Quantitative assessment of cerebella ataxia through automated upper limb functional tests

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Ragil Krishna, Pubudu N. Pathirana, Malcolm Horne, Laura Power, David Szmulewicz


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Quantitative Assessment of Cerebella Ataxia through Automated Upper Limb Functional Tests

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ABSTRACT

Neurological disorders typically exhibit movement disabilities and disorders such as cerebellar ataxia (CA) can cause coordination inaccuracies often manifested as disabilities associated with gait, balance and speech. Since the severity assessment of the disorder is based on the expert clinical opinion, it is likely to be subjective. Automated versions of two upper limb tests: Finger to Nose test (FNT) and Diadochokinesia (DDK) test are investigated in this paper. Inertial Measurement Units (IMU) (BioKin™) are employed to capture the disability by measuring limb movements. Translational and rotational accelerations considered as kinematic parameters provided the features relevant to characteristic movements intrinsic to the disability. Principal Component Analysis (PCA) and multi-class Linear Discriminant classifier (LDA) were instrumental in dominant features correlating with the clinical scores. The relationship between clinicians assessment and the objective analysis is examined using Pearson Correlation. This study found that although FNT predominantly consist of translational movements, rotation was the dominant feature while for the case of DDK that predominantly consist of rotational movements, acceleration was the dominant feature. The degree of correlation in each test was also enhanced by combining the features in different tests.

Keywords: Finger-to-Nose (FNT), Diadochokinesia (DDK), Fast Fourier Transforms (FFT), Linear Discriminant Analysis (LDA)

1. INTRODUCTION

The region in the human brain primarily responsible for balance, gait, goal-oriented movements and its coordination is the cerebellum. The characteristic disturbance of these movements are used to ascertain the dysfunction of the cerebellum also known as cerebellar ataxia. Cerebellar defects in appendicular and axial movements during the patient’s performance to specific motor tasks are assessed by the clinicians and are subjectively graded. The standard motor tasks for upper limb that include the Finger-to-Nose Test (FNT) and test for upper limb Dysdiadochokinesia (DDK) is the focus of this study. The common features of these tests include “actions requiring movement across peripheral limb joints” and “accuracy of repetition and rhythm in stopping and starting”.

The accuracy and the rhythmicity of the movements are the performance parameters assessed by the clinicians. The extent to which there is undershoot and overshoot of the target or trajectory, is the criterion used to assess accuracy. The term Dysmetria refers to inaccuracies of movement and also implies a disturbance causing displacement. Inability to judge a target is a main attribution of the impairment along with variable or increased execution times as seen in the Finger Nose Test. This also suggests that the acceleration is also affected. Rhythmicity is evaluated by asking the subject to perform a series of repetitive movements such as striking one hand with Dasal and palmer sides of the other hand.

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alternatively. The stability and accuracy of these rhythmic movements are the main focus during the tapping iterations. The movement impairment associated are usually described as Dysdiadochokinesia.8

The upper limb tests involve certain movements aimed at extracting the disability by instigating repetitive action involving multiple muscles across limb joints where the cerebellar damage is typically manifested. Hence, quantification of the disability is necessary for progressive treatment plans and rehabilitation. Manual pattern recognition is essentially the criterion used by the clinicians rather than any objective measurement at the bedside. Thus there is no clarity for the kinematic parameters whether it is acceleration, displacement, timing or the accuracy measurement contributing to the impairment. Clinical scales such as the Scale for the Assessment and Rating of Ataxia (SARA) formalises the bedside assessments although they are explicit about the test performance with relatively hard constraints. The absence of an objective measure for characteristic movements that is clinically applicable to a proven degree of validity for upper limb tests is an existing gap. In clinical settings, complex and expensive rehabilitation tools requiring large infrastructures and technical expertise have generally been used for measuring movement impairments. Earlier studies have shown that the use of multiple sensors can limit the usability as it can be cumbersome while considering it as performance assessment tool.9 Inertial measurement units (IMU) are the most frequently used technologies (84%)10 where feature extraction is inherently an integral aspect. Parameters extracted from such measures have tremendous diagnostic value as it senses human physiological signs, movements and can also be translated into meaningful clinical measures for rehabilitation programmes.11

In this work, we engage the use of BioKin\textsuperscript{TM} sensors equipped with accelerometers and gyroscopes with Wi-Fi communication for real time transmission to cloud storages to capture the disability related characteristic information during the tests. Also, this work is aimed at assisting the diagnosis as well as the severity using features extracted from the sensors. The kinematic information from the sensor is low-pass filtered and subjected to time-domain analysis, entropy and frequency domain analysis. The dimensionality of the feature space is reduced using Principal Component Analysis (PCA) with the clustering of the dominant cohorts (patients and controls) is attained. Linear Discriminant Analysis (LDA) enhanced the correlation with the expert clinical scores as well as ascertaining the severity information contained in the features pertaining to cerebellar disorder. As a result of machine learning approaches, generally, the level of classification was enhanced.

