Neural Reorganization Underlies Improvement in Stroke-induced Motor Dysfunction by Music-supported Therapy

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Motor impairments are common after stroke, but efficacious therapies for these dysfunctions are scarce. By extending an earlier study on the effects of music-supported therapy, behavioral indices of motor function as well as electrophysiological measures were obtained before and after a series of therapy sessions to assess whether this new treatment leads to neural reorganization and motor recovery in patients after stroke. The study group comprised 32 stroke patients in a large rehabilitation hospital; they had moderately impaired motor function and no previous musical experience. Over a period of 3 weeks, these patients received 15 sessions of music-supported therapy using a manualized step-by-step approach. For comparison 30 additional patients received standard rehabilitation procedures. Fine as well as gross motor skills were trained by using either a MIDI-piano or electronic drum pads programmed to emit piano tones. Motor functions were assessed by an extensive test battery. In addition, we studied event-related desynchronization/synchronization and coherences from all 62 patients performing self-paced movements of the index finger (MIDI-piano) and of the whole arm (drum pads). Results showed that music-supported therapy yielded significant improvement in fine as well as gross motor skills with respect to speed, precision, and smoothness of movements. Neurophysiological data showed a more pronounced event-related desynchronization before movement onset and a more pronounced coherence in the music-supported therapy group in the post-training assessment, whereas almost no differences were observed in the control group. Thus we see that music-supported therapy leads to marked improvements of motor function after stroke and that these are accompanied by electrophysiological changes indicative of a better cortical connectivity and improved activation of the motor cortex.

Key words: **neurorehabilitation; plasticity; event-related desynchronization and coherence; stroke; music-supported therapy**

The effectiveness of standard physiotherapeutic approaches in stroke rehabilitation has been found to be quite limited, thus calling for innovative motor rehabilitation approaches.[1–4] Data have accumulated indicating that repetitive massed practice of movements leads to improvement in motor function,[4–8] with changes being attributed to neural reorganization.[9–11]

A different line of studies has shown rapid plastic adaptation due to music performance, which is not restricted to cortical motor areas but also involves auditory and integrative auditory–sensorimotor circuits.[12–15]

This suggests that music-making, even in unskilled patients, might be an effective means to induce plastic changes in the motor system.

While sharing the repetitive character of movements with other therapies, music could in addition shape movements through the immediate auditory feedback. Moreover, the high motivational value of music and, possibly, audio–sensorimotor coupling imply that music might be useful in the rehabilitation process.[12,13]

We therefore designed a music-supported therapy program for the recovery of motor functions after stroke.[16]

The present study seeks to extend our previous findings[16] to a larger group of patients and to assess whether neural reorganization is induced by music-supported treatment. To this end we analyzed therapy-induced changes in oscillatory neural activity reflected in event-related desynchronization/synchronization (ERD/ERS)[17–20] and event-related coherence during movement execution. The role of neural rhythms in movement-related EEG activity has been mainly demonstrated by the study of modulation of spectral power responses, allowing the inference that movement-related brain potentials could implicate specific EEG oscillatory patterns.[21] Chen and colleagues found a clear association of increased cortical excitability and ERD during self-paced movements.[22]

We hypothesized that neural reorganization, indexed by an increase of ERD, should be more pronounced in the music-supported therapy group compared to the control group.

Methods

Patients

Sixty-two inpatients in a neurologic rehabilitation hospital who had moderate impairment of motor function of the upper extremities after a stroke and who had no previous musical experience participated after giving informed consent. Inclusion criteria were specified similar to those adopted for constraint-induced movement therapy (CIMT).[23] In particular, (a) pa-

TABLE 1. Relevant Clinical and Sociodemographic Parameters of MG and CG

	MG	CG
Affected extremity: left/right	17/15	15/15
Sex: F/M[a]	16/16	6 /24
Age: mean (SD)	55.7 (12.3)	53 (11.8)
School education (y)	9.8 (1.6)	9.1 (1.3)
Handedness: right/left/ ambidextrous	30/1/1	28/1/1
Ischemia /hemorrhage	26/6	27/3
Months after onset of disease	1.9 (1.3)	1.9 (1.4)
Barthel Index: mean (SD)	85.9 (15.9)	84.3 (16)

