Impaired sensorimotor integration in focal hand dystonia patients in the absence of symptoms

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ABSTRACT

Background Functional imaging studies of people with focal hand dystonia (FHD) have indicated abnormal activity in sensorimotor brain regions. Few studies however, have examined FHD during movements that do not provoke symptoms of the disorder. It is possible, therefore, that any differences between FHD and controls are confounded by activity due to the occurrence of symptoms. Thus, in order to characterise impairments in patients with FHD during movements that do not induce dystonic symptoms, we investigated the neural correlates of externally paced finger tapping movements.

Methods Functional MRI (fMRI) was used to compare patients with FHD to controls with respect to activation in networks modulated by task complexity and hand used to perform simple and complex tapping movements.

Results In the 'complexity network,' patients with FHD showed significantly less activity relative to controls in posterior parietal cortex, medial supplementary motor area (SMA), anterior putamen and cerebellum. In the 'hand network,' patients with FHD showed less activation than controls in primary motor (M1) and somatosensory (S1) cortices, SMA and cerebellum. Conjunction analysis revealed that patients with FHD demonstrated reduced activation in the majority of combined network regions (M1, S1 and cerebellum).

Conclusion Dysfunction in FHD is widespread in both complexity and hand networks, and impairments are demonstrated even when performing tasks that do not evoke dystonic symptoms. These results suggest that such impairments are inherent to, rather than symptomatic of, the disorder.

INTRODUCTION

Focal hand dystonia (FHD) is a movement disorder characterised by excessive co-contraction of agonist and antagonist muscles during specific tasks, such as writing or playing an instrument.[1 2] The underlying causes of the disorder are still unclear, although impairments in sensorimotor regions of the brain are evident in patients with FHD.[3–8] However, conflicting findings exist in the literature. Both abnormally increased and decreased functional activation have been reported in sensorimotor regions. For example, studies that have implemented symptom-inducing tasks (eg, writing and playing guitar) have demonstrated reduced activation in the contralateral primary motor (M1), supplementary motor area (SMA)[3] and premotor areas[7] of patients with FHD compared with healthy control participants. In contrast, other studies have reported abnormally increased activation in the above regions,[5] as well as in the cerebellum and thalamus.[6] Another study reported less activation in SMA, but increased activation in M1 and primary somatosensory cortex (S1), in their FHD group compared with controls.[4] These contradictory results may be accounted for by the variability in tasks and degree of symptoms that were induced in these studies. For example, factors such as duration of tapping or writing can influence the severity of dystonia.[4] Moreover, sustained excitability in the basal ganglia has been found after the cessation of movement during bimanual finger tapping tasks that induced dystonia, and the resultant delayed return to baseline may mask dysfunction in these regions in some studies.[9]

Less is known about changes in sensorimotor function during non-symptomatic movement in FHD. Investigating the effects of FHD using tasks that do not induce dystonic symptoms may contribute to understanding the neurological abnormalities of the disorder, as it ensures that variability in performance is controlled for and avoids discomfort for patients. A previous functional MRI (fMRI) study used such a task, where patients with FHD held their right wrist horizontally and either bent their wrist downward (relaxation) or upward (contraction).[10] Compared with healthy controls, decreased activity was found during the tasks in M1, S1 and SMA in patients with FHD. However, such tasks do not elucidate dysfunction that may arise during finer movement of the fingers. These finer finger movements have been addressed using PET, which demonstrated significantly decreased activation for patients with FHD compared with control participants during writing tasks that induced dystonic movements, but not a finger-tapping task which did not induce dystonia.[3] However, abnormalities in EEG have been found during similar finger tapping tasks that did not induce dystonic symptoms.[11] In the present study, we used fMRI to investigate these types of finer movement tasks to ensure that movement performance was similar in patients and controls, and included simple and complex movements in order to examine possible complexity effects.

