://www.ageing.oxfordjournals.org/).

Computer-based assessment

Overview

All participants in the study undertook computer-based assessment, which comprises two parts: data acquisition and data processing. Data acquisition stage is the digitisation of the patient’s drawing in attempting a conventional figure-copying task, the task domain. Once the patient’s response has been acquired in digital form, data processing is applied to extract and quantify the symptoms of interest, the tremor.

Test environment and infrastructure

One of the aims of this work is to preserve, as far as possible, a conventional writing environment. This will avoid unnecessary distress to the patient, while allowing comparison with other traditional tests. To help achieve this aim, a commercially available digitising tablet with stylus interface was employed. The Wacom series of tablets uses a stylus with ball point refills, similar to a conventional ball-point pen, thus reproducing a conventional ‘pen and paper’ environment (Figure 1).

The digitising tablet is interfaced to a PC, and transmits information in real-time regarding the:

- stylus position, in terms of x-y co-ordinate pairs
- pressure applied to the stylus
- tilt of the stylus from the vertical in both x and y planes
- precise time at which these measurements were made

Custom designed software was used to manage data acquisition; this enables the test administrator to ensure data is being correctly recorded and facilitates efficient and reliable storage onto removable media. The software can be used to digitise patient responses from a range of figure-copying tests, task domain.

![Figure 1. Use of Wacom digitising tablet and pen to preserve traditional ‘paper and pencil’ test environment.](http://www.ageing.oxfordjournals.org/).
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Task domain

The task domain is particular to the test being conducted and hence the neurological condition of interest. The object of a task domain is to accentuate those symptoms of the neurological disorder to be evaluated. The figure required to be copied by the patient is placed on the digitising tablet in printed form and covered with a sheet of tracing paper on which the patient traces a copy. The experimental protocol required patients to trace the shape as fast as they could. Patients were asked to attempt the figure-copying task three times.

The geometric shape presented for the patient to copy in this study is based on the Archimedes spiral (Appendix 2; supplementary data), which is commonly used in assessing tremor in PD patients [7]. Agostino et al. [5] used a simple pentagon (Appendix 2; supplementary data) for measuring bradykinesia and observed a slowing in the last two edges of the shape drawn by the patient. By combining the pentagon and Archimedes spiral in this way it was hoped further evidence of tremor-related behaviour may be observed.

Data analysis

Patient’s response to the drawing task is digitised in real-time as a set of x–y co-ordinate pairs giving information about pen position. In addition, information regarding pen pressure and pen tilt are provided. The present study uses only the positional information. Data analysis was applied to the patients’ responses to quantify the presence of tremor.

Tremor

The rhythmic nature of Parkinsonian tremor makes it suitable for a spectral analysis. The digitised x–y spatial co-ordinates of the pen position were pre-processed to remove the linear trend due to the gross movement when copying the pentagon leaving only the smaller moment-to-moment fluctuations in the position signal. These oscillations were subjected to a statistical spectral analysis to determine if the tremulous oscillations could be detected in the output from the digitising tablet. This analysis used the methodology of Halliday et al. [6] where each record was divided into a number of disjointed sections of equal duration and the power spectral density function estimated by averaging across these discrete sections. The record of each position, after removal of trend, was assumed to be a realisation of a time series, which was stationary in the wide sense, denoted by \( x(t) \). The autospectrum was estimated by dividing the complete record into L non-overlapping segments, each of length T point.

For each segment, \( l (1 \leq l \leq L) \), the discrete Fourier transform, at frequency \( \lambda_l \), denoted \( d_l^T (\lambda_l) \), was calculated. The complex-valued nature of the Fourier transform was exploited to analyse the x–y co-ordinate data in a single transform. This was achieved by mapping the x co-ordinates to real axes, and the y co-ordinates to the imaginary axis. This has the additional advantage and flexibility to analyse complex 2D movements without further pre-processing to extract the separate x and y movements. The autospectra, denoted by \( \hat{f}_{xx}(\lambda_l) \), was then estimated by performing an ensemble average across the L sections:

\[
\hat{f}_{xx}(\lambda_l) = \frac{1}{2\pi LT} \sum_{j=1}^{L} |d_l^T (\lambda_l)|^2
\]

In practice, the analysis involves splitting the complete record into a number of non-overlapping sections each of the same length. Each section is Fourier transformed and the magnitude squared of each Fourier transform calculated as an estimate of the power in each section. The overall power is calculated by averaging the power across all sections. The averaging process is required to give statistically reliable estimates as described next. An important aspect of the present analysis was the use of a confidence interval to assess the significance of distinct features in each spectral estimate. Construction of a confidence interval for the spectral estimate in Equation (1) was done through the use of a log transform, which acts as a variance stabilising transform, in that, the variance of the log transform of the above spectral estimate is constant across all frequencies, allowing a confidence interval to be set at the desired level of significance. Thus, upper and lower 95% confidence limits for the above estimate were given by:

\[
\log_{10}(\hat{f}_{xx}(\lambda_l)) \pm \frac{0.851 L^{-1/2}}{702}
\]

In practice a 95% confidence interval, given by the constant \( \frac{0.851 L^{-1/2}}{702} \), could be used as a scale bar to determine if local peaks in the spectral estimate represented statistically significant rhythmic components in the position signal. This line was included in plots of the spectral estimates and used to assess the probable significance of spectral peaks relating to the presence of the tremor frequency. The segment length T used in the present analysis was 128, this, along with the sampling interval of 10 ms, determined the spectral resolution of 0.78 Hz.