Abbreviations: MG = music-supported therapy plus conventional treatment; CG = conventional treatment only.
[a] Significant difference.

tients had to have residual function of the affected extremity (i.e. the ability to move the affected arm and index finger without help from the healthy side). Moreover, (b) an overall Barthel Index over 50 was required; and (c) performance on the Nine-Hole Pegboard Test had to be slower than that of the mean minus 2 SD of a healthy control group (mean peg/s 0.68, SD 0.14).[24] Patients were assigned pseudo-randomly by occupational therapists not involved in the study to two groups receiving either conventional treatment only ($n = 30$, henceforth CG) or music-supported therapy in addition to conventional therapy ($n = 32$, henceforth MG) according to the following constraints: (1) nearly equal number of patients in CG and MG and (2) nearly equal number of left- and right-affected participants in each group. Tables 1 and 2 show pertinent clinical and demographic data. Except for the gender distribution, no significant differences were found between the MG and CG groups. The majority of left-hemisphere patients ($n = 8$ in MG; $n = 9$ in CG) showed a mild to moderate aphasia (as assessed by Aachen Aphasia Test), but all of these patients were able to understand the instructions during assessment and therapy. Eight additional potential participants were excluded because of severe perceptual or cognitive deficits revealed by neuropsychological testing. None of the remaining patients had

TABLE 2. Etiology and Stroke Location in MG and CG

Etiology	Stroke location	Number of patients in:	
		MG group	CG group
Ischemia	Cortical	12	14
	Subcortical (basal ganglia)	9	9
	Cortical + subcortical	1	1
	Cerebellum, pons	4	3
Hemorrhage	Cortical	1	1
	Subcortical (basal ganglia)	5	2

been diagnosed with depression or other psychiatric or neurologic diseases. They were all native speakers of German. All of the 62 patients enrolled in the study completed the whole treatment and assessment program, except for eight patients (1 MG and 7 CG) who missed computerized movement analysis during post-treatment assessment.

The study was approved by the ethics review board of the University Hospital of Magdeburg.

Evaluation of Motor Functions

Electrophysiology — EEG Recording

Recordings. Electroencephalograms were recorded from 26 electrodes embedded in an elastic cap positioned according to the extended 10–20 system with 256 points/s and a resolution of 22 bits, 71.5 nV per bit.

Procedure. Two different input devices were used for recording, a muted MIDI-piano and a muted electronic drum set. Patients were seated in front of the muted instruments on a chair without armrests or in their own wheelchair. They were asked to perform self-paced index finger movements on a defined piano key or gross movements with the whole arm by hitting a defined drum pad each 3–5 s. One-hundred responses were obtained for each movement and for the affected and nonaffected extremity.

By pressing the key on the piano or hitting a pad, an event-marker was sent to the acquisition computer. Each run lasted approximately 5 min. The entire experiment lasted about 1 h, including positioning of electrodes and breaks.

ERD/ERS analysis. Epochs of 4 s (starting 2 s before pressing the key or hitting the drum) were extracted from data. The base line was set from 1.5 s to 1 s before trigger. Following the classical methodology for studying ERD, single trials were band-pass filtered in the alpha (9–11 Hz) and beta (18–22 Hz) bands and squared to obtain power samples.[25] The power of single trials was then averaged. Finally, smoothing over 15 time samples was performed to reduce the variability.

Three spatial clusters were defined to increase the signal–noise ratio of signals: central electrodes (Fz, Fcz and Cz), ipsilesional electrodes, and contralesional electrodes. In the case of patients with right-sided motor deficits, ipsilesional electrodes were C3, F3, and Fc3, whereas C4, F4, and Fc4 were the contralesional sites (for left-affected patients the assignment was reversed). For analysis, the lateral electrodes of the right-affected group were mirrored and considered together with the unmirrored electrodes of the left-affected patients. To test the effect of the music-supported therapy, comparisons between pre- and post-treatment brain electrical activity responses were computed using Student's *t*-test in 100-ms time windows.