2. METHODOLOGY

2.1 Participants
Seventy subjects consisting of 39 patients diagnosed with Cerebellar Ataxia to varying severity levels (patients: 19 males and 20 females) aged 60±20 years and 31 controls (controls: 13 males and 18 females) aged 50±25) years participated in this trial. All subjects performed both the tests and the movements were captured using the BioKin\textsuperscript{TM} sensor. The study was approved by the Human Research and Ethics Committee, Royal Victorian Eye and Ear Hospital, East Melbourne, Australia (HREC Reference Number: 11/994H/16). All the participants formally consented to the participation in the study.

2.2 Experimental Task
The data capture is conducted using BioKin\textsuperscript{12} wearable module that consists of a built-in IEEE802.11b/g/n wireless communication interface running on a 32-bit ARM processor. With the sensor module is tied around suitable limb positions for each of the tests, the participants performs the following neurological assessment tests:

2.2.1 Finger to Nose Test:
The clinician’s index finger is positioned in front of the subject as given in figure 1 (Data Colection). For approximately 15 seconds, the subject was instructed to use their index finger to first touch the stationary clinician’s finger and then their own nose and repeat the process\textsuperscript{13} The test is performed with both left and right limbs consecutively. The BioKin\textsuperscript{TM} is tied around the subject’s dorsal surface of the hand.

2.2.2 Test for upper limb Dysdiadochokinesia:
The subjects were instructed to place the dorsal side of one hand on the palm of the other hand as given in figure 1. Then the subject is instructed to pronate the hand so that the palm rest on the palm of the other hand. With maximum speed, the subject is also instructed to pronate and supinate between these two positions, and the rate of alternation is extracted from the BioKin\textsuperscript{TM} which is tied around the wrist.
2.3 Data Analysis

The translational and rotational motion can vary between controls and patients and hence all the orthogonal axes are considered separately. The BioKin\textsuperscript{TM} sensor was sampled at 50 Hz and initially low pass filtered with a cut-off frequency 10 Hz. As the significant frequency range was identified to be the band between 2Hz and 5Hz containing most of the characteristic information a 6\textsuperscript{th} order bandpass Butterworth filter was used. Along with the sensor measures of angular velocity and linear acceleration, angular acceleration and angle is also deduced as kinematic features. The frequency domain analysis was conducted using Fast Fourier Transforms (FFT). The features captured from the respective FFT waveform to find the peaks include resonant frequency (RF) and the magnitude of the frequency at resonance (MR). There were 24 main features for each axes from the sensor measures when considering both left and right limbs for each test. The data analysis is outlined in figure 1.

Using hypothesis testing for p-values (p<0.05), the most significant kinematic features for each test were selected. The features were investigated to find out the correlation with clinician’s score using Pearson correlation coefficient. Coefficient values ≥0.5 considered to be indicative of a reasonable correlation. The separation of subject data into cohort of patients and controls is achieved through Principal Component Analysis (PCA).\textsuperscript{14} PCA combines the dominant features in each test and reduces the dimensionality as it uses linear orthogonal transformation for transforming data into a new coordinate system and data projection is as per the diagonal covariance matrix-maximizing the feature variance. Further analysis was attained using principal components identified to have maximum features contribution with PCA and extended to perform feature classification. The PCA separation obtained was quantified using Silhouette’s value (S\textsubscript{sil}) which validates data consistency within clusters.

Based on the extent of the disorder, a detailed severity assessment of patients can be ascertained using classification techniques. The modelling of severity of data is obtained using supervised Linear Discriminant Analysis (LDA) classifier.\textsuperscript{15} The LDA classifier was used to evaluate the PCA-derived dominant data distributions in terms of discriminating and severity estimation. For a given population with probability density function of \(x\) is a multivariate normal with mean vector \(\mu\) and variance-covariance matrix \(\Sigma\), the linear discriminant function is given as,

\[
d^\text{LDA}(x) = -\frac{1}{2} \mu_i^T \Sigma^{-1} \mu_i + \mu_i^T \Sigma^{-1} x = d_{i0} + \sum_{j=1}^{p} d_{ij} x_j, \tag{1}
\]

