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Cortical pattern of complex but not simple movements is affected in writer's cramp: A parametric event-related fMRI study

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HIGHLIGHTS

- The sensorimotor network in writer's cramp shows dualistic behavior during simple and complex movements.
- The aberrant cortical pattern during complex movements was independent of the character of graphic expression or the visual feedback.
- Parametric fMRI design using kinematic parameters of writing is necessary for compensation of the inter-individual variability of hand movements.

ABSTRACT

Objective: Patients with writer's cramp (WC) were studied for differences in cortical activation during movements likely to induce WC (complex movements) and movements which rarely lead to dystonia (simple movements).
Methods: Eleven WC patients (10 F, 1 M, mean age 41.5 ± (SD)7.2 years) and eleven age matched controls were examined for Blood oxygenation-level dependent (BOLD) 1.5 T fMRI. The complex task consisted of writing a single letter or random drawing using an especially adapted joystick with the line of trajectory visualized or hidden. The simple task consisted of self-initiated fingers flexion/extension using the affected hand.
Results: Unlike the controls, WC patients performing complex movements exhibited a lower BOLD signal in the primary sensorimotor cortex and in the posterior parietal cortex bilaterally. A hypoactivation was also observed in the right secondary somatosensory area, in the right anterior insula and in the left premotor cortex ($p < 0.05$ corrected). No significant inter-group differences were found for simple movements.
Conclusions: Although WC patients' complex movements during fMRI were never associated with dystonic cramp, they exhibited an abnormally low cortical activity. This phenomenon was not observed in simple movements and was unrelated to the character of handwriting or to visual feedback.
Significance: Our results support the dualistic behavior in the sensorimotor system in WC.

1. Introduction

Writer's cramp (WC) is the most common type of task-specific focal dystonia. Manifested by involuntary muscle contraction of agonists and antagonists of the forearm and hand, it is usually associated with writing as it is the most frequent complex movement (Marsden and Sheehy, 1990). Predisposed individuals are likely to develop WC with a combination of risk factors and excessive writing effort (Roze et al., 2009). However, the pathophysiological mechanisms of WC remain unclear. WC is probably caused by the involvement of the motor as well as the sensory system and their aberrant mutual integration (Abbruzzese et al., 2001; Vidailhet et al., 2009).

WC arises from a selective disorder of motor programming for writing as a result of impaired motor learning. The execution of all other movements is little affected or not at all. This supports the theory of the motor system's dualistic behavior in task-specific dystonia in which the execution of a specific dystonia-inducing movement is associated with a different cortical pattern than

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Table 1
Summary of previous functional imaging studies on task-specific focal dystonia.

Study	N	Type	Imaging	Task	Results	Cramp
Ceballos-Baumann et al. (1995)	6	ID#	PET (ED)	Joystick movements	↑ PMC, SMA, DLPFC, ant. cingulate ↓ caudal SMA, posterior cingulate, mesial parietal c.	Y1
Ceballos-Baumann et al. (1997)	6	WC	PET (ED)	Writing	↑ S1, PMC, mesial parietal c., vermis ↓ M1, caud. SMA, mesial parietal c., ant. cingulate, mesial prefrontal c., thalamus	Y
Odergren et al. 1998	4	WC	PET (PA)	Writing	↑ SM1*, cerebellum ↓ supramarginal g., angular g.	Y
				Drawing	no changes	N
Ibáñez et al. 1999	7	WC	PET (ED)	Writing	↓ PMC	Y
				Wrist + finger flexion	↓ SM1	N
				Tapping	no changes	N
Pujol et al. (2000)	5	MC	fMRI (ED)	Music instrument playing	↑ SM1 ↓ PMC	Y
Preibisch et al. (2001)	12	WC	fMRI (ED)	Writing	↑ Cerebellum ↓ sup.+middle temporal g., lingual g.	Y?
Oga et al. 2002	8	WC	fMRI (ERD)	Right wrist relaxation	↓ SM1, SMA	N
				Right wrist contraction	↓ SM1, SMA	N
Butterworth et al. (2003)	9	WC	fMRI (ED)	2nd Digit vibrotact. stimul.	↓ S2, PPC	N
				5nd Digit vibrotact. stimul.	↓ S2	N
Lerner et al. (2004)	10	WC	PET (PA)	Writing	↑ SM1 ↓ SMA	Y
				Tapping	No changes	Y7
Hu et al. (2006)	10	WC	fMRI (ED)	Writing with pen	↑ Cerebellum ↓ thalamus	Y
				Writing with finger	No changes	Y
				Mental writing	No changes	Y
Peller et al. (2006)	17	WC	fMRI (ED)	2nd Digit tactile stimul.	↑ BG, insula, parietal c., Posterior visual c., frontal operculum	N
Islam et al. (2009)	17	WC	fMRI (ED)	Tapping	↓ SM1, SMA, S2	N
				2nd Digit flexion	↓ S1	N
				Median nerve stimul.	No changes	N
Wu et al. (2010)	11	WC, MC	fMRI (ED)	Complex tapping	↓ PPC, SMA, cerebellum	N
				Simple tapping	↓ SM1, SMA, cerebellum	N
Havránková et al. (this study)	*11*	*WC*	*fMRI* (ERD, PA)	Complex (writing/drawing)	↓ *SM1, S1, S2, SMA, PMC, PPC, insula*	*N*
				Simple (hand grips)	*No changes*	*N*