Coherence analysis. In order to determine whether there was an increase in the coherence as an effect of the therapy, we computed the coherence between electrodes (Fcz, C3, F3, Cz, C4, Cpz, Fz, F4, P3, Pz, P4, Cp4, Cp3, Fc4, Fc3) in the studied frequency ranges in both groups (MG and CG) and conditions (pre-therapy versus post-therapy) using the following expression:

$$C_{xy}(f) = \frac{\left|G_{xy}(f)\right|^2}{G_{xx}(f)G_{yy}(f)}$$

TABLE 3. Results of the Pretesting of Motor Functions between Groups: Mean (SD)

Motor test/parameter	MG	CG	$F(1,52)$
FREQ finger tapping in Hz	2 (1.4)	1.6 (1.4)	0.07, n.s.
VMAX finger tapping in °/s	160.2 (105.5)	126.8 (112.1)	0.59, n.s.
NIV finger tapping[a]	1.7 (0.3)	2.1 (0.4)	0.81, n.s.
FREQ hand tapping in Hz	1.8 (1.4)	1.5 (1.4)	0.06, n.s.
VMAX hand tapping in °/s	102.5 (80.1)	100.6 (110.8)	0.55, n.s.
NIV hand tapping[a]	1.9 (0.3)	2.5 (0.4)	0.74, n.s.
FREQ pronation/supination in Hz	1.2 (0.8)	1.2 (1.1)	0.27, n.s.
VMAX pronation/supination in °/s	398.8 (354.7)	423.1 (462.2)	0.19, n.s.
NIV pronation/supination [a]	2 (0.3)	2.3 (0.4)	0.13, n.s.
V2 target movement 5cm in mm/s	456.7 (232.1)	479.4 (373.9)	0.3, n.s.
V2 target movement 0.8cm in mm/s	487.5 (243.4)	464.4 (366.8)	0.04, n.s.
	MG	CG	$F(1,60)$
ARAT (score)	33.3 (23.9)	36.4 (23.3)	0.27, n.s.
Arm paresis (score)	4.5 (2.8)	4.7 (2.8)	0.04, n.s.
BBT (score)	25.1 (17.6)	30.8 (21)	1.35, n.s.
9HPT (score)	4.1 (4)	4.9 (4.1)	0.51, n.s.

Abbreviation: n.s. = nonsignificant.

[a]The best value that could be reached was 1.

where *x* and *y* are different electrodes, *f* is the studied frequency band, and

$$G_{xx}(f) = \frac{1}{N}\sum_{n=1}^{N}|X_n(f)|^2$$

$$G_{yy}(f) = \frac{1}{N}\sum_{n=1}^{N}|Y_n(f)|^2$$

$$G_{xy}(f) = \frac{1}{N}\sum_{n=1}^{N}|X_n(f)Y_n^*(f)|$$

where $X_n(f)$ and $Y_n(f)$ are the fast Fourier transform values for the desired frequency bands for the *x* and *y* electrode at the *n*th trial.[26] Differences between pre- and post-therapy measurements were assessed using the Mann–Wilcoxon U-test.

Behavioral Measurements

As previously reported, motor functions were assessed by an extensive test battery: Action Research Arm Test (ARAT), Arm Paresis Score, Box and Block Test (BBT), and Nine Hole Peg-board Test (9HPT).[16] A computerized movement analysis system (CMS 50; Zebris, Isny, Germany) was used to test each hand: whole-hand tapping, index-finger tapping, and pronation/supination. In addition, patients had to perform two target movements to either a 5-cm or a 0.8-cm diameter target. Data analysis was performed yielding the following measures: frequency (FREQ), number of inversions of velocity profiles per movement segment (NIV), average maximum angular velocity (VMAX), and maximum velocity of the wrist (V2).[16] There were no significant differences in pretesting of motor functions between groups (Table 3).

The measures derived from the motor test battery (CMS, ARAT, Arm Paresis Score, BBT, 9HPT) were used to assess the effect of the music-supported therapy and constituted the dependent variables. These were entered into an ANOVA design with group (MG versus CG) as between-subjects factor and timepoint (pre versus post) as within-subjects factor. Group × timepoint interaction effects were taken as evidence of differential effects of treatment in the

two groups. Moreover, to determine the size of the treatment effects Cohen's d was computed for each group separately.[27]

Conventional therapy. All participants, CG and MG, received standard therapies according to the instructions of the attending neurologists, including individual physical therapy, individual occupational therapy using different materials, and group therapies, each 30 min in duration. MG patients received 29.2 units and CG patients 28.3 of conventional therapies within the 3-week study period.