where \(d_{i0}=-\frac{1}{2} \mu_i^T \Sigma^{-1} \mu_i\) and \(d_{ij}\) is the \(j\textsuperscript{th}\) element in \(\mu_i^T \Sigma^{-1}\) with \(i \in [0, 1, 2]\). For the purpose of supervised classification, the subject data was categorised into three different classes- controls (severity score of 0), patients (severity score of 1) with mild ataxia and patients (severity score of 2) with a significant level of ataxia. The k-fold cross-validation technique was also applied for evaluating the classifier performance. True Positive Rate (TPR) is the number of patients accurately classified and False Positive rate (FPR) is the number of healthy subjects identified as patients. These parameters were used to evaluate the performance in the form of accuracy (max value = 1) and sensitivity. The over-fitting and misclassification issues were also addressed along with the performance parameters.
3. RESULTS

The frequency domain analysis of the primary measures are given in table 1. The resonant frequency (RF) and the magnitude of the resonant frequency (MR) were the features analysed for kinematic parameters such as angular and linear acceleration and angle. The p-values (p<0.05) for hypothesis testing are denoted in table 1.

Table 1. Pearson correlation values and P-values of extracted features

<table>
<thead>
<tr>
<th>Test</th>
<th>Axes</th>
<th>L/R</th>
<th>P-val</th>
<th>Acceleration</th>
<th>Angular</th>
<th>Angle</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RF</td>
<td>MR</td>
<td>RF</td>
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<tr>
<td>FNT</td>
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<td>-0.2128</td>
<td>-0.0209</td>
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<td></td>
<td></td>
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<td>0.65</td>
<td>0.58</td>
<td>0.75</td>
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<tr>
<td></td>
<td></td>
<td>R</td>
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<td>0.192</td>
<td>-0.1777</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Rp</td>
<td>0.63</td>
<td>0.59</td>
<td>0.51</td>
<td>0.71</td>
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<tr>
<td></td>
<td>Y</td>
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<td>-0.0256</td>
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<td></td>
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<tr>
<td></td>
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<tr>
<td></td>
<td>Z</td>
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<td>0.0411</td>
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<td></td>
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<td>Lp</td>
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<td>0.29</td>
<td>0.72</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
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<td>0.0316</td>
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<td></td>
<td></td>
<td>Rp</td>
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<td>0.76</td>
<td>0.56</td>
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<tr>
<td>DDK</td>
<td>X</td>
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<td>-0.2619</td>
<td>-0.0184</td>
<td>0.2253</td>
<td>-0.3416</td>
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<tr>
<td></td>
<td></td>
<td>Lp</td>
<td>0.63</td>
<td>0.71</td>
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<td>R</td>
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<td></td>
<td></td>
<td>Rp</td>
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<td>Y</td>
<td>L</td>
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<td>-0.5846</td>
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<td>-0.0865</td>
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<tr>
<td></td>
<td></td>
<td>Rp</td>
<td>0.25</td>
<td>0.32</td>
<td>0.74</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Correlation value for L- Left limb, R- Right limb
RF- Frequency at Resonance, MR- Magnitude of Frequency At Resonance, Rp- P-value of right limb, Lp- P-value of left limb.

The hypothesis testing selected the features of significance for each test in table 2. These features represented the ability of subject data to be separated into two cohorts. For clarity, following notational abbreviation for the selected features are adhered: Frequency Feature (RF)MR(\text{Axis},\text{KinematicParameter})

The quantified information of the separation is given in table 2 using Silhouette’s value for the separation obtained using PCA given in figure 2 (c) and (d). Features of good correlation coefficient values (≥0.5) gave separation as plotted in figure 2 (a) and (b). RF(FNT(L,R)); MR(FNT(L,R)) are plotted in x,y axes in figure 2(a) for the FNT, and with RF(DDK(L,R)); MR(DDK(L,R)) for DDK test in figure 2(b).

Classification: The linear discriminant analysis classifier results are depicted in figure 3 (i). In Finger to nose test, the best classification of FNT was given by the angular acceleration features RF(X,An)(DDK(L,R)) and MR(Z,An)(DDK(L,R)) as indicated in figure 3(b). The feature input to LDA included combination of both left and right limbs using PCA which obtained highest correlation with expert clinician score (0.7782). The angle, RF(Y,An)(FNT(L,R)); MR(Y,An)(FNT(L,R)) resulted in noticeable classification relevant to severity as in figure 3(c). In the test for upper limb Dysdiadochokinesia, superior discrimination and correlation with the expert clinicians score was obtained for features of the accelerometer i.e. RF(X,An)(DDK(L,R)); MR(X,An)(DDK(L,R)) and RF(Y,An)(DDK(L,R)); MR(Y,An)(DDK(L,R)) as given in figure 3(d). The angle features RF(Z,An)(DDK(L,R)) and MR(Z,An)(DDK(L,R)) as given in figure

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Figure 2. Figures 2(a) and 2(c) depict Resonant Frequency (RF) versus Magnitude (MR) from FFT analysis using features of high correlation and figures 2(b) and 2(d) denote the best separation using PCA analysis of kinematic parameters in FNT. Figure 2(a) depicts Y-axis of gyroscope in FNT, Figure 2(b) Z-axis of accelerometer in DDK.

