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FINGER-SPECIFIC LOSS OF INDEPENDENT CONTROL OF MOVEMENTS IN MUSICIANS WITH FOCAL DYSTONIA

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Abstract—The loss of independent control of finger movements impairs the dexterous use of the hand. Focal hand dystonia is characterised by abnormal structural and functional changes at the cortical and subcortical regions responsible for individuated finger movements and by the loss of surround inhibition in the finger muscles. However, little is known about the pathophysiological impact of focal dystonia on the independent control of finger movements. Here we addressed this issue by asking pianists with and without focal dystonia to repetitively strike a piano key with one of the four fingers as fast as possible while the remaining digits kept the adjacent keys depressed. Using principal component analysis and cluster analysis to the derived keystroke data, we successfully classified pianists according to the presence or absence of dystonic symptoms with classification rates and cross-validation scores of approximately 90%. This confirmed the effects of focal dystonia on the individuated finger movements. Interestingly, the movement features that contributed to successful classification differed across fingers. Compared to healthy pianists, pianists with an affected index finger were characterised predominantly by stronger keystrokes, whereas pianists with affected middle or ring fingers exhibited abnormal temporal control of the keystrokes, such as slowness and rhythmic inconsistency. The selective alternation of the movement features indicates a finger-specific loss of the independent control of finger movements in focal dystonia of musicians.

Key words: hand dexterity, fine motor control, movement disorder, neuroplasticity, machine learning, music.

INTRODUCTION

The independent control of finger movements is a key feature of the dexterous use of the hand. A superior independence of finger movements in humans over non-human primates indicates the development of this motor function in parallel with the evolution of an ability to manipulate various tools (van Duinen and Gandevia, 2011). However, damages in cortical and subcortical regions caused by stroke (Lang and Schieber, 2004), cerebellar dysfunction (Brandauer et al., 2012), or Parkinson's disease (Park et al., 2012) yield a loss of individuated finger movements, which severely impairs the quality of life. To unravel its neural mechanisms is therefore essential.

As a further highly interesting example of central nervous sensory-motor dysfunction, focal hand dystonia in musicians (MD) is a task-specific movement disorder that frequently manifests as a deterioration of dexterous finger movements. This is due to the loss of voluntary control of extensively trained movements that musicians performed during playing their instrument (Altenmüller and Jabusch, 2010; Altenmüller et al., 2012). For those who are affected, the disorder is highly disabling and often terminates their professional musical careers (Jabusch et al., 2004). Patients with focal hand dystonia displayed atypical activity in motor-related cortical and subcortical regions during individuated finger movements (Oga et al., 2002; Garraux et al., 2004; Lerner et al., 2004; Moore et al., 2012) and reduced central nervous surround inhibition in the finger muscles when investigated with motor cortex stimulation (Rosenkranz et al., 2005; Beck and Hallett, 2010). These findings suggest an impairment of individuated finger movements that play a crucial role in expert musical performance (Slobounov et al., 2002; Furuya et al., 2011; Furuya and Soechting, 2012; Furuya and Altenmüller, 2013). However, it has not been characterised how MD influences the individuated finger movements.

The present study aims to identify the pathophysiological impact of MD on the individuated movements of each of the fingers. Individuated finger movements require moving one particular finger while keeping the remaining fingers voluntarily immobilised. A lack of independence across fingers hinders the dynamic finger movement due to a spill-over of the stabilising force of production, and vice versa. MD can therefore disrupt the spatio-temporal features of the movements. However, potential problems to evaluate it reliably were limited sample size of the patient group and large number of candidate movement features affected by MD. The latter renders it difficult to determine with conventional statistical techniques whether a particular combination of multiple movement

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Abbreviations: ANOVA, analysis of variance; IKI, inter-keystroke interval; LDA, linear discriminant analysis; LOOCV, leave-one-out cross-validation; MD, musicians' dystonia; MIDI, Musical Instrument Digital Interface; NBC, naïve Bayesian classifier; PC1, first principal component; PCA, principal component analysis; PCs, principal components; SD, standard deviation; SVM, support vector machine.

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features characterises MD. In addition it implies the problem of multiple comparisons. Here, a novel approach using principal component analysis (PCA) and cluster analysis is proposed as a solution for these problems. It allows us not only to determine whether MD degrades the individuated finger movements by accounting for abundant spatio-temporal features of movements, but also to identify a particular set of movement features that are specifically affected by MD. Therefore, we were particularly interested first to assess whether individuated finger movements are affected by MD using a cluster analysis, and second whether the effect of MD on movements is similar or different across fingers using PCA. The results of these analyses may well contribute to correctly diagnosing and monitoring the effect of treatment of MD. This is of practical relevance, because frequently the symptoms are difficult to recognise for clinicians. Especially the correct identification of the affected finger can be problematic, because non-affected fingers also move atypically to compensate for the symptoms (Elbert et al., 1998; Candia et al., 2005). However, misdiagnosing the dystonic movement can have severe consequences, since for example successful treatment with local injections of botulinum-toxin A into the cramping finger flexors or extensors relies on correct identification of the dystonic movements (Schuele et al., 2005).

EXPERIMENTAL PROCEDURES

Patients and controls

Pianists who had one or two of their fingers affected by MD were recruited from the outpatient clinic of the Institute of Music Physiology and Musicians' Medicine at the Hannover University of Music, Drama, and Media. Each patient underwent a thorough neurological examination and was diagnosed by one of the authors (E.A.) who is specialised in movement disorders of musicians. Patients with other neurological, orthopaedic or psychiatric disorders were excluded from the study. In accordance with the Declaration of Helsinki, the experimental procedures were explained to all participants. Informed consent was obtained from all participants prior to participation in the experiment, and the experimental protocol was approved by the local ethics committee located in the Hannover Medical University.

