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B. Haslinger, E. Altenmüller, F. Castrop, C. Zimmer and C. Dresel

Neurology 2010;74;1790-1797
DOI: 10.1212/WNL.0b013e3181e0f784

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B. Haslinger, MD
E. Altenmüller, MD
F. Castrop, MD
C. Zimmer, MD
C. Dresel, MD

Address correspondence and reprint requests to Dr. Bernhard Haslinger, Neurologische Klinik, Klinikum rechts der Isar, Technische Universität München, Ismaninger Strasse 22, D-81675 München, Germany
haslinger@lrz.tum.de

ABSTRACT

Background: *Embouchure dystonia* is a focal task-specific dystonia affecting the complex interplay of lower facial, jaw, and tongue muscles in musicians playing brass or woodwind instruments. Although it is highly disabling for affected patients, little is known about the pathophysiologic basis of this rare movement disorder.

Methods: We therefore studied sensorimotor activation patterns during 2 orofacial motor tasks in brass players with embouchure dystonia by using fMRI. A "dystonia-specific" task involved buzzing at an instrument-specific, fully functional mouthpiece. A "neutral" task involved simply blowing into a tube.

Results: Compared with healthy brass players, patients with embouchure dystonia showed significantly increased activation of somatotopic face representations within the bilateral primary sensorimotor cortex and of the bilateral premotor cortex during buzzing at the mouthpiece. Interestingly, a similar activation pattern was present during the neutral task when patients were clinically asymptomatic.

Conclusion: Sensorimotor overactivity could reflect deficient subcortical and intracortical inhibition as well as abnormal sensorimotor integration and reorganization in musicians with embouchure dystonia. Because this overactivity was also found during the neutral task, it could be a crucial pathophysiologic factor predisposing for the development of orofacial dystonia rather than a mere correlate of dystonic motor output. ***Neurology*® 2010;74:1790–1797**

GLOSSARY

BA = Brodmann area; **ED** = embouchure dystonia; **FHD** = focal hand dystonia; **MD** = musician's dystonia; **MNI** = Montreal Neurological Institute.

Embouchure dystonia (ED) is a rare focal task-specific dystonia that affects wind players and manifests as playing-related involuntary movements of the orofacial muscles that control the airflow into the mouthpiece.[1,2] Despite its high impact on musical careers, the pathophysiology of ED or other musician's dystonias (MDs) remains poorly understood. A multifactorial concept combines an individual predisposition[3] with extrinsic factors and intrinsic abnormalities of sensorimotor inhibition and integration or dysfunctional brain plasticity.[4] However, the latter have mainly been indirectly inferred from findings in more frequent forms of focal dystonia, such as nonmusician's focal hand dystonia (FHD) or blepharospasm.[5] The diverse findings suggest distinct pathophysiologic traits requiring a separate investigation of different forms of focal dystonia to account for anatomical and clinical differences.

Few studies have directly investigated the pathophysiology of MD, especially of the rare patients with ED. Musicians with FHD showed abnormal processing of sensory stimuli[6] and dysfunctional sensorimotor integration.[7] fMRI detected increased sensorimotor activity in guitarists with FHD.[8] A disorganization of cortical somatosensory representations in musicians with FHD[9] and ED[10] was revealed by magnetoencephalography.

In the present fMRI study, we aimed to investigate whether brass players with ED reveal characteristic abnormalities of cortical sensorimotor activation during a dystonia-provoking

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Supplemental data at www.neurology.org

From the Departments of Neurology (B.H., F.C., C.D.) and Neuroradiology (C.Z.), Klinikum rechts der Isar, Technische Universität München; and Institute for Music Physiology and Musician's Medicine (E.A.), University for Music and Drama, Hannover, Germany.

Study funding: Supported by the Deutsche Forschungsgemeinschaft (HA 3370/3-1).

Disclosure: Author disclosures are provided at the end of the article.

Table 1 Demographic and clinical characteristics of healthy controls and patients with embouchure dystonia[a]

Group/patient	Sex	Age, y	Instrument	Duration of disorder, mo	Brass playing history, y	Daily practice, h	Dystonia score	Buzzing score
Healthy controls								
C1	F	34	Trombone	NA	24	1.5	1	1
C2	M	28	French horn	NA	13	2	1	1
C3	M	42	French horn	NA	28	2.5	2	2
C4	M	43	Trumpet	NA	30	1	1	2
C5	F	30	French horn	NA	21	3	1	1
C6	M	41	French horn	NA	28	4	1	1
C7	M	37	French horn	NA	23	4.5	1	1
C8	M	52	French horn	NA	43	2.5	1	1
C9	M	23	Trombone	NA	17	3.5	2	1
C10	M	45	Trumpet	NA	34	2.5	1	1
Mean (SD)	NA	37.5 (8.8)	NA	NA	26.1 (8.6)	2.7 (1.1)	1.2 (0.4)	1.2 (0.4)
Patients with ED								
D1	M	55	Trombone	29	43	0	2	2
D2	M	36	French horn	12	23	2	5	4
D3	M	44	Trumpet	30	36	3	5	5
D4	M	27	Trombone	24	17	1.5	2	2
D5	F	41	French horn	72	31	3	3	2
D6	M	46	Trumpet	28	34	1	3	4
D7	F	48	French horn	72	36	3	2	2
D8	M	36	Trombone	28	21	2.5	2	1
D9	M	29	French horn	41	18	1	4	4
D10	M	33	Trombone	54	20	2	2	2
Mean (SD)	NA	39.5 (8.9)	NA	39.0 (20.5)	27.9 (9.2)	1.9 (1.0)	3.0 (1.2)	2.8 (1.3)