Previous PET and fMRI research has demonstrated that the extent of brain motor activation is reflected in the complexity of the movement. For example, simple tasks (eg, tapping one finger against the thumb) require activity of the contralateral M1, S1 and ipsilateral cerebellum.[12–14] In contrast, complex unimanual movements (eg, sequential tapping of the fingers) additionally

involve the ipsilateral M1, S1, the SMA, premotor area, bilateral posterior parietal area and the precuneus.[12 14–16] These regions further interact with the basal ganglia. Specifically, selection of movement is associated with bilateral caudate nucleus activation, whereas the bilateral anterior putamen is involved in the preparation of movements.[17] The contralateral posterior putamen is associated with movement execution.[17] The cerebellum is also crucial for the selection, preparation and execution of movement, and basal ganglia structures such as the putamen may influence the cerebellum, as they are both involved in timing and the learning of new skills.[18] Patients with FHD are thought to have deficits in these regions,[19 20] and so in the current study, we examined regions with activity reflecting the complexity of movement (complex compared with simple movements). In addition, we investigated regions with differential activation depending on the hand used to perform the movement (left compared with right hand). The dissociation between these complexity and hand networks has been studied previously, revealing that complexity affected activation in a distributed cortical network of SMA, lateral premotor and posterior parietal cortices, independent of the performing hand.[21] The network of regions with activity that was dependent on the hand performing the movement regardless of complexity of movement incorporated M1 and S1 regions as well as the thalamus and putamen.[21]

We predicted that when performing tasks that do not induce symptoms of dystonia, patients would nevertheless show abnormalities in both complexity and hand networks. In this way, we aimed to elucidate mechanisms of the disorder that relate to hand specificity, as well as those related to the formulation and planning of complex movements.

METHOD

Participants

Eleven patients with FHD participated (five women, mean age 49.1, SD 12.83 years, mean duration of disorder 13.3, SD 8.74 years). Their clinical characteristics are summarised in table 1. Nine patients were right-handed, one patient was left-handed, and one was mixed-handed, according to the laterality score from the Edinburgh Handedness Inventory.[22] Patients 2 and 6 were undergoing botulinum toxin treatment and had their last injection 4 months prior to this study (when the clinical effects had worn off), as treatment has been shown to reverse abnormalities in cortical representation and white matter within the period of clinical effectiveness.[23 24] Patient 5 tried botulinum toxin treatment unsuccessfully 3 years prior to this study. All other patients had never had botulinum toxin treatment.

Eleven healthy participants (five women, mean age 48.8, SD 12.38 years) matched the patients for age, gender, handedness and musical instrument (for musician's cramp patients). The study was approved by the Northern X Regional Ethics Committee.

Experimental design

Simple and complex unimanual and bimanual tapping movements were used, resulting in six movement conditions (20 s periods) alternated with rest periods (10 s). Simple tapping consisted of repeatedly tapping the thumb to the index finger. The complex movement required participants to tap their thumb to their second, third, fourth and fifth fingers in sequence (2-3-4-5-5-4-3-2-2 and so on, known as the Luria apposition task). The experimental design was almost identical to that of a previously reported EEG experiment[11] with the exception that movements were audio-paced through headphones using a computer-generated metronome. The tones were also played during rest. The pace was set externally to ensure that the tapping frequency remained consistent between participants. The frequency used (1 Hz) was based on previous research in order to maximise signal recordings and set a comfortable pace for patient populations to perform.[25]

Conditions were randomised, and each presented twice within a block. The participants completed four blocks (approximately 7 min duration each). Participants fixated on a cross which was present in the middle of the screen at all times. Prior to the scanning session, participants undertook a practice trial which was observed and videotaped to ensure task compliance. During the time in the scanner, the participant's movements were monitored by an experimenter, and practice sessions were video-recorded. The experimenter ensured that the movements were in the appropriate sequence for the condition (complex/simple) and were paced with the auditory metronome at 1 Hz (although without polymyography, we acknowledge that we cannot be absolutely certain that there were no subclinical symptoms of dystonia, particularly when it has been shown that there is abnormal motor synchronisation in the co-contraction of dystonia[26]).