Music-supported therapy. The music-supported therapy comprised 15 sessions of 30-min duration over 3 weeks and was administered individually in addition to conventional treatment. The CG only received conventional therapy.

Two different input devices were used, a MIDI-piano and an electronic drum set consisting of 8 pads, each with a 20-cm diameter, arranged in front of the patient. The drum pads (designated by numbers 1–8) were used to produce piano (G/A/B/C/D/E/F/G) rather than drum sounds. Similarly, the MIDI-piano was arranged in such a way that only 8 white keys (G/A/B/C/D/E/F/G) could be played by the subject. This offers the advantage of an input device practicing fine-motor skills (piano) and another input instrument practicing gross-motor skills (drum set), while keeping the output constant. From experience gathered in a number of pilot patients, a modular training regime with stepwise increase of complexity was designed (described below).

Because of the different impairment patterns, some patients received treatment exclusively on the MIDI-piano ($n = 16$) or the drum set ($n = 2$), while others were treated using both instruments ($n = 14$, 15 min per instrument during each session).

For drum training, patients were seated on a chair without armrests or in their own wheelchair in front of 8 drum pads. The height and proximity of the drum pads were individually adjustable, because at the beginning of the experiment only some of the participants were able to hit the drums with their extended arm and some could only reach the lower drum pads. Each exercise was first played by the instructor (S.S.) and was subsequently repeated by the patient, starting with the affected extremity and then played with the affected and healthy extremity together. Similarly, patients were seated in front of the MIDI-piano and did the exercises.

The treatment was adaptable to the needs of the patients, in terms of the number of tones they were required to play, velocity, order, and limb used for playing. Furthermore, the degree of difficulty was systematically increased using 10 set levels. Every patient started the exercises (between 8 and 12 per session) at the lowest level by playing single tones or the same tone on the same drum pad or key. If patients successfully managed this task, they continued on to the next level; if not, the previous task was repeated.

In the subsequent levels, patients were required to use an increasing number of tones until all 8 tones could be played in varied sequences. The most difficult level required patients to play children's or folk songs consisting of 5 to 8 tones with the paretic hand. Twenty different songs were available for the 8 tones (e.g., "Ode to Joy"). Frequent repetitions of identical movements, which have been proven essential for motor learning, were required. All therapy sessions were applied and monitored by the instructor and documented for later analysis.
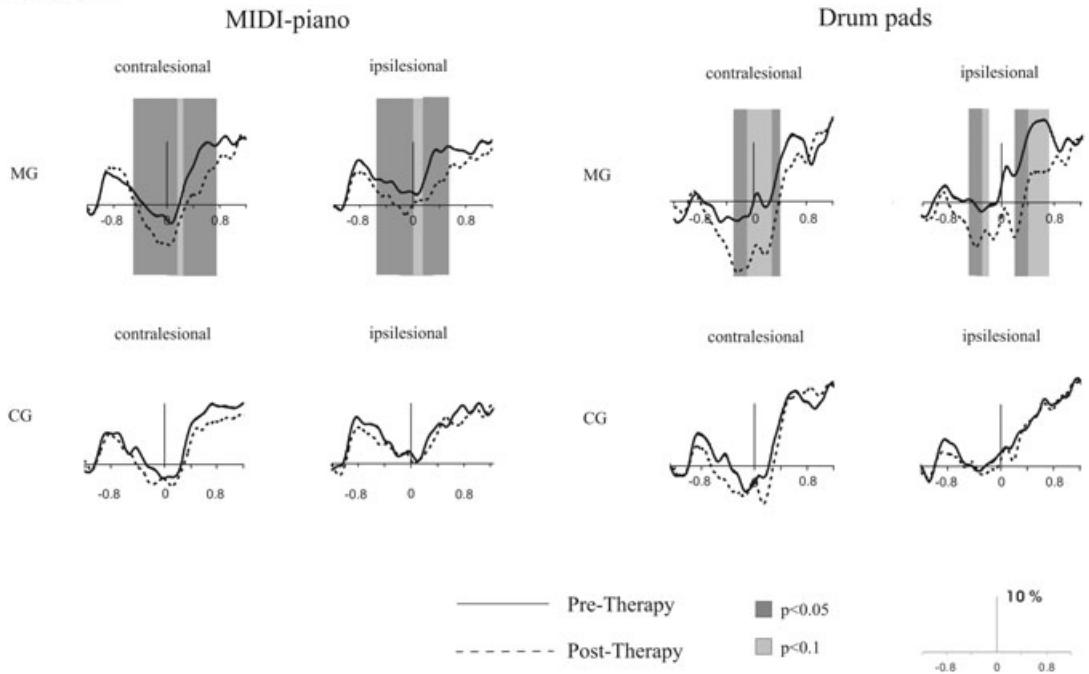
Results