Abbreviations: ED = embouchure dystonia; NA = not applicable.
[a] Actual daily practice at the time of study is indicated. Dystonia score and buzzing score are scored by blinded rating of the video recordings (dystonia score: 1 = no dystonia; 2 = possible ED; 3 = definite ED, minor degree; 4 = definite ED, medium degree; 5 = definite ED, severe degree; buzzing score: 1 = normal buzzing; 2 = degraded buzzing but no visible dystonic movements; 3 = degraded buzzing and dystonic movements visible; 4 = severely degraded buzzing and compensatory movements, strong tremor; 5 = no sound production possible).

orofacial motor task as a functional correlate of clinical ED. We were further interested in whether these patients show a more generalized sensorimotor dysfunction during a nondystonic motor task, indicating a subclinical predisposition for developing this highly specific disorder.

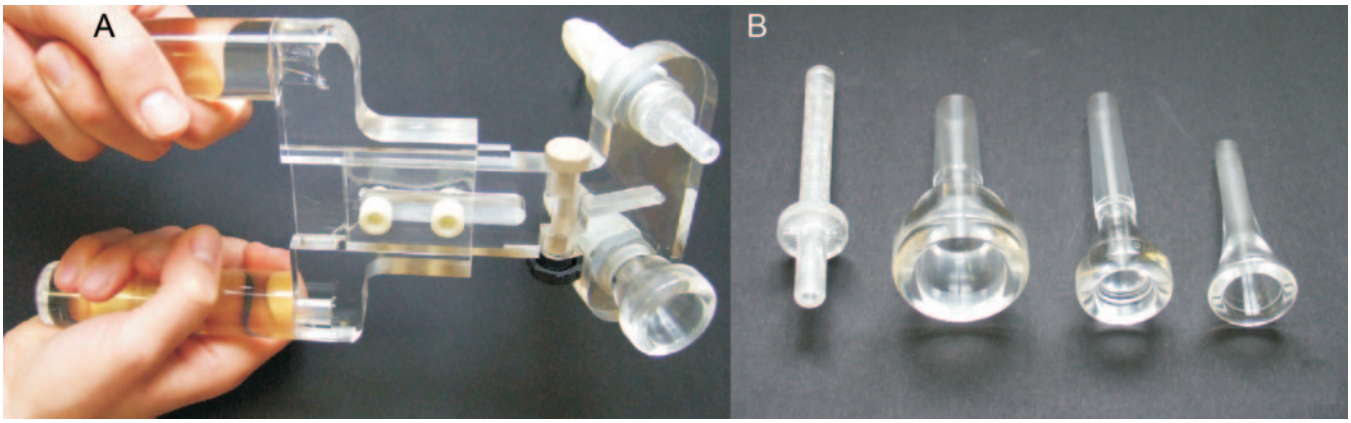
METHODS **Subjects.** We studied 10 professional brass players with ED and 10 healthy professional brass players, all right-handed (table 1).

Musical professionalism was defined as having at least a completed conservatory degree in brass playing. Patients with idiopathic ED were recruited from the movement disorders outpatient clinic at the Institute for Music Physiology and Musicians' Medicine, Hannover. We included patients with mild to moderate ED not completely incapacitating them to play their instrument and assuring that they were able to adequately perform the experimental task. One patient had stopped playing his instrument because of ED; the rest were still active at the time of investigation, albeit on a reduced level. No patient noticed orofacial dystonic symptoms in activities other than brass playing. Patients with multifocal dystonia, secondary causes for dystonia, and other neurologic disorders were excluded (for a detailed description of ED phenotypes, see table e-1 on the *Neurology*® Web site at www.neurology.org). The healthy brass players were recruited from professional musical orchestras, colleges, or freelance professional musicians. A medical history and examination excluded any sign of neurologic disease.

Standard protocol approvals, registrations, and patient consents. All participants gave their written informed consent in accordance with the guidelines of the Declaration of Helsinki. The study protocol was approved by the institutional ethics board.

Experimental task and fMRI data acquisition. The fMRI paradigm involved 2 externally triggered orofacial motor tasks: a mouthpiece task demanded "buzzing" at the mouthpiece for 6 seconds with a medium pitch and sound intensity. This was

Figure 1 Handhold and tubes used for the fMRI experiment



(A) The acrylic glass handhold with mounted mouthpiece and tube and an incised latex finger stall attached to the outlet of each for producing a comparable resistance. (B) From left to right: acrylic glass tube and instrument-specific mouthpieces for trombone, trumpet, and French horn.

supposed to provoke dystonic symptoms in patients. In a second task, the tube task, not inducing dystonia, subjects had to blow into a plain tube for 6 seconds. Subjects were instructed to buzz or blow with as little strain as possible, use abdominal breathing, and avoid excessive breath taking for reducing head movements. Each task was preceded by a preparatory interval pseudo-randomly varying between 3 and 13 s to avoid anticipation and allow statistical separation from the experimental task.