Twelve highly skilled, healthy pianists who majored or had majored the keyboard and who had no history of neurological disorder (all right-handed) and 17 pianists with MD in the right hand (15 right-handed) participated in the experiments. In pianists, MD usually involves painless involuntary cramping of one or two fingers of the hand while playing the piano; the fingers in which the cramping occurs are defined as the affected finger(s). The duration of the disorder ranged from 1 to 20 years (mean duration ± standard deviation (SD) = 9.5 ± 5.6 years) at the time of the experiment. None of the patients displayed symptoms at their contra-lateral left hand. Ten patients underwent botulinum-toxin A injection therapy, whereas the remaining seven did not. Importantly, the most recent injection was performed at least 3 months prior to the experiment (range: 3–48 months, mean ± SD: 13.2 ± 15.7 months), suggesting the effect of the injection had passed by the time the present experiment began. The patients displayed symptoms at the index, middle, or ring fingers. The numbers of the patients whose symptoms were primarily at the index, middle and ring fingers were seven, five, and seven, respectively (two with multiple fingers affected). Note that none of the patients who participated in the current experiment had the little finger affected by MD. The total period of piano playing was 22.8 ± 2.2 and 39.2 ± 10.7 years for the healthy pianists and pianists with MD, respectively (*t*-test: $p = 2 \times 10^{-5}$). For a cluster analysis, two groups of pianists whose tapping finger is unaffected and affected were 32.5 ± 12.7 and 32.1 ± 8.2 years for the index finger tapping ($p = 0.94$), 31.5 ± 11.6 and 38.2 ± 11.6 years for the middle finger tapping ($p = 0.28$), and 28.4 ± 9.1 and 45.0 ± 10.1 years for the ring finger tapping ($p = 0.003$), respectively. We admit that this group difference could be a confounding factor, but we were unable to recruit perfectly age-matched groups due to highly limited populations. Furthermore, with respect to pianists' fine motor skills there is evidence that during early and middle adulthood motor skills remain extremely constant, given that the pianists are continuously practicing as it was the case in our sample (Jabusch et al., 2004, 2009).

Experimental design and data acquisition

Each participant performed a finger tapping task, which consists of successive keystrokes with one finger as fast and accurate as possible while the remaining four digits keep the adjacent keys depressed. This task enabled us to probe multifaceted features of the dynamic independence of finger movements (Aoki et al., 2005). In this case, the term ''fastest keystrokes'' and ''most accurate keystroke'' means to strike with the shortest inter-keystroke interval (IKI) and with the highest rhythmic accuracy, respectively. The tapping was performed in a staccato manner (i.e. a stroke of shortened finger-key contact duration), and no instruction regarding loudness of a tone was provided. Each of the four fingers of the right hand performed the tapping for 6 s, and the order was randomised across participants. Following each trial, there was a 10-s interval used to circumvent muscular fatigue. If participants released the non-tapping finger(s) during a trial, they were asked to repeat the trial. To assess the repeatability of tapping performance and to increase the sample size, each trial was repeated twice for each of the four fingers.

The pianists played a digital piano (MP 9000; Kawai, Krefeld, Germany) that was connected to a Windows computer (SONY VAIO VGN-Z90PS) via a Musical Instrument Digital Interface (MIDI) (Roland EDIROL UA-4FX). We recorded MIDI data from the keyboard by using a custom-made script in LabVIEW (National Instruments), running at 500 Hz (Furuya and Soechting,

2010). The pianists were provided with the tasks notated as scores of each of the tapping fingers on a computer monitor located in front of the piano.

Data analysis

During the experiment, we recorded the time at which each key was depressed and the time when it was released. In addition, we also recorded the speed with which each key was depressed, i.e. MIDI velocities provided by the interface, ranging from 1 to 127 (loudness). Using these data, we computed the duration of finger-key contact (from keypress to key-release) and IKI (from keypress to keypress). We excluded outliers that were greater than twofold of the SD within a trial from further analyses.

Statistical analysis

To test whether MD affects the individuated finger movements, a one-way analysis of variance (ANOVA) with unequal sample sizes using GROUP (healthy pianists, MD tapping with an unaffected finger, MD tapping with an affected finger) as independent variable was performed for each of the MIDI variables during tapping with each of the fingers. Tukey post-hoc tests were performed in the case of significant results of the ANOVA.

Cluster analysis

We performed binary classification to assess whether a finger tapping dataset was capable of specifying an affected finger (Fig. 1), in order to test that focal dystonia alters the individuated finger movements. We were also interested in identifying movement features affected by MD through determining a particular set of tapping variables that elicit the best classification. As an input for the cluster analysis, we computed the mean and SD of the IKI, MIDI velocity (i.e. loudness), and finger-key contact duration within a trial for each of the four fingers and for each of the two trials. For each of these dependent variables, a *t*-test confirmed no effect of trial on any dependent variables ($p > 0.05$), confirming the repeatability of the tapping performance across trials and the lack of a fatigue effect.

To probe for pathophysiological impacts on the independent control of finger movements, the cluster analysis was repeated using two different inputs (i.e. feature vectors) for each of the fingers. The first cluster analysis was performed using six variables (i.e. Mean/