ERD/ERS

In line with previous studies, a decrease of power prior to the response was observed for both studied frequency bands (Fig. 1). Pre- and post-treatment responses showed only small differences in the alpha band. However, in the beta band several differences between pre- and post-therapy conditions in the MG were observed, whereas there were almost no differences in the
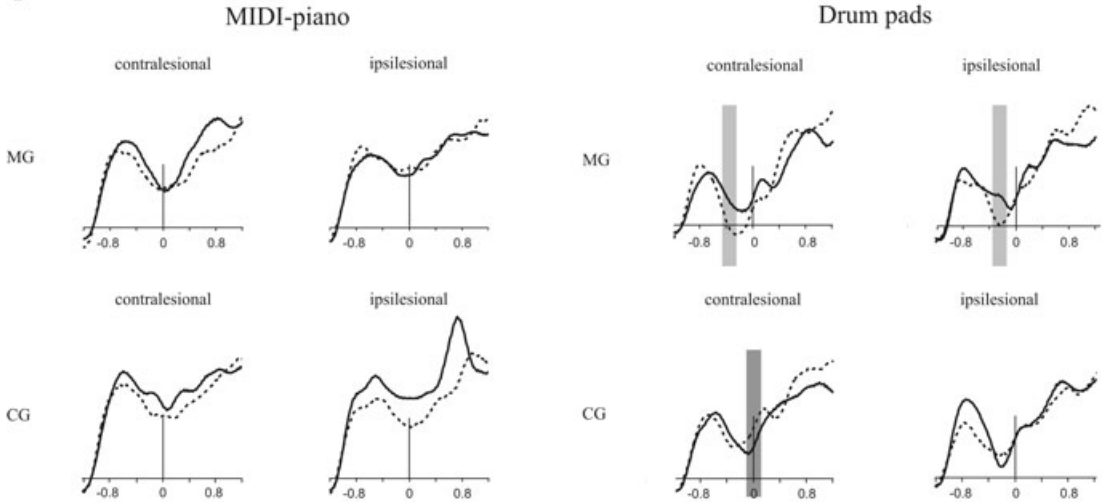
Figure 1. The results of the ERD/ERS analysis: differences of pre- and post-therapy responses in the alpha and beta band between MG and CG for the MIDI-piano and the drum pad condition in the affected extremity.

CG. Specifically, the MG showed a more pronounced decrease of beta power around the response (from -500 ms to 500 ms) in the post-treatment registration. This effect was more pronounced for movements with the affected limb.

Coherence

Figure 2 illustrates the electrode pairs that showed greater coherence in the post-measurement compared to the pre-assessment. Clearly, the MG presents a more pronounced
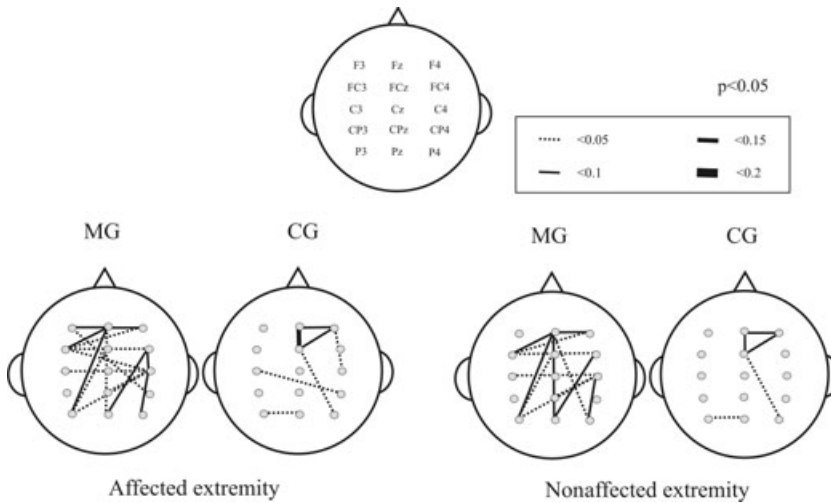
Figure 2. Topographic task-related coherence maps for the MG compared to the CG during self-paced arm movements for the drum pad condition in the beta band (18–22 Hz).

enhancement of coherence after the therapy compared to the CG, in particular for the drum conditions.