A fully functional acrylic glass mouthpiece and a tube were mounted on a purpose-built magnetic resonance–compatible acrylic glass handhold (figure 1). The mouthpieces were chosen according to the subject's instrument. Incised latex finger stalls were attached at the end of the mouthpiece and tube to obtain a flow resistance comparable to the individual's musical instrument. At rest, subjects were instructed to lie supine with their eyes open, the upper arms supported by the thorax, and the flexed forearms holding the handhold in a median position in front of their lips. Bitonal tone sequences indicated the appropriate preparation phase for the following condition, prompting the subjects to position the mouthpiece or tube in front of their lips by a short wrist movement. Further sound signals indicated the start (i.e., drawing breath, forming the embouchure, and starting to buzz or blow) and the end (i.e., repositioning the handhold in a median position) of the experimental task.

Training sessions ensured that patients and controls performed the task correctly. Task performance during fMRI was monitored by videotaping the participants from the control room to identify the correct type and timing of each handhold movement. After fMRI, the lower face of all subjects was anonymously videotaped during 1) buzzing at the mouthpiece and blowing into the tube as during fMRI; 2) playing scales, fifths, and fourths on their instrument; and 3) buzzing fifths and fourths at the mouthpiece. These video sequences were used for monitoring the occurrence of dystonic symptoms during the experimental tasks off-line. Afterward, they were blindly rated by a specialist in MD (E.A.) for determining a buzzing score as a rating of dystonia during buzzing and an overall dystonia score (table 1).

For the functional scans, T2*-weighted whole-brain echo planar images were acquired on a 1.5-T Siemens Symphony scanner (Erlangen, Germany) with an 8-channel head coil (repetition time/echo time 2,480/50 milliseconds, $\alpha = 90°$, field of view 224 mm, matrix 64×64, 28 slices at 4.5 mm, 10% slice gap). Each subject performed 3 runs each including 320 scans. For each of the 2 experimental tasks, 18 trials were pseudo-randomly distributed across each run with an intertrial interval pseudo-randomly jittered between 2 and 12 seconds. A whole-brain 3-dimensional T1-weighted data set was obtained for anatomical reference.

Data analysis. Imaging data were analyzed using SPM5 (www.fil.ion.ucl.ac.uk/spm/software/spm5) and MATLAB 7.1 (The Mathworks Inc., Natick, MA). After discarding the first 2 images of each run, images of all runs were realigned to the first image of the series, stereotactically normalized to the Montreal Neurological Institute (MNI) template and smoothed with an isotropic gaussian kernel of 6 mm full-width at half-maximum.

A second-level random-effects approach was used for statistical analysis.[11] On the first level, the 3 functional runs were entered into an individual design matrix including 3 conditions for each subject. For the mouthpiece and tube conditions, each trial was modeled as a miniblock of 6 seconds. For covering the short hand movements at the beginning of the preparation, these trials were modeled as events of 0 seconds. The onset functions were convolved with the canonical hemodynamic response function. For desensitizing the analysis for spatially varying hemodynamic delays or slice-timing differences, the temporal and dispersion derivatives of the hemodynamic response function were included in the model.[12] To capture residual motion-related artifacts, spatial transformation matrices estimated during realignment preprocessing were included in the model. A temporal high-pass filter (cutoff 128 seconds) was applied to remove low-frequency noise.

T contrast images for each of the 3 conditions (mouthpiece, tube, and preparation) vs rest were calculated for each subject. These contrast images were entered into a second level full-factorial design with the between-subjects factor "group" and the within-subject factor "task" to make inferences at the population level. Statistical parametric maps were estimated by applying appropriate t contrasts for both tasks (mouthpiece and tube) vs baseline and for the comparison mouthpiece vs tube separately within each group as well as between groups.

To test whether activation levels in patients with ED during buzzing at the mouthpiece covary with the severity of dystonia or with the brass playing practice, we calculated regression models correlating the individual contrast images (including voxel-wise β values across the whole brain) for mouthpiece vs rest with the individual dystonia and buzzing score across all patients or with the individual mean daily practice across all patients and con-

trols. For that analysis, we applied a mask of voxels that survived an uncorrected threshold of $p < 0.001$ in the between-groups comparison mouthpiece vs rest in patients vs controls.