Data acquisition

Echo-planar images (EPIs) were collected on a 1.5 T scanner (Siemens Magnetom Avanto 1.5 T, Erlangen, Germany) using

Table 1 Clinical characteristics of focal dystonia patients

Patient no	Age (years)	Duration (years)	Gender	Handedness	Side affected	Severity (%)*	Type	Botulinum toxin (Dysport (R)) treatment (months, m) (target muscle, dosage, mu)
1	56	18	F	Right	Right	74	WC	–
2	58	15	M	Right	Right	69	WC	4 m prior: FPL: 10 mu; FPD1–2: 40 mu
3	27	1	F	Right	Right	79	WC	–
4	63	25	F	Right	Right	77	WC	–
5	49	29	M	Mixed	Both	L=74 R=60	WC	–
6	58	19	F	Left	Left	85	WC	4 m prior: FPL and FPD1 both 15 mu
7	54	5	M	Right	Right	42	WC+other	–
8	56	8	M	Right	Right	53	WC+MC	–
9	40	10	M	Right	Right	77	MC	–
10	25	6	F	Right	Right	74	MC+T	–
11	54	10	M	Right	Right	81	MC+T	–

*Severity Scale[2].
FDP1-2, flexor digitorum profundus (index and middle finger combined); FPL, flexor pollicis longus; L, left hand; MC, musician's cramp; other, incoordination in other tasks involving fine manipulation; R, right hand; T, typing; WC, writer's cramp.

the standard head coil. Imaging parameters were: repetition time (TR)=2570 ms, echo time (TE)=50 ms, flip angle=90°, field of view (FOV)=192×192 mm^2, slice thickness=3 mm, imaging matrix=64×64, voxel size=3 mm×3 mm×3 mm and 30 parallel axial slices. The first two images from each block were discarded to allow for T1 stabilisation effects. Before functional scans were recorded, T1-weighted anatomical scans (Magnetisation Prepared Rapid Gradient Echo (MPRAGE)) were acquired from each participant with the following parameters: 176 axial slices, slice thickness 1 mm, FOV=256×256 mm^2, TR=11 ms, TE=4.94 ms.

Imaging data were preprocessed and analysed using SPM5 (Wellcome Department of Cognitive Neurology, London; http://www.fil.ion.ucl.ac.uk). Functional EPIs from each participant were realigned to the first volume in order to correct for between-scans movement. Each participant's T1 was aligned to the functional scans and spatially normalised into a standard space using the Montreal Neurological Institute (MNI) template brain. The normalised EPIs were then smoothed with an 8 mm full-width-at-half-maximum Gaussian spatial filter to account for individual variability.

Statistical analysis

At the first (single subject) level, boxcar regressors were fitted to the occurrence of each of the six experimental conditions. Regressors were then convolved with a canonical haemodynamic response function and a high-pass filter of 256 s applied. Regressors were entered into a general linear model to identify the haemodynamic response associated with each condition compared with rest. At the second (group) level, beta values for each of the six conditions were entered into a mixed within-between-subject factorial design. Regressors were separately modelled for the between-subjects factor of group, within-subjects factor of condition and the mixed-factors of group-by-condition (using a subject-specific constant to remove overall intrasubject variability within groups). Main effects and interactions of the factors group, effector and complexity were then identified using weighted contrasts.

There were two subsequent stages of analysis. First, a voxelwise analysis of the factors complexity (one-tailed t test: complex>simple) and hand (F test capturing any regions that had a differential response during left-hand and right-hand movements) pooled across all participants was performed in order to characterise the networks differentially activated by these two factors. The bimanual condition was not included in this part of the analysis, as we were interested in isolating regions which show altered activity with respect to the laterality of output. Including the bimanual condition did not reveal different regions involved in the hand network. A conjunction analysis was performed to identify regions responsive to both factors (threshold of $p<0.05$, controlled for familywise error). This allowed us to assess the influence of FHD within the differentiated regions biased towards planning complex movements or those modulated by the hand used, and to examine differences within regions showing no bias. Comparisons between patients with FHD and control groups within the above regions were analysed both at a voxelwise level within

Table 2 Regions showing the main effect of complexity of movement (voxelwise analysis)