Motor Functions

As summarized in Table 4, significant improvements were restricted to the MG and found for all parameters with the exception of pronation/supination.

Effect sizes for MG patients were moderate (between 0.4 and 0.6, Cohen's d[27]) for all parameters with the exception of pronation/supination (VMAX) and 9HPT, for which effect sizes must be considered small. For the CG, all effect sizes were extremely small.

Discussion

Preliminary data have shown positive effects of music-supported therapy.[16] The present work extends these findings to a larger group of patients suffering from incomplete paresis of an upper extremity. For the MG, but not for the CG, we found clear improvements regarding the range of possible movement and, the speed and quality of movements as well as the generalization of treatment benefits to real-world situations.

Electrophysiology

Electrophysiological measures, that is, movement-induced ERD/ERS and coherence, showed profound therapy-related changes. For hand movements, ERD typically starts about 1–2 s prior to movement onset over contralateral sensorimotor areas and becomes bilateral at the time of movement onset[18,19] and is followed by ERS.[17] It has been proposed that ERD during movement preparation and execution is linked to cortical activation,[20] whereas postmovement ERS visible primarily in the beta band is a correlate of cortical resting state. We found a significant decrease of power (ERD) predominantly in the beta range before movement onset in the post-therapy session in the MG. In accordance with previous studies, this can be interpreted as an increased activity of motor regions, which corresponds to the more pronounced improvement of motor functions in this group.

Moreover, there was a significant enhancement of the coherence in the post-therapy session in the MG. Coherence has previously been

TABLE 4. Results of the Motor Tests: Mean (SD)

Motor tests/parameter	MG		CG	
	Pre	Post	Pre	Post
FREQ finger tapping in Hz**	2 (1.4)	2.8 (1.5)	1.6 (1.4)	1.6 (1.5)
VMAX finger tapping in °/s *	160.2 (105.5)	216.9 (105.1)	126.8 (112.1)	112.7 (114)
NIV finger tapping*	1.7 (0.3)	1.3 (0.3)	2.1 (0.4)	2.4 (0.4)
FREQ hand tapping in HZ*	1.8 (1.4)	2.4 (1.6)	1.5 (1.4)	1.4 (1.6)
VMAX hand tapping in °/s *	102.5 (80.1)	158.9 (152.8)	100.6 (110.8)	67 (72.1)
NIV hand tapping*	1.9 (0.3)	1.5 (0.3)	2.5 (0.4)	2.9 (0.4)
FREQ pronation/supination in Hz	1.2 (0.8)	1.6 (1)	1.2 (1.1)	1.2 (1.1)
VMAX pronation/supination in °/s	398.8 (354.7)	420.8 (298.7)	423.1 (462.2)	395.5 (380.5)
NIV pronation/supination *	2 (0.3)	1.5 (0.3)	2.3 (0.4)	2.3 (0.4)
V2 target movement 5 cm in mm/s **	456.7 (232.1)	614.1 (276.8)	479.4 (373.9)	463.1 (373.6)
V2 target movement 0.8 cm in mm/s *	487.5 (243.4)	595.9 (284)	464.4 (366.8)	451.3 (363.3)
ARAT (score)**	33.3 (23.9)	41.4 (17.6)	36.4 (23.3)	36.9 (23.3)
Arm paresis (score)*	4.5 (2.8)	5.9 (1.8)	4.7 (2.8)	4.8 (2.8)
BBT (score)**	25.12 (17.6)	35.1 (18.3)	30.8 (21)	32.5 (20.9)
9HPT (score)*	4.1 (4)	5.4 (3.5)	4.9 (4.1)	4.9 (4.1)

Note: Group by timepoint interaction **$P < 0.001$, *$P < 0.05$.

used to characterize functional interactions between brain areas during motor behavior,[28–30] and it has been argued that changes in functional connectivity can be used to infer shifts of interregional information communication.[30] In particular, coherence in the beta band has been demonstrated to have a strong association with motor function.[31] We found a dramatic therapy-related increase in coherence in the beta band in the MG but not in the CG, which suggests that interregional communication or, in other words, neural reorganization, was induced to a much greater extent in the MG.