Based on previous imaging studies in focal dystonia, we expected activation abnormalities in primary motor, premotor, and primary and secondary somatosensory cortices.[8,13-17] We therefore did not apply a statistical correction for multiple comparisons across the whole brain but restricted the correction to a smaller volume of interest according to our anatomical hypotheses. First, we applied a threshold of $p < 0.001$ uncorrected (extent threshold k = 5 voxels) to search for significant activation in these areas. Activations in other areas are reported for descriptive purposes and are discussed in the e-Discussion. For critical areas of interest, a small volume correction ($p_{svc} < 0.05$, false discovery rate corrected[18]) was then applied to a set of anatomically defined regions of interest, which were activated in healthy controls during an orofacial motor task similar to the current tasks.[19] Spherical regions of interest of 10-mm radius were bilaterally centered around stereotactic coordinates (Talairach) of $x = \pm 58$, $y = -10$, $z = 28$ for the orofacial primary motor area (Brodmann area [BA] 4); $x = \pm 59$, $y = -10$, $z = 24$ for the primary somatosensory (BA3); and $x = \pm 55$, $y = -5$, $z = 15$ for the secondary somatosensory cortex (BA43). Applying the WFU PickAtlas tool (http://fmri.wfubmc.edu),[20] these coordinates were transformed into MNI coordinates, and the targeted cortical regions of interest were combined into 1 mask to correct for multiple comparisons within this restricted volume.

Table 2 Areas with stronger activation in patients with embouchure dystonia compared with healthy controls[a]

	Mouthpiece > rest Patients > controls				Tube > rest Patients > controls			
Area (BA)	x	y	z	t Score	x	y	z	t Score
R precentral (4/6)	56	−8	32	4.47*	58	−10	30	3.62*
L precentral (4)	−56	−10	30	3.62*				
L precentral (6)	−52	−10	48	3.50	−52	−8	46	4.05
R inferior frontal (44)					60	12	18	3.73
L inferior frontal (44)					−56	14	16	3.34
L mesial frontal, SMA (6)	−12	−14	78	3.49				
L middle frontal (46/45)					−46	22	28	4.10
R postcentral (43/3)	54	−22	14	3.50				
L postcentral (3)	−52	−10	22	3.79*	−66	−16	34	3.73*
L parietal operculum (43)	−62	−6	16	3.93*	−58	−10	18	3.55*
L inferior parietal (40)					−44	−44	52	3.62
R middle temporal (22)	58	−10	−4	4.14				
L superior temporal (22, 21)	−58	−12	0	4.02	−56	−8	−4	3.77
R transverse temporal (41)	52	−22	12	3.34				
L transverse temporal (41)	−46	−20	10	3.49	−46	−20	10	3.33
L middle temporal (37/39)					−56	−60	6	3.58
R insula	38	8	−2	3.41				
L anterior insula					−28	24	6	3.64
L posterior insula					−36	−16	14	3.42
R thalamus					16	−18	2	3.61
L thalamus					−12	−18	−2	3.50
L caudate nucleus	−8	2	10	3.48	−8	4	10	3.54

Abbreviations: BA = Brodmann area; SMA = supplementary motor area.
[a] Coordinates (in millimeters) refer to peak activation in Montreal Neurological Institute space. All activations are significant at $p < 0.001$ uncorrected (extent threshold, k = 5) or *$p_{svc} < 0.05$ small volume corrected for multiple spatial comparisons within a set of critical areas of interest.

RESULTS Clinical data and task performance. There was no significant between-groups difference in history ($F_{6,13} = 0.21$, $p = 0.66$) or mean daily practice ($F_{6,13} = 2.88$, $p = 0.11$) of brass playing at the time of study.