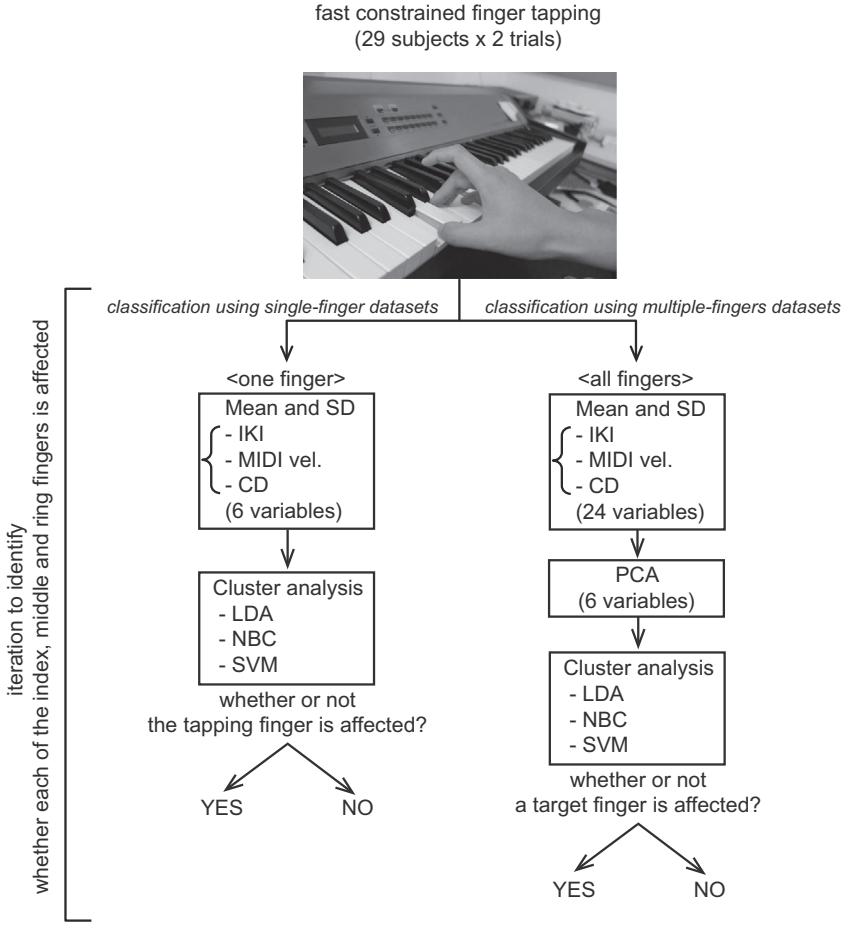

Fig. 1. Flow chart of the data analysis to identify whether each of the fingers is affected by focal hand dystonia by using a finger-tapping test and cluster analysis. LDA, linear discriminant analysis; NBC, naïve Bayesian classifier; SVM, support vector machine; IKI, inter-keystroke interval; MIDI vel., MIDI velocity; CD, finger-key contact duration.

SD × IKI/velocity/contact duration) of a tapping finger, derived from the two trials from all participants, as an inputted feature vector (Fig. 1 left). This analysis aimed to assess whether MD at a tapping finger affects tapping behaviour in itself and is referred to as "*classification using single-finger datasets*". For example, we assessed whether the datasets from the index finger of pianists with an affected index finger formed a separate cluster from those of the index-tapping datasets of the healthy pianists and the MD pianists with unaffected index fingers. This analysis was performed to identify the symptoms of each of the index, middle and ring fingers.

The second cluster analysis was performed to test whether MD at a non-tapping finger affects the motion of the non-affected tapping fingers (Fig. 1, right). Due to the dependence of movement control across fingers at both the peripheral and central levels (Schieber and Santello, 2004), voluntary immobilisation of a dystonic finger possibly disrupts the tapping motion of a non-affected finger. For example, if MD at the middle finger lowers the independent control of movements across fingers, muscular force exerted to keep the middle finger depressing a key can impede extension motion of the tapping finger. Furthermore, it is also likely that information of the tapping with an unaffected finger of the MD patients highlights abnormality of movement features of the tapping with an affected finger. In line with these arguments, we hypothesised a better identification of an affected finger when using the datasets acquired from tapping with both the affected and non-affected fingers in the cluster analysis ("*classification using multiple-finger datasets*"). Again, this analysis using the tapping datasets of all fingers was performed to identify the symptoms of each of the index, middle, and ring finger. In this analysis, the input matrix represents 58 (two trials × 29 participants) × 24 (six variables × four fingers) datasets. To decrease the dimensionality of the matrix, a PCA was performed. PCA is a well-established mathematical technique that transforms a set of observations of possibly correlated variables (i.e. MIDI variables) into a set of values of linearly uncorrelated (orthogonal) variables (i.e. principal components, PCs). The PCs are ranked such that the first principal component (PC1) accounts for the largest portion of the variance. The derived weighting coefficients and PC scores represent the contribution of each of the 24 variables to an individual PC and a linearly uncorrelated variable that was converted from a set of original variables for each trial, respectively. In addition to the dimensionality reduction that yields a better classification, the PCA enables to identify a set of multiple variables that represent the symptom of MD for each of the fingers affected. The mathematical expression of this procedure is as follows;

$$X_{var} = PC1 \times WC1_{var} + \cdots + PC24 \times WC24_{var}$$

where X_{var} is the standardised input vector at a particular movement variable, and WC1–WC24 are the weighting coefficients of a certain variable.

A cluster analysis is a method used to determine the parameters that represent an individual classifier based on a training dataset so as to minimise erroneous assignments of a dataset into an inappropriate class. For each of the index, middle, and ring fingers, we performed a Fisher's linear discriminant analysis (LDA), a naïve Bayesian classifier (NBC) assuming Kernel density function, and a support vector machine (SVM), and compared the results in order to determine the best classifier in terms of successful classification and cross-validation. A rationale to use the different classifiers was a lack of any prior information on distribution of datasets of the finger tapping in a hyperspace, and the classifiers differ in the shapes of the boundary that separates the datasets in a hyperspace. In addition, to determine the best classifier for the datasets is essential for accurate diagnosis of MD based on the tapping behaviours. The input feature vector consisted of either the movement variables derived from a single finger or a fraction of the PCs that represented the movement variables of all the fingers in a certain trial. The classifier assigns the movement data into one of two classes; whether or not a certain finger is affected by MD.

The LDA discriminates the movement data in terms of hyperplanes that maximise the ratio of between-class over within-class variance of the data (Misaki et al., 2010). The NBC applies Bayesian probability theory to data classification based on an automatically constructed statistical probability model (Murakami and Mizuguchi, 2010). Here, we used Kernel density estimation, a non-parametric method of estimating the probability density function population. The SVM chooses the hyperplane that has the maximum margin, i.e. the hyperplane that separates the classes with maximum safety clearance to the closest training patterns on either side (Vapnik, 1995). We used the MATLAB statistical and bioinformatics toolboxes for the cluster analyses.