Cluster Equiv k	Voxel p(family-wise error corrected, FWE-corr)	Voxel Equiv Z	Montreal Neurological Institute coordinates of peak voxel			Main Effect (ME) group difference (at peak voxel) p(corr)	Region	
			x	y	z			
Cortical areas								
1329	<0.001	Inf	−27	−12	57		Left	Middle frontal gyrus (BA6)
	<0.001	Inf	30	−12	57		Right	Precentral gyrus (BA6)
	<0.001	Inf	3	−6	57		Right	Medial frontal gyrus (BA6)
966	<0.001	Inf	60	−21	42		Right	Precentral gyrus (BA4)
155	<0.001	7.84	60	6	21		Right	Inferior frontal gyrus (BA44)
	<0.001	7.33	60	6	30		Right	Inferior frontal gyrus (BA9)
7	0.007	5.12	−36	39	27		Left	Middle frontal gyrus (BA10)
1395	<0.001	Inf	**−45**	**−42**	**51**	**0.009**	**Left**	**Inferior parietal lobule (BA40)**
	<0.001	Inf	−60	−21	33		Left	Postcentral gyrus (BA2)
	<0.001	Inf	**−24**	**−63**	**63**	**<0.001**	**Left**	**Superior parietal lobule (BA7)**
	<0.001	Inf	**24**	**−66**	**66**	**<0.001**	**Right**	**Superior parietal lobule (BA7)**
	<0.001	Inf	**48**	**−39**	**54**	**0.009**	**Right**	**Inferior parietal lobule (BA40)**
Subcortical areas								
51	0.001	5.58	**−24**	**3**	**12**	**0.002**	**Left**	**Putamen**
	0.004	5.24	−15	−9	18		Left	
	0.01	5.04	−21	−3	21		Left	
15	0.001	5.57	6	−6	12		Right	Thalamus (anterior nucleus)
10	0.007	5.11	18	0	3		Right	Globus pallidus
5	0.008	5.09	12	−9	0		Right	Thalamus
Cerebellum								
154	<0.001	Inf	27	−60	−24		Right	Posterior lobe
	<0.001	6.49	**3**	**−66**	**−15**	**<0.001**	**Right**	**Anterior lobe**
	<0.001	5.63	−3	−51	−18		Left	Anterior lobe
30	<0.001	7.61	**−24**	**−66**	**−24**	**<0.001**	**Left**	Posterior lobe

ME group difference: reported only for peak voxel of regions, with p(corr) only displayed if a significant group effect was reached. These regions of significant difference at the peak voxel are shown in bold.

Table 3 Regions showing main effect of hand used (voxelwise analysis)

Cluster Equiv k	Voxel p(FWE-corr)	Voxel equiv Z	Montreal Neurological Institute coordinates of peak voxel x	y	z	ME group difference (at peak voxel) p(corr)	Region	
Cortical areas								
697	<0.001	Inf	**36**	**−27**	**51**	**<0.001**	**Right**	**Precentral gyrus (BA4)**
	<0.001	Inf	**36**	**−33**	**66**	**<0.001**	**Right**	**Precentral gyrus (BA4)**
40	<0.001	6.34	**−6**	**−18**	**51**	**<0.001**	**Left**	**Medial frontal gyrus (BA6)**
	<0.001	5.93	**−9**	**−30**	**51**	**<0.002**	**Left**	**Paracentral lobule (BA6)**
382	<0.001	Inf	−39	−27	51		Left	Postcentral gyrus (BA3)
	<0.001	Inf	−33	−33	72		Left	Postcentral gyrus (BA3)
	<0.001	Inf	**−33**	**−36**	**60**	**<0.002**	**Left**	**Postcentral gyrus (BA3)**
	<0.001	Inf	45	−21	63		Right	Precentral gyrus (BA6)
Subcortical areas								
175	<0.001	7.46	42	−18	18		Right	Insula
34	<0.001	7.15	18	−21	3		Right	Thalamus (VPL nucleus)
34	<0.001	6.78	−15	−21	6		Left	Thalamus (VPM nucleus)
	0.011	5.03	−27	−24	9		Left	
59	<0.001	6.61	30	−12	0		Right	Putamen
48	<0.001	6.43	−33	−12	3		Left	Extranuclear/putamen
20	<0.001	5.92	**−45**	**−24**	**18**	**<0.003**	**Left**	**Insula**
Cerebellum								
222	<0.001	Inf	**−15**	**−54**	**−15**	**<0.002**	**Left**	**Anterior lobe**
	<0.001	Inf	−12	−57	−24		Left	Anterior lobe
	<0.001	7.72	**−27**	**−42**	**−24**	**<0.001**	**Left**	**Anterior lobe**
119	<0.001	Inf	**18**	**−48**	**−15**	**<0.03**	**Right**	**Anterior lobe**
	<0.001	Inf	12	−57	−24		Right	Anterior lobe
	<0.001	Inf	**9**	**−63**	**−12**	**<0.002**	**Right**	**Anterior lobe**