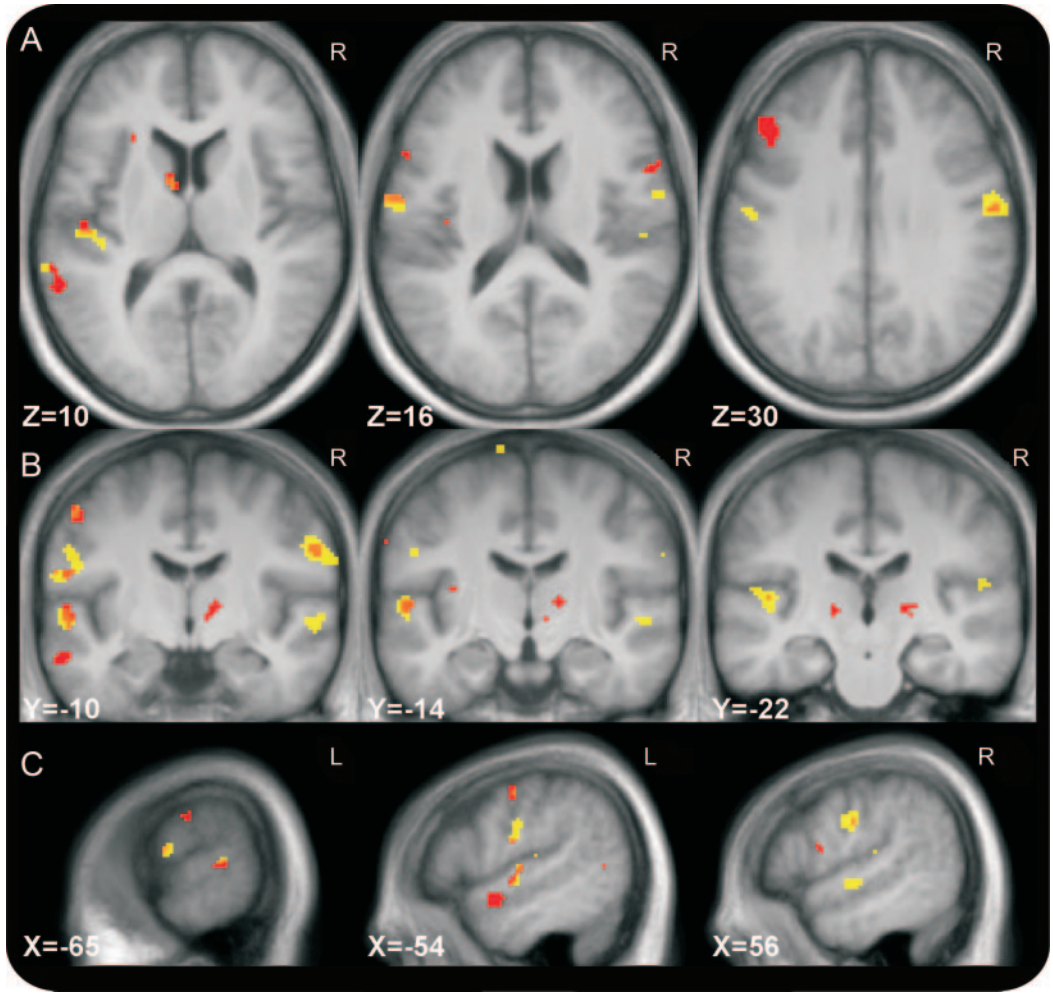
As monitored during the training sessions and by questioning post fMRI scanning, all patients could perform the experimental tasks adequately without an increased strain for producing a tone. All subjects affirmed that their performance for both experimental tasks during the off-line video session reflected their actual performance during fMRI scanning regarding the occurrence of dystonic symptoms. No control subject showed any signs of dystonia during instrument playing or either of the experimental tasks. Nine of 10 patients with ED revealed clear signs of dystonia during the mouthpiece task. No patient displayed any signs of dystonia during the tube task. The mean dystonia score ($F_{6,13} = 18.69$, $p < 0.001$) and the mean buzzing score ($F_{6,13} = 13.40$, $p = 0.002$) were significantly higher in patients (table 1).

Functional imaging data. ***Within-group analyses.*** The comparisons of buzzing at the mouthpiece vs rest, blowing into the tube vs rest, and mouthpiece vs tube yielded similar cortical-subcortical sensorimotor activation patterns in both groups (tables e-2–e-4).

Between-groups analysis of buzzing at the mouthpiece vs rest. The direct between-groups comparison between patients with ED and healthy controls for buzzing at the mouthpiece vs rest revealed stronger activation in patients within bilateral precentral (primary motor, lateral premotor) cortex, mesial premotor cortex (supplementary motor area), left primary somatosensory and bilateral secondary somatosensory areas, bilateral superior and mesial temporal cortices, right insula, and left caudate nucleus (table 2 and figure 2). No stronger activations were found in healthy controls compared with patients.

Between-groups analysis of blowing into the tube vs rest. When comparing activation in both groups during blowing into the tube vs rest, patients with ED showed stronger activation within right precentral (primary motor, lateral premotor) cortex, left lateral premotor cortex, bilateral ventral premotor cortex, left primary and secondary somatosensory cortex, left inferior parietal cortex, left prefrontal cortex, left superior and mesial temporal cortex, left occipitotemporal cortex, left insula, bilateral thalamus, and left caudate nucleus (table 2 and figure 2). No stronger

Figure 2 Activation differences between patients with embouchure dystonia and healthy controls



Areas with significantly stronger activation ($p < 0.001$ uncorrected, 5 voxels extent threshold) in patients with embouchure dystonia compared with healthy controls during buzzing at the mouthpiece (yellow) and blowing into the tube (red). Overlapping areas appear in orange. Areas of stronger activation in patients with dystonia are overlaid onto axial (A), coronal (B), and sagittal (C) sections of a stereotactically normalized T1-weighted mean magnetic resonance image of all 20 subjects investigated in the study. The slice position is given in Montreal Neurological Institute coordinates (x = lateral distance in millimeters from the midline, + right, − left; y = anteroposterior distance from the anterior commissure [AC], + anterior, − posterior; z = height relative to the AC line, + above, − below).

activations were found in healthy controls compared with patients.

Between-groups analysis of mouthpiece vs tube and correlation analyses. When directly comparing buzzing at the mouthpiece vs blowing into the tube between both groups, patients with ED showed stronger activation than controls in only a small cluster within the left dorsal (paracentral) precentral cortex. We detected no stronger signal increases in patients for this comparison within any of the hypothesized areas of interest, nor did the analysis show any areas with higher activation levels in healthy controls.

The correlation analyses did not display any significant positive or negative correlations between the dystonia/buzzing score or the daily brass playing practice and the buzzing-related activation in areas that were overactive in patients compared with controls during the dystonia-specific mouthpiece task.