Leave-one-out cross-validation (LOOCV)

A typical concern of a cluster analysis is overfitting, which may perfectly classify the training dataset but may fail to produce a successful prediction for a novel dataset. To evaluate the predictability of a classifier, a LOOCV was performed. A LOOCV uses pairs of original datasets from a single subject as the testing dataset, and the remaining datasets form the training set. Possible parameters are then tuned based only on the training set and the binary class label on the leave-out testing dataset is predicted from the classification model built upon the training set. This procedure is repeated so that each dataset (i.e. each subject) is used exactly once as the testing dataset. The LOOCV error rate was computed by dividing the number of misclassified testing datasets (subjects) by the total number of datasets (subjects). This value was subtracted from 1 and then multiplied by 100, and the result was defined as the LOOCV score, which represents the predictability of the classifier for a dataset derived from a novel player. Note that we also performed a LOOCV that

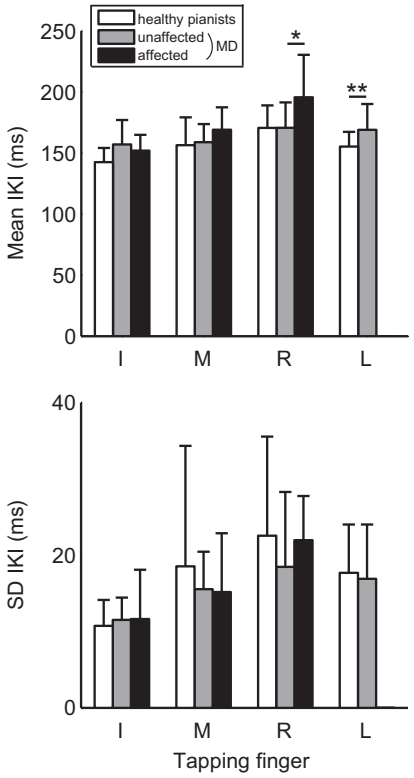

Fig. 2. The group mean (top) and standard deviation (bottom) of the inter-keystroke interval of the tapping movements across the healthy pianists (white), the MD pianists without symptoms at the tapping finger (grey, unaffected MD), and the MD pianists with symptoms at the tapping finger (black, affected MD) during fastest finger tapping with each of the index (I), middle (M), ring (R) and little (L) fingers (*x*-axis). An error bar indicates one SD within each group. $^{*}p < 0.05$, $^{**}p < 0.01$. Results of the other four MIDI variables (mean and SD of the MIDI velocity and finger-key contact duration) are summarised in Table 1.

excluded the dataset of one trial from a subject, which did not largely affect the results.

RESULTS

Comparison across affected and non-affected fingers

To describe the movement characteristics of the affected and unaffected fingers, the mean and SD of each of the six movement variables within a trial during tapping with each of the four fingers were computed (Fig. 2 and Table 1). As a representative result, Fig. 2 displays the group means of mean and SD of the IKI across the healthy pianists (white), the MD pianists without symptoms at the tapping finger (grey), and the MD pianists with symptoms at the tapping finger (black). The results demonstrated that values at some of the variables were larger or smaller when a tapping finger was affected as compared to tapping with an unaffected finger, although this difference depended on which finger was used for tapping. For example, the mean IKI value was relatively larger at the affected finger when tapping with the ring finger, which was not discernible during the index finger tapping. One-way ANOVA revealed no significant group effect for each of the six variables, except for the mean IKI at the ring ($F^{2,26} = 3.77$, $p = 0.04$) and little ($F^{1,27} = 7.88$, $p = 0.01$) fingers and the mean MIDI velocity at the little finger (Table 1). A post-hoc test for the mean IKI of the ring finger showed a difference only between the pianists with the tapping-finger affected and pianists with the tapping-finger unaffected.

To summarise, the findings indicate firstly that none of the variables can segregate between the three distinct groups, and secondly that the MD patients tap

Table 1. Group mean and SD of the MIDI velocity and contact duration, and results of ANOVA

		Healthy pianists		MD: unaffected finger		MD: affected finger		ANOVA	
		Mean	SD	Mean	SD	Mean	SD	*F*	*p*
MIDI velocity									
Mean	I	59.7	10.9	66.2	10.7	64.7	8.0	2.14	0.14
	M	52.8	13.3	55.5	8.9	62.8	9.4	2.58	0.10
	R	49.3	14.3	58.3	7.9	50.8	10.2	1.42	0.26
	L	51.5	14.8	60.5	9.6			5.74	**0.02**
SD	I	8.5	2.7	8.1	2.2	9.3	3.5	1.76	0.19
	M	9.8	3.1	10.1	2.6	8.4	2.4	1.21	0.31
	R	10.3	3.4	10.0	2.6	9.2	2.3	2.72	0.08
	L	10.3	2.2	10.1	2.6			0.08	0.79
Contact duration									
Mean	I	47.3	20.5	50.0	16.4	39.6	3.1	1.15	0.33
	M	68.0	40.7	60.1	21.9	65.4	20.4	0.34	0.71
	R	72.2	22.9	59.6	18.3	74.7	25.0	2.08	0.15
	L	61.5	20.6	63.7	20.6			0.33	0.57
SD	I	6.6	4.1	10.1	6.3	6.4	2.4	2.63	0.09
	M	10.2	6.1	10.9	5.7	14.5	8.4	0.95	0.40
	R	14.9	8.6	11.9	5.2	17.1	5.7	2.09	0.14
	L	10.8	4.4	13.2	4.4			1.72	0.20

A bold number indicates $p < 0.05$.
A unit of the finger-key contact duration is millisecond.
F and *p* indicates *F* value and *p* value derived from one-way ANOVA, respectively. I, M, R, L indicates the index, middle, ring and little finger, respectively.
I, M, R, L indicates the index, middle, ring and little finger, respectively.

differently from the healthy pianists even with the non-affected finger. A limitation of this conventional statistics is therefore that it is not apparent if a tapping finger is affected when examining only one single variable, possibly due to a large inter-subject variability and a lack of data from a sufficient number of patients. This motivated us to determine if a combination of multiple variables would be better at characterising the differences between the affected and unaffected fingers as compared to a single variable. We tested this idea by means of a cluster analysis using multiple variables as input datasets to determine whether or not a certain finger is affected. We expected that a particular set of the movement variables sensitive to MD would contribute to a successful classification according to the presence of dystonic symptoms at a finger.

Classification using single-finger datasets

To determine the effects of MD on the movement characteristics of a tapping finger, we performed a cluster analysis. The analysis aimed to segregate the affected and unaffected fingers based on the six movement variables derived from the tapping finger (i.e. the mean and SD of each of the IKI, the keystroke velocity, and the finger-key contact duration) (i.e. Fig. 1 left). Table 2 summarises both the successful classification rate for each of the two classifiers and the LOOCV scores during tapping with each of the index, middle, and ring fingers. Overall, NBC and SVM yielded substantially better rates of successful classification and cross-validation than LDA for all three fingers. The following section therefore focuses only on the results of NBC and SVM, which indeed provided converging findings.