ME group difference: reported only for peak voxel of regions, with p(corr) only displayed if a significant group effect was reached. These regions of significant difference at the peak voxel are shown in bold.

each of these networks (threshold $p<0.05$ cluster-level) and at peak voxels within regions in these networks responsive to complexity, hand and the regions showing no bias ($p<0.05$, Bonferroni corrected). Anatomical T1 coordinates of the MNI brain were transformed to Talairach coordinates in order to identify regions of activation (http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach).[27] These Talairach coordinates were used to confirm anatomical regions of activation using Talairach Daemon.[28]

RESULTS

All patients and control participants were observed to have performed the tasks accurately. Importantly, no dystonic

Table 4 Regions unbiased towards complexity and hand networks (ie, complexity+hand conjunction)

Cluster Equiv k	Voxel p(FWE-corr)	Voxel Equiv Z	Montreal Neurological Institute coordinates of peak voxel x	y	z	ME group difference (at peak voxel) p(corr)	Region	
Cortical areas								
588	<0.001	Inf	**45**	**−36**	**60**	**0.03**	**Right**	**Postcentral gyrus (BA40)**
	<0.001	7.51	33	−18	60		Right	Precentral gyrus (BA6)
	<0.001	7.38	54	−27	48		Right	Postcentral gyrus (BA2)
529	<0.001	Inf	**−42**	**−39**	**57**	**0.002**	**Left**	**Inferior parietal lobule (BA40)**
	<0.001	Inf	**−42**	**−27**	**60**	**<0.001**	**Left**	**Postcentral gyrus (BA3)**
	<0.001	Inf	−27	−21	66		Left	Precentral gyrus (BA6)
14	<0.001	6.03	**−6**	**−15**	**54**	**<0.001**	**Left**	**Medial frontal gyrus (BA6)**
12	<0.001	5.83	**−51**	**−21**	**15**	**0.02**	**Left**	**Insula**
30	<0.001	5.76	**6**	**−9**	**51**	**<0.001**	**Right**	**Cingulate gyrus (BA24)**
	0.015	4.97	**6**	**−21**	**60**	**<0.001**	**Right**	**Medial frontal gyrus (BA6)**
Subcortical areas								
1	0.032	4.79	−15	−18	9		Left	Thalamus (VPL nucleus)
Cerebellum								
225	<0.001	Inf	**−27**	**−51**	**−27**	**<0.001**	**Left**	**Anterior lobe**
	<0.001	6.58	**−6**	**−57**	**−15**	**<0.001**	**Left**	**Anterior lobe**
236	<0.001	7.74	**24**	**−48**	**−24**	**<0.002**	**Right**	**Anterior lobe**
	<0.001	6.83	**6**	**−63**	**−18**	**<0.002**	**Right**	**Posterior lobe**

ME group difference: reported only for peak voxel of regions, with p(corr) only displayed if a significant group effect was reached. These regions of significant difference at the peak voxel are shown in bold.