DISCUSSION This study demonstrates increased activation of primary motor, premotor, and primary and secondary somatosensory cortices in brass players with ED compared with healthy musicians. This was evident during a dystonia-provoking orofacial motor task simulating actual instrument playing and also partly during the neutral task when patients were clinically asymptomatic. Both findings advance our understanding of this rare disease because they reveal abnormal sensorimotor activation patterns within orofacial representations as an intrinsic predisposing trait as well as dystonia-specific effects.

The task-specificity of functional activation patterns in focal dystonia is supported by previous imaging studies that found varying results depending on the task and type of focal dystonia. Some studies reported a decreased activation of the primary motor cortex in nonmusicians with focal hand, laryngeal, or orofacial dystonia.[13,14,16,17] Many of these studies examined motor tasks that did not provoke dystonia. In those studies where the experimental task induced dystonic symptoms akin to our mouthpiece task, e.g., guitar playing in musicians with FHD[8] or long-term writing in patients with writer's cramp,[15] a similar pattern of increased sensorimotor activation was found.

Because we were likewise interested in activation patterns of patients with ED without overt dystonic symptoms, considering the high variability of previous imaging findings, we also investigated a neutral task, i.e., blowing into a tube. We could thereby avoid the interpretative dilemma of distinguishing between dystonia-induced and dystonia-unrelated activation, because the patients were asymptomatic during this task. A similar pattern of increased sensorimotor activation in patients with ED was found during this neutral task. This finding is corroborated by the direct between-groups comparison of mouthpiece vs tube, which did not reveal significant activation differences in cortical sensorimotor areas. Post hoc analyses did not find a correlation between the level of sensorimotor activation and the severity of task-induced dystonia or daily brass playing practice. These results suggest that the overactivity of orofacial sensorimotor representations is an intrinsic abnormality predisposing for developing ED rather than being secondary to the presence of dystonic motor output or compensatory motor strategies after a possible lack of practice. Such a predisposition is clinically supported by a small incidence of dystonia in other body parts like task-induced FHD in some patients with ED.[2]

Sensorimotor overactivity in patients with ED is likely to mirror a multifactorial interplay of functional abnormalities within sensorimotor networks. Cortical sensorimotor overactivity is congruent with the concept of increased excitability and reduced intracortical inhibition[21-23] along with a reduced inhibitory γ-aminobutyric acid neurotransmission in the sensorimotor cortex as shown in FHD.[24] In line with these findings, overexcitation of the premotor cortex was demonstrated during movement preparation in pianists with MD.[25] This may further explain increased activation of premotor cortices in our patients with ED, similar to previous imaging findings in different forms of nonmusician's dystonia.[13,15] Overactive premotor cortices have been demonstrated concomitantly with overactive basal ganglia in PET studies of dystonic patients at rest.[26] This has been interpreted as an intrinsic abnormal modulation of the cortico-striato-pallido-thalamo-cortical circuit in dystonia finally resulting in premotor overactivity.[26]

Increased sensorimotor activation during a dystonic and a nondystonic task in patients with ED might also be a correlate of an abnormal interaction between motor and somatosensory areas. Consistent with the concept of dysfunctional sensorimotor integration as previously shown in nonmusicians with FHD,[27,28] an increased and spatially dedifferentiated facilitation of corticospinal motor output after focal somatosensory input has been reported in musicians with FHD.[7] Such an alteration of sensorimotor integration could be due to a failure of the basal ganglia to efficiently focus incoming sensory information, as suggested by basal ganglia hyperactivity during a sensory discrimination task in patients with writer's cramp.[29] Impaired sensory gating of the basal ganglia could contribute to an excessive activation of sensorimotor cortical areas during motor execution in ED.

Finally, sensorimotor overactivation in musicians with ED might be secondary to a pathologic reorganization of cortical sensorimotor representations. An abnormal functional plasticity has been detected within the somatosensory cortex in musicians with ED[10] and FHD[9] similar to findings in nonmusicians with FHD,[30-32] whereas morphometric analyses revealed a structural reorganization in form of an increased gray matter density within the primary somatosensory cortex in patients with FHD, 5 of them with MD.[33] Increased activation of primary and secondary somatosensory areas in our patients during both experimental tasks highlights the importance of the somatosensory system in the pathophysiology of ED analog to previous clinical and electrophysiologic findings in musicians[6] and nonmusicians[34,35] with FHD. This interpretation is supported by the coincidence of the initial manifestation of dystonia with alterations of somatosensory input due to trauma or changes of musical technique in some patients with ED and the sensory trick whereby some patients experience a clinical improvement by touching their face.[4]

A somatotopic distortion of cortical somatosensory representations has been demonstrated as a consequence of repetitive stereotyped movements in a primate model of FHD.[36] Intensive training of repetitive movement sequences is also a key feature of musicians who reach professional skillfulness. Many years of intensive motor training in healthy musicians physiologically lead to a beneficial sensorimotor reorganization. This includes an increased excitabil-

ity of the motor cortex[37] and a partial reorganization of sensorimotor interaction with a higher potential of sensorimotor cortical plasticity.[7,37] Healthy musicians show an (orderly) increase of representational fields of individual fingers within the somatosensory cortex[38] and an increase of gray matter density within primary sensorimotor and premotor cortices.[39,40] These findings reveal some common features between healthy musicians and patients with focal dystonia that were discussed above. It is therefore not surprising that musicians are at risk to develop dystonia when there is an individual susceptibility for physiologic, originally beneficial brain plasticity to go too far and shift to a maladaptation that may lead to abnormal sensorimotor processing.