For ring-finger tapping, the NBC demonstrated remarkably good performance in both the classification and the cross-validation. To further identify which movement features were specifically affected by the dystonic symptoms at the ring finger, NBC was iterated by changing the input variables. None of the variables could successfully classify, with classification scores ranging from 79% to 83%. This corroborates the finding shown in Fig. 2 and Table 1. Next, a combination of two variables yielded classification scores ranging from 76% to 90%. In particular, using both the mean and SD of the IKI yielded the best performance in terms of classification (90%) and cross-validation (90%) as compared to using all six variables. Similarly, SVM elicited the best classification and cross-validation when using these two variables, although the LOOCV score was slightly lower than the NBC (86%). These findings provided converging evidence indicating that both tempo and rhythmic accuracy of tapping were affected by MD at the ring finger.

For the middle finger, although the classification appeared to be successful (93%), a relatively low LOOCV score suggested overfitting, which means that the classifier failed to predict based on a new dataset. This was even more likely for the index finger, which had the worst LOOCV scores for all the classifiers (Table 2). These results indicate that for the index and middle fingers, MD does not necessarily affect fine motor control only of the affected finger, in a strict sense. However, it is also possible that immobilising the affected finger voluntarily influences the tapping behaviour of a non-affected finger, as argued in the Methods. If so, the movement features of tapping with a non-affected finger should also serve to better segregate the healthy pianists and the pianists with MD. We tested this hypothesis by using datasets that represented the tapping with both the affected and non-affected fingers in a cluster analysis (Fig. 1, right).

PC analysis

Prior to the cluster analyses, we decreased the dimensionality of the input dataset by performing a PC analysis. The dataset consisted of 58 (29 participants $\times$ two trials) and 24 (six variables $\times$ four fingers) matrices. The variance accounted for by each of the first six PCs was 24.0%, 17.2%, 13.4%, 6.8%, 6.4%, and 5.5%, respectively. This indicates that the first six PCs accounted for more than 70% of the total variance. Therefore, we decided to use these six PCs as inputs for the subsequent cluster analyses.

Table 3 summarises the weighting coefficients of the first six PCs. The value of WCi represents the contributions of the individual variables to the PCi. WC1 consisted mostly of a positive contribution from the mean and SD of the finger-key contact duration during tapping with each of the four fingers, and a negative contribution from the mean IKI at the middle and ring fingers. WC2 consisted mostly of a positive contribution from the mean keystroke velocity during tapping with each of the four fingers. For WC3, the positive and negative contributions of the mean IKI and SD of the keystroke velocity dominated, respectively, particularly when the middle finger kept a key depressed as a non-tapping finger. WC4 was characterised by the negative SD of the keystroke velocity at the index and ring fingers, the positive SD of the contact duration at the middle and little fingers, the negative SD of the IKI at the index finger, and the negative mean of the IKI at the

Table 2. Successful classification rates and cross-validation rates when using single-finger datasets

	Index	Middle	Ring
Linear discriminant analysis	65.5 (56.9)	81.0 (70.7)	75.9 (67.2)
Naïve Baysian classifier	82.8 (69.0)	93.1 (79.3)	89.7 (86.2)
Support vector machine	91.4 (72.4)	93.1 (84.5)	98.3 (81.0)

A number in parenthesis indicates a LOOCV score derived from the cross validation test.

Table 3. Weighting coefficients of the first six principal components

	Index						Middle						Ring						Little					
	IKI		Keystr Vel		Contact Dur		IKI		Keystr Vel		Contact Dur		IKI		Keystr Vel		Contact Dur		IKI		Keystr Vel		Contact Dur	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
WC1	0.10	0.20	0.03	0.22	**0.26**	**0.27**	0.23	0.21	0.05	0.20	**0.30**	**0.25**	**0.28**	0.13	0.11	0.07	**0.33**	**0.28**	0.11	0.06	0.19	0.08	**0.27**	0.22
WC2	−0.09	−0.11	**0.35**	−0.04	0.00	0.02	−0.23	**−0.25**	**0.43**	0.17	−0.18	−0.05	−0.20	**−0.30**	**0.41**	0.16	0.03	0.12	0.01	−0.02	**0.34**	0.11	0.10	0.12
WC3	**0.39**	−0.20	−0.04	**−0.25**	0.09	0.13	0.24	−0.24	0.08	−0.20	−0.06	−0.05	0.23	−0.23	0.02	**−0.27**	−0.01	−0.11	**0.41**	−0.20	0.08	**−0.33**	0.16	0.08
WC4	−0.20	**−0.40**	−0.05	**−0.36**	0.06	−0.05	0.05	0.10	0.05	−0.15	0.24	**0.35**	−0.18	−0.17	−0.05	**−0.30**	0.08	−0.03	**−0.25**	0.17	−0.12	0.20	0.18	**0.31**
WC5	0.13	−0.06	**0.41**	−0.09	**−0.32**	−0.03	**0.37**	0.24	0.15	−0.04	0.20	**0.26**	0.04	0.11	0.20	−0.12	−0.12	−0.07	−0.05	−0.08	0.16	0.03	**−0.37**	**−0.33**
WC6	−0.04	0.16	−0.02	**0.26**	**0.32**	**0.25**	−0.01	0.06	0.07	0.01	0.09	0.18	−0.24	**−0.25**	0.06	−0.08	−0.09	−0.20	**−0.36**	**−0.52**	−0.14	**−0.29**	−0.07	−0.01

A bold number indicates a weighting coefficient larger than 0.25.
IKI, inter-keystroke interval; Keystr Vel, MIDI velocity; Contact Dur, finger-key contact duration.

little finger. WC5 and WC6, which characterise particular trials and/or players, had no representative pattern across fingers.