Table 2. Features selected based on hypothesis testing and Separation measure using the Silhouettes value ($S_v$)

<table>
<thead>
<tr>
<th>TEST</th>
<th>ABBREVIATION</th>
<th>DESCRIPTION (L,R)</th>
<th>SILHOUETTE VALUE</th>
<th>TEST</th>
<th>ABBREVIATION</th>
<th>DESCRIPTION (L,R)</th>
<th>SILHOUETTE VALUE</th>
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</thead>
<tbody>
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<td>FNT</td>
<td>$RF^{Y,A_n}_{FNT(L,R)}$</td>
<td>RF of $A_n$ in Y-axis</td>
<td>Parameters</td>
<td>FNT</td>
<td>$RF^{Y,A_n}_{FNT(L,R)}$</td>
<td>RF of $A_n$ in Y-axis</td>
<td>acceleration 0.513 0.772*</td>
</tr>
<tr>
<td></td>
<td>$MR^{Y,A_n}_{FNT(L,R)}$</td>
<td>MR of $A_n$ in Y-axis</td>
<td>FNT</td>
<td>DDK</td>
<td>$MR^{X,A_n}_{DDK(L,R)}$</td>
<td>MR of $A_n$ in Y-axis</td>
<td>Velocity 0.535 0.521</td>
</tr>
<tr>
<td></td>
<td>$RF^{Y,A_n}_{FNT(L,R)}$</td>
<td>RF of $A_n$ in Y-axis</td>
<td>DDK</td>
<td></td>
<td>$RF^{X,A_n}_{DDK(L,R)}$</td>
<td>RF of $A_n$ in Y-axis</td>
<td>Angular Acceleration 0.784* 0.651</td>
</tr>
<tr>
<td></td>
<td>$MR^{Y,A_n}_{FNT(L,R)}$</td>
<td>MR of $A_n$ in Y-axis</td>
<td></td>
<td></td>
<td>$MR^{X,A_n}_{DDK(L,R)}$</td>
<td>MR of $A_n$ in Y-axis</td>
<td>Angular Velocity 0.708 0.711</td>
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<tr>
<td></td>
<td>$RF^{Z,A_n}_{DDK(L,R)}$</td>
<td>RF of $A_n$ in Z-axis</td>
<td></td>
<td></td>
<td>$RF^{Y,A_n}_{DDK(L,R)}$</td>
<td>RF of $A_n$ in Y-axis</td>
<td>Angle 0.762* 0.783*</td>
</tr>
<tr>
<td>DDK</td>
<td>$MR^{X,A_n}_{DDK(L,R)}$</td>
<td>MR of $A_n$ in X-axis</td>
<td></td>
<td></td>
<td>$MR^{Z,A_n}_{DDK(L,R)}$</td>
<td>MR of $A_n$ in Z-axis</td>
<td>All Combined 0.617 0.701</td>
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<tr>
<td></td>
<td>$MR^{Y,A_n}_{DDK(L,R)}$</td>
<td>MR of $A_n$ in Y-axis</td>
<td></td>
<td></td>
<td>$MR^{X,A_n}_{DDK(L,R)}$</td>
<td>MR of $A_n$ in Y-axis</td>
<td>Upper Limb Combined 0.754 0.754</td>
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</tbody>
</table>

3(f), showed convincing separation for the subject data in DDK in terms of classification but the correlation with expert clinician scores were low compared to the acceleration.

The feature vector obtained from acceleration and angle can discriminate the subject data independently although combination of both affects adversely. The LDA results were also correlated with the expert clinician scores using Pearson correlation coefficient. FNT gave $C_p = 0.7782$ and DDK gave 0.5668 in frequency domain analysis whereas in time-domain the correlation was less than 0.65. The two upper limb tests (FNT and DDK) were also PCA combined resulting in a Silhouette separation value of 0.754 as depicted in figure 3(ii). Further, the combination is classified in terms of patient.