AUTHOR CONTRIBUTIONS

B. Haslinger and C. Dresel completed the statistical analysis.

ACKNOWLEDGMENT

We are grateful to Christoph Rimpau (Institute of Machine Tools and Industrial Management, TU-Muenchen) for his support in manufacturing the acrylic glass handhold and Anna Eckerskorn for her help in recruiting study participants.

DISCLOSURE

Dr. Haslinger serves on a scientific board for Merz Pharmaceuticals, LLC; has received funding for travel from Ipsen, Merz Pharmaceuticals, LLC, and Medtronic, Inc.; has received speaker honoraria from Novartis, GlaxoSmithKline, Desitin Pharmaceuticals, GmbH, Ipsen, and Allergan, Inc.; and receives research support from Ipsen and from the German Research Foundation (DFG). Prof. Dr. Altenmüller serves on the editorial boards of the *Journal of Interdisciplinary Music Studies*, *Medical Problems of Performing Artists*, *Musicae Scientiae*, and *Music and Medicine*; receives royalties from the publication of *Music, Motor Control and the Brain* (Oxford University Press, 2006); has received honoraria from Allergan, Inc., Ipsen, Desitin Pharmaceuticals, GmbH, and Merz Pharmaceuticals, LLC; and receives research support from the DFG, the European Marie Curie Actions, the Lichtenberg Scholarship Program of Lower Saxony, and the Dystonia Medical Research Foundation. Dr. Castrop has received funding for travel from Novartis, Merck Serono, Medtronic, Inc., Solvay Pharmaceuticals, Inc., Merz Pharmaceuticals, LLC, Ipsen, and Allegan, Inc. Prof. Dr. Zimmer receives research support from CCBR- SYNARC, Wyeth, Bayer Schering Pharma, Novartis, Merz Pharmaceuticals, LLC, Medivation, Inc., Quintiles, AC Immune SA, Actelion Pharmaceuticals Ltd, Biogen Idec, Genzyme Corporation, Merck Serono, FGK Clinical Research GmbH, the DFG, and the Bavarian government. Dr. Dresel has received funding for travel from Ipsen and Merz Pharmaceuticals, LLC; has filed patent DE 10.2005.023.121A1 (filed: 2005): MR-compatible stimulation device; and receives research support from the DFG.

Received September 8, 2009. Accepted in final form February 3, 2010.

REFERENCES

1. Jankovic J, Ashoori A. Movement disorders in musicians. Mov Disord 2008;23:1957–1965.
2. Frucht SJ. Embouchure dystonia: portrait of a task-specific cranial dystonia. Mov Disord 2009;24:1752–1762.
3. Schmidt A, Jabusch HC, Altenmuller E, et al. Etiology of musician's dystonia: familial or environmental? Neurology 2009;72:1248–1254.
4. Altenmuller E, Jabusch HC. Focal hand dystonia in musicians: phenomenology, etiology, and psychological trigger factors. J Hand Ther 2009;22:144–154.
5. Breakefield XO, Blood AJ, Li Y, Hallett M, Hanson PI, Standaert DG. The pathophysiological basis of dystonias. Nat Rev Neurosci 2008;9:222–234.
6. Lim VK, Bradshaw JL, Nicholls ME, Altenmuller E. Perceptual differences in sequential stimuli across patients with musician's and writer's cramp. Mov Disord 2003;18:1286–1293.
7. Rosenkranz K, Williamon A, Butler K, Cordivari C, Lees AJ, Rothwell JC. Pathophysiological differences between musician's dystonia and writer's cramp. Brain 2005;128:918–931.
8. Pujol J, Roset-Llobet J, Rosines-Cubells D, et al. Brain cortical activation during guitar-induced hand dystonia studied by functional MRI. Neuroimage 2000;12:257–267.
9. Elbert T, Candia V, Altenmuller E, et al. Alteration of digital representations in somatosensory cortex in focal hand dystonia. Neuroreport 1998;9:3571–3575.
10. Hirata Y, Schulz M, Altenmuller E, Elbert T, Pantev C. Sensory mapping of lip representation in brass musicians with embouchure dystonia. Neuroreport 2004;15:815–818.
11. Strange BA, Portas CM, Dolan RJ, Holmes AP, Friston KJ. Random effects analyses for event-related fMRI. Neuroimage 1999;9:36.
12. Calhoun VD, Stevens MC, Pearlson GD, Kiehl KA. fMRI analysis with the general linear model: removal of latency-induced amplitude bias by incorporation of hemodynamic derivative terms. Neuroimage 2004;22:252–257.
13. Ceballos-Baumann AO, Sheean G, Passingham RE, Marsden CD, Brooks DJ. Botulinum toxin does not reverse the cortical dysfunction associated with writer's cramp: a PET study. Brain 1997;120(pt 4):571–582.
14. Ibanez V, Sadato N, Karp B, Deiber MP, Hallett M. Deficient activation of the motor cortical network in patients with writer's cramp. Neurology 1999;53:96–105.
15. Odergren T, Stone-Elander S, Ingvar M. Cerebral and cerebellar activation in correlation to the action-induced dystonia in writer's cramp. Mov Disord 1998;13:497–508.
16. Dresel C, Haslinger B, Castrop F, Wohlschlaeger AM, Ceballos-Baumann AO. Silent event-related fMRI reveals deficient motor and enhanced somatosensory activation in orofacial dystonia. Brain 2006;129:36–46.
17. Haslinger B, Erhard P, Dresel C, Castrop F, Roettinger M, Ceballos-Baumann AO. "Silent event-related" fMRI reveals reduced sensorimotor activation in laryngeal dystonia. Neurology 2005;65:1562–1569.
18. Genovese CR, Lazar NA, Nichols T. Thresholding of statistical maps in functional neuroimaging using the false discovery rate. Neuroimage 2002;15:870–878.
19. Dresel C, Castrop F, Haslinger B, Wohlschlaeger AM, Hennenlotter A, Ceballos-Baumann AO. The functional neuroanatomy of coordinated orofacial movements: sparse sampling fMRI of whistling. Neuroimage 2005;28:588–597.
20. Maldjian JA, Laurienti PJ, Kraft RA, Burdette JH. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. Neuroimage 2003;19:1233–1239.
21. Siebner HR, Tormos JM, Ceballos-Baumann AO, et al. Low-frequency repetitive transcranial magnetic stimulation of the motor cortex in writer's cramp. Neurology 1999;52:529–537.