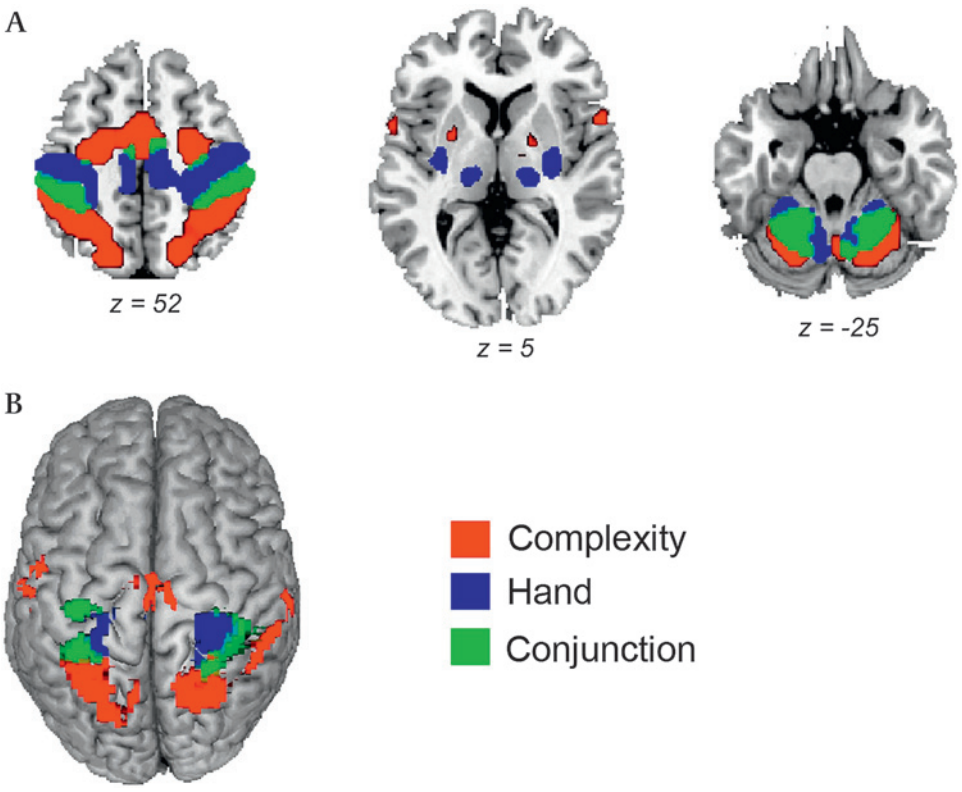

Figure 1 (A) Networks modulated by complexity, hand used and a conjunction of the two displayed on average Montreal Neurological Institute T1 at z=52, z=5 and z=−25. (B) Using functional masks for the complexity, hand and conjunction networks. Areas showing the main effect of group are displayed.

postures were observed or reported during any task for patients with FHD. Tables 2–4 display regions identified in complexity, hand and conjunction networks, with group differences highlighted in bold.

Networks for complexity and hand

Figure 1A displays the networks for complexity, hand and the conjunction of the two factors. Voxelwise analysis revealed a network showing a main effect of complexity in the SMA, bilateral lateral premotor areas, posterior parietal regions, left anterior putamen, right anterior globus pallidus, right thalamus and bilateral cerebellum (table 2). Areas differentially activated by either hand were bilateral M1, S1, SMA, bilateral posterior putamen, bilateral thalamus (ventroposterior nuclei), insula and bilateral cerebellum (table 3). Regions involved in both networks included parts of bilateral M1, S1, premotor, posterior parietal regions, right cingulate, left thalamus (ventroposterior nucleus) and bilateral cerebellum (table 4).

Patients with FHD compared with controls

Group analysis within networks using masks of functional regions of interest (ROIs) revealed a significant main effect of group ($p<0.05$, Bonferroni-corrected) at the peak voxel of activation in regions within the complexity, hand and conjunction network as shown in tables 2–4 and figure 1B. The main effect of group captures all cortical activity relating to simple and complex, uni- and bimanual responses. Common across all these conditions, patients with FHD demonstrated less activation than the controls in these networks. There were no significant interactions between group and any other factor at the voxel level. In the peak voxel of regions analysis, for areas modulated by complexity, regions demonstrating a group effect included bilateral superior parietal cortex (Brodmann Area (BA)7, BA40), left anterior putamen and bilateral cerebellum. Within the hand network, M1 (BA4) and S1 (BA3), SMA (BA6), left insula and bilateral cerebellum were the regions that had differential activation between patient and control groups.