To identify the PCs that represented a pathophysiological impact of MD on finger movements, the average values of each of the first four PCs across the subjects were computed at each of the unaffected and affected fingers (Fig. 3). The results described the differences in the PC values depending on which finger was affected, which characterised finger-specific symptoms of MD. The PC1 showed a positive value only for the pianists who had symptoms at the ring finger. This indicates that MD at the ring finger is associated with a slower tapping speed of this finger and with longer and more variable finger-key contact durations during tapping with each of the four fingers (see Table 3). PC2 differed in sign according to whether the individuals had symptoms at the index finger, which indicates stronger keystrokes during tapping with each of the fingers by the pianists with an affected index finger. PC3 showed the largest positive value for patients with symptoms at the middle finger, which indicates slower tapping pace and more variable keystroke velocity during tapping. PC4 displayed a negative value only for patients with symptoms at the ring finger, being characterised by larger rhythmic inaccuracy during index finger tapping, slower tapping

Fig. 3. Group means of each of the first four principal components (PCs) across pianists without MD (white) and with MD at the index (light grey), middle (dark grey), and ring fingers (black). An error bar indicates one SD within each group. MD, musician's dystonia. Each of the principal components characterises which finger is affected.

with the little finger, larger variability in the keystroke velocity during index and ring finger tapping, and smaller variability in contact duration during middle and little finger tapping. In sum, these results indicated that MD elicited force abnormality for the index finger and temporal abnormality for the ring finger.

Classification using multiple-fingers datasets

To explore the possibility of substantial impacts of immobilising the affected finger on tapping behaviours of a non-affected finger, a cluster analysis was performed using the PC datasets obtained from the movement features derived from all the fingers (Fig. 1 right). We iterated the cluster analysis by changing the number of PCs from one to six, in order to determine the number of PCs that would allow for the best classification. The results are summarised in Table 4. Similar to the classification using a single finger dataset, NBC and SVM were remarkably better classifiers than LDA for all the fingers. We therefore focus on the results of NBC and SVM.

For the index finger, NBC with three or four PCs showed considerably good performance in terms of both classification and cross-validation. These scores were remarkably higher than those of the classification using a dataset from a single finger (16% higher for the classification rate and 24% higher for the cross-validation value). Indeed, NBC using the first three and four PCs yielded misclassification that amounts to only two and one trials, respectively. This confirmed that immobilisation of the affected finger impaired fine motor control during tapping with the adjacent non-affected fingers. Note that these classifications are unlikely to be an overfitting due to the high LOOCV scores of approximately 90%. Similar to NBC, SVM yielded a fairly good classification score that even amounted to 100%. However, the LOOCV score was not higher than that of the NBC, even though the value was 16% higher as compared to the classification using a single finger dataset. This indicates better predictability of the NBC compared to the SVM.

Fig. 4 displays a classification of the movement features of tapping by all players in terms of whether the index finger is affected (blue-dotted area) using NBC in the PC space. The white and black plot indicates the movement features derived from one trial of a healthy pianist and a pianist with MD, respectively. This classifier, using the first three PCs, yielded a 97% successful classification rate and a 93% LOOCV score (Table 4). Note that some of the white plots that appear to be in the blue-dotted area do not belong to it; instead, they are located either in front of or behind it.

For the middle finger, both the NBC and SVM yielded classification scores of greater than 90% when using the first three PCs. They also elicited the best LOOCV score for NBC. When increasing the number of PCs up to six, both of these classifiers demonstrated their best performance in terms of classification and cross-validation. These scores were again higher than those obtained using a dataset from a single finger, indicating that MD at the middle finger influenced on the tapping movements in both the affected and unaffected fingers.

For the ring finger, in contrast, the results of the classification and cross-validation were similar when using the tapping data from a single finger (Table 2) or from multiple fingers (Table 4). For the NBC, the LOOCV score was even better when using only two original keystroke variables from a single finger (i.e. the mean and SD of the IKI during ring finger tapping; 90% of LOOCV score). This implies that MD at the ring finger did not affect fine motor control of the adjacent non-affected fingers.

Effect of botulinum toxin injections on the individuated finger movements

In order to determine whether past injections of botulinum toxin influenced the individuated finger movements of the

Table 4. Successful classification rates and cross-validation rates when using multiple-finger datasets

	PC 1	PC 1 + 2	PC 1 + 2 + 3	PC 1+…+4	PC 1+…+5	PC 1+…+6
Index						
Linear discriminant analysis	58.6 **(58.6)**	58.6 (55.2)	55.2 (50.0)	55.2 (51.7)	58.6 (53.4)	**60.3** (53.4)
Naive Baysian classifier	75.9 (72.4)	93.1 (86.2)	96.6 **(93.1)**	98.3 (87.9)	96.6 (87.9)	96.6 (84.5)
Support vector machine	75.9 (75.9)	89.7 (84.5)	93.1 **(87.9)**	96.6 (79.3)	96.6 (82.8)	**100.0** (81.0)
Middle						
Linear discriminant analysis	63.8 (63.8)	56.9 (53.4)	79.3 (79.3)	81.0 **(81.0)**	81.0 (75.9)	**82.8** (77.6)
Naive Baysian classifier	86.2 (86.2)	86.2 (86.2)	91.4 **(89.7)**	91.4 (89.7)	91.4 (89.7)	**94.8** (89.7)
Support vector machine	86.2 (86.2)	86.2 (86.2)	91.4 (86.2)	96.6 (86.2)	**100.0** (86.2)	100.0 **(89.7)**
Ring						
Linear discriminant analysis	65.5 (63.8)	65.5 (62.1)	72.4 (67.2)	67.2 (63.8)	67.2 (63.8)	**74.1 (70.7)**
Naive Baysian classifier	79.3 (79.3)	79.3 (77.6)	87.9 (81.0)	87.9 (79.3)	91.4 (82.8)	**93.1 (86.2)**
Support vector machine	79.3 (79.3)	81.0 (77.6)	87.9 **(81.0)**	87.9 (79.3)	**96.6** (81.0)	96.6 (81.0)

A number in parenthesis indicates a LOOCV score derived from the cross validation test.
PC, principal components inputted in the cluster analysis (from 1 to 6).
A bold number indicates the largest value across different number of PCs.
A successful classification indicates that MD altered the tapping not only of the affected finger, but also of the unaffected fingers.