22. Chen R, Wassermann EM, Canos M, Hallett M. Impaired inhibition in writer's cramp during voluntary muscle activation. Neurology 1997;49:1054–1059.
23. Gilio F, Curra A, Lorenzano C, Modugno N, Manfredi M, Berardelli A. Effects of botulinum toxin type A on intracortical inhibition in patients with dystonia. Ann Neurol 2000;48:20–26.
24. Levy LM, Hallett M. Impaired brain GABA in focal dystonia. Ann Neurol 2002;51:93–101.
25. Lim VK, Bradshaw JL, Nicholls ME, Altenmuller E. Abnormal sensorimotor processing in pianists with focal dystonia. Adv Neurol 2004;94:267–273.
26. Eidelberg D, Moeller JR, Antonini A, et al. Functional brain networks in DYT1 dystonia. Ann Neurol 1998;44:303–312.
27. Abbruzzese G, Marchese R, Buccolieri A, Gasparetto B, Trompetto C. Abnormalities of sensorimotor integration in focal dystonia: a transcranial magnetic stimulation study. Brain 2001;124:537–545.
28. Quartarone A, Bagnato S, Rizzo V, et al. Abnormal associative plasticity of the human motor cortex in writer's cramp. Brain 2003;126:2586–2596.
29. Peller M, Zeuner KE, Munchau A, et al. The basal ganglia are hyperactive during the discrimination of tactile stimuli in writer's cramp. Brain 2006;129:2697–2708.
30. Meunier S, Garnero L, Ducorps A, et al. Human brain mapping in dystonia reveals both endophenotypic traits and adaptive reorganization. Ann Neurol 2001;50:521–527.
31. Butterworth S, Francis S, Kelly E, McGlone F, Bowtell R, Sawle GV. Abnormal cortical sensory activation in dystonia: an fMRI study. Mov Disord 2003;18:673–682.
32. Bara-Jimenez W, Catalan MJ, Hallett M, Gerloff C. Abnormal somatosensory homunculus in dystonia of the hand. Ann Neurol 1998;44:828–831.
33. Garraux G, Bauer A, Hanakawa T, Wu T, Kansaku K, Hallett M. Changes in brain anatomy in focal hand dystonia. Ann Neurol 2004;55:736–739.
34. Bara-Jimenez W, Shelton P, Sanger TD, Hallett M. Sensory discrimination capabilities in patients with focal hand dystonia. Ann Neurol 2000;47:377–380.
35. Fiorio M, Tinazzi M, Bertolasi L, Aglioti SM. Temporal processing of visuotactile and tactile stimuli in writer's cramp. Ann Neurol 2003;53:630–635.
36. Byl NN, Merzenich MM, Jenkins WM. A primate genesis model of focal dystonia and repetitive strain injury, I: learning-induced dedifferentiation of the representation of the hand in the primary somatosensory cortex in adult monkeys. Neurology 1996;47:508–520.
37. Rosenkranz K, Williamon A, Rothwell JC. Motorcortical excitability and synaptic plasticity is enhanced in professional musicians. J Neurosci 2007;27:5200–5206.
38. Elbert T, Pantev C, Wienbruch C, Rockstroh B, Taub E. Increased cortical representation of the fingers of the left hand in string players. Science 1995;270:305–307.
39. Amunts K, Schlaug G, Jäncke L, et al. Motor cortex and hand motor skills: structural compliance in the human brain. Hum Brain Mapp 1997;5:206–215.
40. Gaser C, Schlaug G. Brain structures differ between musicians and non-musicians. J Neurosci 2003;23:9240–9245.