Results

The average UPDRS (motor sections) score was 45.2 ± 9.2 and 2.8 ± 0.8 for the modified Hoehn and Yahr Scale in PD patients (Appendix 1 in supplementary data). All participants were able to perform the shape-tracing task according to the instructions, using a graphic tablet attached to a laptop.

Figure 2. Example control (left) and PD patient’s (right) drawing responses.
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Figure 3. Example PD patient’s (a) and a control (b) power spectrum analysis of \( x-y \) position data during spiral pentagon tracing task. The solid vertical line in the top right of each figure gives the approximate magnitude of a 95% confidence limit for each estimate. Local fluctuations which exceed the magnitude of this line can be interpreted as a distinct frequency component. The feature around 6 Hz in the spectrum of the PD patient is such a feature, and can be interpreted as an indication of tremor in the position data. (c) shows a population spectrum, calculated as the average across all patients & controls. The estimate for the patients has increased power in the 4–6 Hz region compared with the controls.

They traced a five-sided spiral-pentagon in a clockwise direction. Generally, patients with PD took longer than the age-matched controls to execute the tracing task. Results are presented for responses to the spiral-pentagon tasks for age-matched controls and PD patients. Individual examples of each are given in Figure 2. A statistical spectral analysis of the moment-to-moment fluctuations in the position signal of the collected data was performed and power spectrums obtained for the controls and patients groups. The power spectrums of the two groups were compared; Figure 3a and b show the power spectrums obtained from the control and patient responses respectively. In addition, Figure 3c shows a population spectrum, calculated as the average across all patients and controls. The estimate for the patients has increased power in the 4–6 Hz region compared with the controls. A peak in log power between the 5 Hz and 6 Hz can clearly be seen in the patient’s spectrum (Figure 3a) and is indicative of Parkinsonism tremor. No such peak can be seen in the control’s spectrum (Figure 3b). The tremor in Parkinson’s disease occurs at rest and is characterised by a frequency of 4–6 Hz and medium amplitude. It is classically referred to as a ‘pill rolling’ tremor of the hands but can also affect the head, trunk, jaw and lips [9]. Although rare, a rest tremor may also be found in patients with other neurodegenerative diseases, such as multiple-systems atrophy and progressive supranuclear palsy. The tremor associated with these disorders is usually symmetric and not as prominent as the tremor that accompanies Parkinson’s disease [9].

Discussion

Idiopathic Parkinson’s disease is a chronic neurodegenerative disease predominantly affecting older people. Its diagnosis is based on clinical features which can have poor sensitivity with about 25% of patients diagnosed as having the disease actually having other conditions [10]. An accurate diagnosis is important because long term-use of anti-Parkinson’s medication is known to be associated with the development of on-off motor fluctuations and/or dopa-induced dyskinesia, and about 50% of patients will experience
such side effects within 5 years of starting L-dopa therapy [11]. For these reasons, any clinical tool which can help in confirming the diagnosis of the disease and in assessing response to therapy will be useful in avoiding inappropriate medication and the side effects associated with them. We aimed in this project to recreate an experiment developed and performed by Agostini et al. [5] at Rome University, but instead of using a two-arm articulated structure we have used a graphic tablet with a standard pen to ease the performance of any motor task, like figure-copying test. We also used a new software to analyse the tremor. This new technique is simple and rapid with an objective assessment of motor parameters, velocity of movement and moment-to-moment fluctuations in the positional signals during testing. The specific aspect of tremor has been assessed in this study, using a statistical spectral analysis of the moment-to-moment fluctuations in the position signal of the output from the digitising tablet during testing. This allowed the comparison of power spectrums obtained from the control and patient responses respectively. In this study, a peak in log power between the 5 Hz & 6 Hz could clearly be identified in the patient’s spectrum and is indicative of PD’s related tremor and no similar peak could be seen in the control’s spectrum. These results suggest that this type of sequential task and automated data analysis may be useful in the diagnosis of tremor in PD. The results indicate that it is possible to measure Parkinsonian tremor using a commercially available graphics tablet. However, our results also show the limitations of using what is essentially a two-dimensional input device to measure a three-dimensional characteristic.

We must emphasise that the technique is not a substitute for a clinical examination or assessment of PD motor features, but it may aid the diagnosis and assess the response to variable therapeutic interventions. In addition, the electronic data can be easily stored then retrieved for response to variable therapeutic interventions. In addition, having established the technique and analytical approach, further assessment is required in a larger study to compare it to other computerised-based motor deficit assessments available and possibly to be used in the future comparison. Having established the technique and analytical approach, further assessment is required in a larger study to compare it to other computerised-based motor deficit assessments available and possibly to be used in the differential diagnosis with other tremulous conditions, such as essential tremor.

Key points

- Figure-copying test using Archimedes spiral is widely used in tremor diagnosis.
- The new technique assesses tremor using a statistical spectral analysis of position signals of the pen during figure-copying on a digitising tablet connected to a laptop.
- This technique may aid the diagnosis and assess the response to variable therapeutic interventions among patients with PD.


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Conflicts of Interest

None

References


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