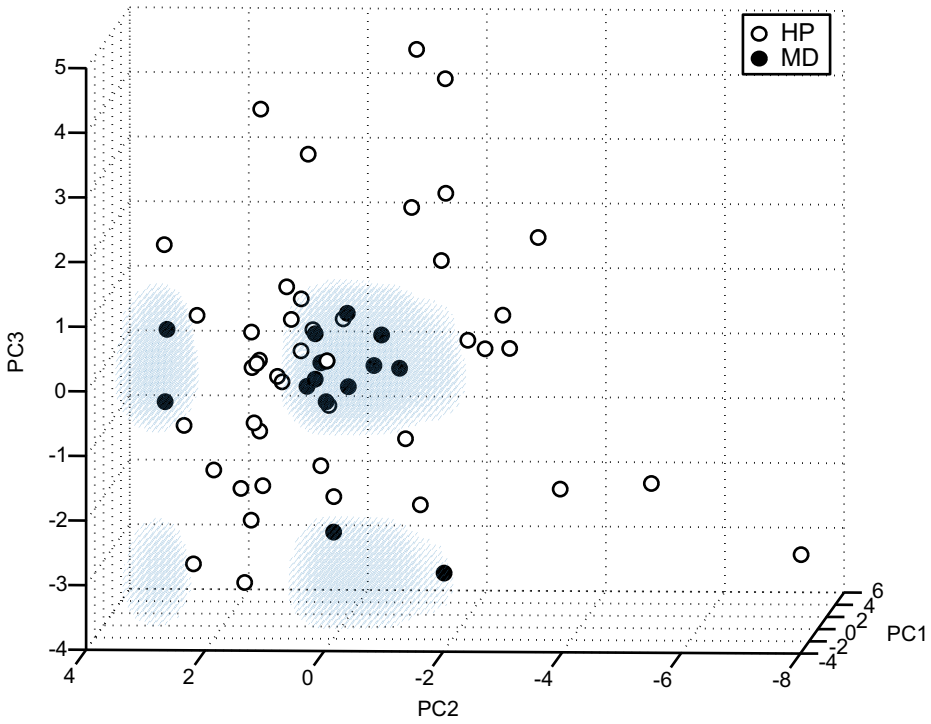

Fig. 4. Results from the naïve Bayesian classifier that predicts MD at the index finger in the principal component space. The blue-dotted area indicates movement features associated with MD in the index finger, which was predicted by the classifier. Each circle corresponds to data representing each trial of the pianists with the index finger unaffected (open circle) and affected (filled circle). HP, healthy pianists; MD, musician's dystonia. Overall, patients belonged to the blue-dotted area.

Table 5. Results of correlation analysis between post-injection duration of botulinum toxin and tapping performance

	Index		Middle		Ring		Little	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
IKI								
Mean	0.23	0.52	0.31	0.39	0.49	0.15	0.06	0.86
SD	0.06	0.87	0.58	0.08	−0.21	0.55	0.63	0.05
VEL								
Mean	−0.17	0.64	0.18	0.63	−0.18	0.62	0.24	0.51
SD	−0.26	0.46	0.07	0.84	−0.59	0.07	0.48	0.16
CD								
Mean	−0.24	0.50	0.35	0.33	0.53	0.12	0.59	0.17
SD	−0.29	0.42	0.46	0.18	−0.04	0.90	0.01	0.97

IKI, inter-keystroke interval; VEL, MIDI velocity; CD, finger-key contact duration. A correlation coefficient (*r*) was computed for 10 patients who have had an injection.
p: *p*-value.

patients with MD, a correlation coefficient was computed between the length of the time interval of the last injection and the present investigation (post-injection duration) and each of the movement variables derived from the tapping with each of the fingers for the 10 patients who had experienced an injection (Table 5). None of the variables demonstrated a significant correlation with the post-injection duration, confirming that a previous injection of botulinum toxin did not influence tapping behaviour.

Effect of duration of the MD on the individuated finger movements

A correlation coefficient was computed between the duration of the MD and each of the movement variables derived from the tapping with each of the fingers for the 10 patients who had experienced an injection (Table 6). A significant correlation was discernible only for the mean IKI of the middle and ring fingers, mean MIDI velocity of the ring finger, and SD of the MIDI velocity of the little finger. These findings indicate that the patients with longer duration of MD showed a slower and weaker tapping with less variable striking force.

DISCUSSION

The present study demonstrated a successful classification of individual fingers between with and without symptoms of MD according to the movement features that characterised constrained and speeded finger tapping. This confirms the impact of MD on individuated finger movements. In addition, the results of PCA and an iteration of the cluster analysis using different variables determined a distinct set of movement features that contributed to the identification of MD, which differed across fingers. A contrasting example is the difference between the index and ring fingers. Pianists with the index finger affected specifically showed a positive PC2 value, which consists mostly of the keystroke velocity of the tapping finger. This indicated stronger keystrokes during tapping by

Table 6. Results of correlation analysis between duration of the disorder and tapping performance

	Index		Middle		Ring		Little	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
IKI								
Mean	0.13	0.61	**0.53**	**0.03**	**0.58**	**0.02**	0.48	0.05
SD	−0.07	0.79	−0.21	0.41	−0.10	0.70	−0.32	0.21
VEL								
Mean	−0.32	0.21	−0.18	0.48	**−0.50**	**0.04**	0.11	067
SD	−0.27	0.30	−0.22	0.39	−0.17	0.53	**−0.54**	**0.03**
CD								
Mean	0.42	0.09	0.35	0.17	0.22	0.40	0.16	0.54
SD	0.22	0.40	−0.06	0.83	0.44	0.07	0.29	0.26

IKI, inter-keystroke interval; VEL, MIDI velocity; CD, finger-key contact duration.
A correlation coefficient (*r*) was computed for 10 patients who have had an injection.
p: *p*-value.
A bold number indicates $p < 0.05$.

these pianists than by unaffected individuals. In contrast, slowness and rhythmic inconsistency in tapping were predominant identifiers of MD at the ring finger, suggesting an impact of MD on the temporal features of the tapping behaviour. These findings highlight the finger-specific effects of MD on the independent control of finger movements, which may provide invaluable information not only for pathophysiological impacts of MD on finger dexterity, but also for accurate diagnosis of MD. While previous studies have described loss of independent control of finger movements in patients with stroke (Lang and Schieber, 2004; Raghavan et al., 2006), cerebellar dysfunction (Konczak et al., 1997; Brandauer et al., 2012), and Parkinson's disease (Elbert et al., 1998), to our best knowledge, the present study is the first to characterise behavioural abnormalities in the independent movement control of each of the fingers in patients with focal hand dystonia.