DISCUSSION

In the current study, we demonstrate that when performing non-symptom-inducing tasks involving sensorimotor integration, patients with FHD show less activation in hand and complexity networks relative to healthy controls. As has been suggested previously, this reduced activation is likely to represent a broad and complex pattern of impaired integration of sensory and motor information within the basal ganglia-thalamo-cortical loop.[29 30] Recent evidence suggests that alterations in proprioceptive input pathways of patients are involved in these sensorimotor impairments, as the effect of motor vibration on cortical activation is reduced in patients with FHD compared with controls.[31] The current findings support a previous fMRI study that reported reduced activation in similar regions (M1, S1 and SMA) when patients with FHD performed a task that did not induce dystonic symptoms.[10] Deficient activation may indicate a duality of behaviour of this region in patients; underactivation during movements without symptoms of the disorder, and overactivation during the presentation of dystonic symptoms.[7]

Patients with FHD showed abnormal activation relative to controls in the majority of regions that comprise both hand and complexity networks. Cortical regions involved in the hand network included M1 and S1 in the putative hand region, as expected.[21] Additionally, activation was also found in the cingulate motor area, which has been reported by a previous study.[32] In patients with FHD, less activation was found in these areas compared with controls, demonstrating dysfunction in this network even when movement performance was similar to controls. In agreement with previous research, cortical areas recruited during more complex movements were found to include SMA and premotor regions, the superior parietal cortex,[12–14 21] as well as putamen, thalamus, globus pallidus and

cerebellum. Within this network, patients with FHD demonstrated less activation bilaterally in superior parietal lobes, extending to inferior parietal lobe. Because SMA and parts of the premotor region were not impaired in our patients with FHD, we suggest that FHD is characterised by only partial deficits in the complexity network, at least when performing movements that do not induce symptoms. The left putamen and bilateral cerebellum also showed less activation for patients with FHD. This finding is consistent with research suggesting that FHD is a disorder involving the basal ganglia, as well as the cerebellum and cortical regions.[19] The conjunction analysis investigated a network comprising regions which demonstrated not only an effect of task complexity but also differential activation, depending on which hand performed the movement. The majority of these cortical areas (M1, S1, SMA, insula, cerebellar regions) were found to be impaired in patients with FHD.

Tasks which induce the symptoms of FHD tend to be of a complex nature, and this may explain the differences in activation that were found between patients with FHD and controls within the complexity network.[7] Interestingly, in contrast to the complexity network, patients with FHD did not show differential activation relative to controls in the more posterior regions of the basal ganglia in the hand network. Subcortical regions affected by dystonia may be distinctly those that a previous study associates with the planning and preparation of movements.[17]

The group differences in the conjunction network are of interest because previous research has found that manual asymmetries during tapping tasks are less pronounced for more complex tasks. Where activation is found predominantly in one hemisphere when one hand performs a simple task, performing unimanual complex tasks utilises widely distributed networks involving both hemispheres.[33] It is not surprising, therefore, that patients with FHD in the current study demonstrated differential activity relative to controls in many cortical areas in this network, as the effect of complexity may differ between the affected and non-affected hand. We also found considerable impairment in the cerebellar regions, consistent with a previous FHD study, although that study used a writing task.[6] The cerebellum is thought to be involved in processes that involve timing.[34] This may explain the differences that patients with FHD demonstrate in temporal discrimination tasks of both auditory and tactile stimuli.[35 36]

In the current study, the majority of patients have right-sided symptoms. Therefore, it was possible that an investigation of affected (majority right) compared with unaffected (left) sides would demonstrate asymmetrical effects. However, although the patients' symptoms were mainly unilateral, abnormal activation in these patients was found bilaterally, a finding which has been reported in previous studies on FHD.[37–39] This pattern remains when the left-side-affected patient and their control were removed from the analyses. This suggests that patients with primarily unilateral symptoms have widely affected regions, and this may provide an explanation for cases where writer's cramp patients develop FHD symptoms in their other hand.[40] Furthermore, in another additional analysis, there was a lack of significant difference between the affected side and asymptomatic side (excluding the mixed-handed patient), which is consistent with previous findings of bilateral cortical abnormalities manifesting as unilateral symptoms.[4 5]

In conclusion, patients with FHD demonstrated widespread functional impairments compared with controls during simple and complex finger movements. Importantly, these impairments were found during movements that did not evoke dystonic symptoms, which suggests that there are inherent bilateral abnormalities in these patients.

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