N – number of patients; type of dystonia: ID – idiopathic dystonia, WC – writer's cramp, MC – musician cramp; functional imaging method: fMRI – functional magnetic resonance imaging, PET – positron emission tomography; study design: (ED – epoch design, ERD – event related design, PA – parametric analysis); type of study task; results – (↑) higher or (↓) lower activity in patients relative to controls (PMC– premotor cortex, SMA – supplementary motor area, DLPFC – dorsolateral prefrontal cortex, SM1 – primary sensorimotor cortex, S1 – primary sensory cortex, M1 – primary motor cortex, S2 – secondary somatosensory cortex, PPC – posterior parietal cortex); cramp – dystonic cramp during the task: Y – yes, N – no, Y1,7 – reported number of patients with dystonic cramp during the task, Y? – presence of dystonic cramp during the task not reported; #one patient with writer's cramp only; *positive correlation with writing duration.

other movements. The motor pattern of cortical activation in WC has repeatedly been studied with methods of functional imaging – functional magnetic resonance (fMRI) and positron emission tomography (PET) (Table 1). The execution of movements unaffected by WC usually revealed hypoactivation in the primary sensorimotor cortex (SM1), the supplementary motor area (SMA) (Butterworth et al., 2003; Islam et al., 2009; Oga et al., 2002; Wu et al., 2009) and the posterior parietal cortex (Butterworth et al., 2003; Wu et al., 2010). Conversely, these areas were found to be hyperactivated during signs of WC (Hu et al., 2006; Lerner et al., 2004; Odergren et al., 1998). Other studies brought rather different results (Ceballos-Baumann et al., 1997; Ibanez et al., 1999; Preibisch et al., 2001) perhaps due to a different task design or technique of functional imaging. Some authors used parametric designs to describe quantitative relationships between the intensity of dysfunctional motor areas and the extent of the movement performed, e.g., the number of words written (Ibanez et al., 1999; Odergren et al., 1998) or the severity of dystonia (Lerner et al., 2004). Hence, fMRI parametric analysis with use of further quantitative variables may improve our understanding of the pathophysiological mechanisms of focal dystonia.

We employed the parametric approach as well. Using two motor tasks with complex and simple movements performed by patients and healthy controls, we searched for the motor system dualistic behavior in WC. It was necessary to make sure that the selected complex movement should be short enough to not induce WC during the experiment. Rather than obtaining an fMRI correlate of focal hand dystonia, we expected to detect an inter-group difference in the cortical pattern during the execution of complex but not in simple movements. The latter consisted of the opening and closing of a hand, for the former we chose writing with a specially adapted joystick held as a pen. In contrast to most of the previous fMRI studies, we used an event-related design which offers the advantage of correct assessment of the start and duration of each single movement.

However other factors may contribute to the fMRI motor pattern, such as writing content or the presence of sensory feedback. It has been reported that drawing lines does not necessarily lead to dystonic cramp (Odergren et al., 1998) similarly, there are only a few reports of focal hand dystonia in painters. Moreover, the process of writing depends on somatosensory proprioception and visual control. While somatosensory perception is known to be altered in WC patients (Bara-Jimenez et al., 2000; Nelson et al., 2009; Sanger et al., 2001) visual feedback is probably not crucial for the clinical manifestation of WC (Chakarov et al., 2006; Prodoehl et al., 2006). Conversely, when WC patients see someone's hand writing it leads to significant changes in motor cortex excitability (Fiorio et al., 2010) suggesting that visual input may play a certain role in WC.

Hence, we studied the execution of complex movements from two aspects. One was the "*character*" of writing with the subject writing a predefined letter or just freely doodling. The idea was to find out whether the motor pattern for writing, i.e., the motor activity which is usually associated with WC, is different from healthy subjects when compared to the motor pattern for random scrawling. The second aspect was the presence or absence of "*visual feedback*" with the subject seeing or not seeing the line trajectory on the screen. Unlike previous studies, we included several