A determination as to whether the index finger is affected was not successful when using any datasets with respect to index finger tapping (Table 2). In contrast, a classification that also used the tapping data that was obtained while keeping a key depressed with the index finger successfully identified whether the index finger was affected or not (Table 4). These findings indicate that MD at the index finger does not necessarily impair tapping behaviour with this affected finger, but substantially lowers independent control across fingers. The results of the PCA further revealed that PC2 was positive only for pianists with the index finger affected (Fig. 3). This PC primarily represented the keystroke velocity of all the fingers, which indicates forceful strokes with both the affected and unaffected fingers in pianists having the index finger affected.

The current task requires the non-tapping digits to keep the keys depressed during repetitive keystrokes with a certain finger. However, patients with focal hand dystonia have a tendency to move multiple fingers together (Rosenkranz et al., 2005; Beck and Hallett, 2010). A lack of independence between the tapping and non-tapping fingers can cause the non-tapping fingers to lift off the keys while the tapping finger underwent lifting. To prevent an unwanted lifting motion in the non-tapping fingers, the muscles connected to this finger have to exert stronger flexion force. This force can not only stabilise the non-striking fingers, but can also accelerate the flexion motion in the tapping finger due to inter-digit dependence at both the neural and biomechanical levels (Schieber and Hibbard, 1993; Kilbreath and Gandevia, 1994; Zatsiorsky et al., 2000; Keen and Fuglevand, 2004; Schieber and Santello, 2004), which possibly leads to forceful keystrokes in pianists with MD. It is also likely that the forceful keystrokes are a strategy used to compensate for the movement inaccuracy caused by MD, because piano keystrokes with a stronger force facilitate rhythmic accuracy (Goebl and Palmer, 2008).

In contrast, a cluster analysis using the tapping data from the ring finger found that MD at the ring finger mostly elicited slowness and rhythmic inconsistency in the tapping movements (90% of classification and cross-validation rates). Even when using tapping data from all the fingers, the results of the PCA showed distinct values, particularly at PC1 and PC4, for pianists with the ring finger affected (Fig. 3), which still indicated abnormalities mostly in the IKI and in the finger-key contact duration. The loss of accuracy in the temporal control of finger movements in pianists with the ring finger affected was also observed when playing a simple tone sequence with five digits (Rosenkranz et al., 2009). They demonstrated prolonged finger-key contact duration during keystrokes with the ring finger.

Pianists who had the middle finger affected displayed the largest positive PC3 value compared to pianists belonging to the other groups (Fig. 3). The PC3 characterised both the large positive IKI and the negative SD of the keystroke velocity, particularly when the middle finger kept a key depressed, indicating keystrokes with slower rates and more consistent articulation. The slow-down can be interpreted as a compensation strategy for the destabilising effect of MD at the middle finger on the dynamic motion of the tapping finger. In light of a speed-accuracy trade-off (Fitts, 1954; Harris and Wolpert, 1998), it is likely that

the improved accuracy of articulation is a mere outcome of this compensatory slow-down.

A puzzling finding in the present study is the different impacts of MD on individuated finger movements across fingers (Fig. 3). To our best knowledge, no study has provided evidence demonstrating finger-specific abnormalities of motor function in the MD-affected finger, which provides novel information that sheds light on the pathophysiological mechanisms of MD. Possible reasons behind this specificity include inherent differences in the muscles and nerves connected to the individual fingers (Leijnse et al., 1993), differences in the neural firing pattern across the extrinsic finger muscles (Winges and Santello, 2004; Winges et al., 2006), and differences in the amount of surround inhibition of the intrinsic finger muscles depending on which finger is being used (Rosenkranz and Rothwell, 2003). A difference in muscular strength across the fingers can also be related to finger-specific symptoms because the resistance of the muscular force against spontaneous noise in the motor commands varies in relation to the muscular strength (Hamilton et al., 2004). Moreover, focal hand dystonia yields different abnormalities in neural processing at the somatosensory cortex across the fingers (Nelson et al., 2009), which may alter sensory-motor integration in a finger-specific fashion, not at rest (Weise et al., 2012), but during movement execution (Rosenkranz et al., 2005, 2009).

The diagnosis and symptom monitoring of MD is challenging for clinicians because of the subtle symptoms that emerge particularly during fast and complex finger movements, and are frequently hardly visible. Furthermore, atypical movements at unaffected fingers so as to compensate for the difficulty in extending the affected finger may render the identification of the dystonic finger more difficult. Accordingly, MD is frequently misdiagnosed (Rosset-Llobet et al., 2009). For instance, misidentification of the affected finger has a risk of injection of botulinum toxin into the muscles connecting to unaffected fingers. Pianists with MD exhibited larger rhythmic variability in keystrokes when playing a simple C-major scale on a keyboard as compared to healthy pianists. We therefore used this scale analysis as a reliable diagnostic tool for MD (Jabusch et al., 2004). The present method extended our previous findings by providing a promising means to identify an affected finger by means of a behavioural task and cluster analysis. The results of cross-validation suggest that even with a limited sample size, the NBC can successfully identify whether a certain finger is affected, with an accuracy of approximately 90%, which was superior over the LDA and SVM. An increased sample size and the inclusion of patients with MD at multiple fingers or with other neuromuscular disorders will be needed in future studies, in order to enable more reliable and successful diagnosis of MD. Further development of an online patient database and user-friendly software may also be needed. These techniques also have the potential to assess the loss of independence of finger movements elicited by other neurological disorders.

The present study may include several limitations to be elaborated upon in future studies. First, the total period of the experience of piano playing can be a confounding factor particularly when identifying MD at the ring finger, which should be controlled. However, we do not believe that this plays an important role, since finger dexterity and tapping speed of adult pianists, but also of non-musicians, remains amazingly stable for many decades when adulthood is reached and regular practice is given. Second, it is possible that the current testing procedure assessed not only the characteristics of the dystonic symptoms, but also results from biomechanical constraints, which are discussed to constitute a risk factor for developing focal hand dystonia (Leijnse et al., 1993). These issues could be resolved by collecting data only from patients with no history of botulinum-toxin injection and adding biomechanical measurements as proposed previously (Leijnse, 1998).

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