Figure 3. Boxplot representing the feature separation of each test with doctors score using Linear Discriminant Analysis and combination of 2 tests.
severity using LDA. This resulted in enhancing the correlation with standard upper limb test scores since it obtained improved coefficient of 0.8253. Evaluating the region of Convergence (ROC) curve, the Area under the Curve (AUC) values were found to be 0.7983 and 0.9132 for FNT and DDK respectively. The accuracy values calculated were 0.9175 and 0.9350 for FNT and DDK respectively were the cross-validation error is 1-accuracy. The True Positive Rate(TPR) is found out to be 0.69 in FNT and 0.75 in DDK.

4. DISCUSSION

The feature extraction and selection process in table 1 using correlation and hypothesis testing found the characteristic features contributing to the disorder from the kinematic measures. The two tests are compared and evaluated using figure 2, 3 and table 2. The rotational motion provides a better separation and correlation with expert clinical scores in FNT. Similarly, acceleration distinguished the patients and control cohorts and correlated with clinician’s score for the case of DDK. The resonant frequency features are dominant as they obtained a high degree of separation (figure 3, table 2) in these upper limb tests compared to the magnitude features.

The gyroscope captures the characteristic disability feature resulting in greater separation in FNT as shown in table 2 and discriminates the subject data based on severity. The task is repeated at a lower frequency by patients than controls, evident from the frequency domain analysis as depicted in figure 3(a). Angular acceleration (figure 3(b)) discriminated the two cohorts effectively along the Y-axis of the gyroscope. The uncoordinated movement of the arm while trying to reach a target in FNT is primarily responsible for this discrimination. The rotation along the Y-axis resulted in uncoordinated movements during the repeated motion of the index finger from the nose to the target and back to the nose. In DDK, the resonant frequency and magnitude of angle captured the difference in the rotational angle between the two cohorts. It suggests range of the angle in the internal/pronation) and external rotation(supination) of the wrist differs for both controls and patients and results in movement bias intrinsic to ataxia. Along the Z-axis of the accelerometer (figure), movement abnormalities were found among the patients during the rapidly alternating movements of the palm. Also, a relatively slower pace of execution of the task by patients than the controls is depicted in figure 3(c). This infers to ataxia manifestations in patients based on the frequency of operation highlighting the difficulty they experiencing in performing the task. The inability of the patients to perform rapid alternating movements is evident from the LDA results that highlights the linear acceleration along X and Z-axis (figure 2(d)).

The analysis demonstrate better separation compared to the existing techniques as given in table 2 (Sv = 0.793 highest value). Also, frequency domain analysis generated more informative features compared to time-domain or other feature extraction techniques. While combining the two tests, high Silhouette value was obtained Sv = 0.754 indicating superior separation (table 2 and figure 3) and the correlation with expert clinical scores was greater than their individual correlation values with the upper limb tests. High degree of classification was demonstrated by the performance parameters resulting from the cross validation given in figure substantiating the higher accuracy and AUC values. Hence, an acceptable level of performance was obtained using this analysis comprising of PCA and LDA supervised classification. The true positive rates acquired confirms the success rate of the model selected during cross-validation. Low error also implies less number of subjects misclassified.

5. CONCLUSIONS

A robust technique using IMU sensor based motion capture is investigated for quantitative assessment of cerebellar ataxia during standard upper-limb bedside tests. Using the IMU sensing in BioKin™, the prominent feature capturing the disability is found out to be acceleration (translational/rotational) for both tests. The combination of gyroscope features gave convincing separation between patient and control cohorts in FNT where angular acceleration produced the best correlation with the expert clinical score. Contrastingly, linear acceleration features produced both separation and correlation for DDK. It is also noticeable that for the FNT with predominantly translational motion, rotational features captured disability and for DDK with predominantly rotational movements linear acceleration captured the disability.

The quantitative assessment of the two tests suggest that cerebellar ataxia is manifested in orthogonal directions other than the direction of dominant limb motion i.e. angular acceleration and angle manifested in Y-axis in the case of FNT and, acceleration manifested in X,Z axis and angle in Y-axis of DDK. The kinematic measures such as angle and the movement artefacts generated as a result of limb motion are the characteristic features not generally observed by the clinicians. The common feature for both the upper limb test is rotational movement around Y-axis associated to angle variation. Comparing the feature domains, frequency domain analysis gave better values of separation (Sv = 0.793) and correlation (Cp = 0.8219) for both the tests as compared to features in the entropy domain (Cp = 0.5668, Sv = 0.533) and in time domain (Cp = 0.6711,
Better correlation with clinical score was obtained for combination of FNT and DDK than their independent correlation values.

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