Thus, evidence for neural reorganization induced by music-supported therapy is provided by the current study. We will therefore consider which aspects of the therapy may be responsible for these neural changes.

Music-supported Therapy as Massed Practice

One important aspect to consider is to which degree the effects observed in the present study are due to the specific aspects of the treatment (e.g., the practice with musical instruments) or to unspecific aspects, such as massed practice. To answer this question, a comparison with CIMT is promising. This approach involves massed practice with (1) motor restriction of the unaffected extremity by a splint/sling for a period of 12 days and (2) training of the affected extremity by a procedure termed "shaping" for approximately 6 h/day for 8 weekdays. Sterr and colleagues investigated the efficiency of CIMT and concluded that the effective factor in the CIMT appears to be the extended and repeated use of the paretic arm, whereas the mechanical restriction of the healthy extremity seemed less important.[5,6] With regard to the "dose" of repetitive movements the CIMT protocol of Sterr and Freivogel called for 6 h/day, 3 h/day or 1.5 h/day of practice, which compares to "only" 15 sessions of 30-min duration in the present study.[6] Standard CIMT treatment protocols have yielded effect sizes of 0.46 and between 0.34 and 0.45 for dexterity of the paretic arm.[3,32] Although the duration of sessions was considerably shorter in the current study, it nevertheless produced effect sizes of up to 0.6. This suggests that in addition to movement repetition, other factors might be important for the effectiveness of music-supported

therapy. We will discuss these factors in the following sections.

External Auditory Feedback: "Melody and Rhythm"

There are at least two relevant aspects of auditory feedback provided by the use of musical instruments. First, the presence of an immediate direct auditory feedback provides additional information about the movement outcome. In the music-supported therapy, each movement and, for complex sequences, each step of the movement is associated with feedback, and thus constant information is provided on the quality of timing of the movement. In as much as stroke has been reported to lead to an impairment of proprioceptive feedback information,[33,34] external musical auditory feedback may serve to counteract this deficit. Second, two types of feedback (pitch contour and rhythm) are provided for more complex movements, which may help to shape the quality of the movements of the disabled limb. In this sense auditory musical feedback might be superior to visual feedback in the shaping of motor functions, which has been investigated in a number of experimental settings.[35–37]

Auditory–Motor Coupling

To perform music, a high-speed mechanism is needed to control complex movement patterns under continuous auditory feedback. As a prerequisite, audiomotor integration at cortical and probably subcortical levels has to be accomplished. This audiomotor coupling is established during the learning and training phases and could be compared to the oral–aural loop in language processing. A number of recent studies attest to the rapid effects of audiomotor coupling during music-making in novice participants.[12–15] A number of further findings strengthen the argument for audiomotor coupling as a powerful mechanism shaping motor functions: (1) the contralateral motor cortex is involuntarily activated in pianists when listening to well-performed piano music,[38] (2) expert violinists when silently tapping a song show activity in the primary auditory regions,[39] (3) novice piano players show enlarged motor cortical regions after 5 days of 2-h piano lessons,[40] and (4) these plasticity effects related to motor skill acquisition appear within minutes after the begin of practice.[41] The idea of audiomotor coupling has some parallels with the mirror neuron concept, which refers to neurons that discharge during the execution of hand actions, during the observation of the same action made by others, or by listening to sounds related to the action.[42]

Conventional Therapy

It may seem odd that the control group, who received 28 units of conventional treatment on average, did not show improvement in any of the measures. This null effect is corroborated by previous observations, however.[1–4] Thus, the current study is not unique in casting doubt on the efficiency of conventional therapies in the remediation of motor deficits after stroke.

Conclusions and Open Questions

The present study demonstrated a pronounced effect of music-supported therapy on the recovery of motor functions paralleled by changes in electrophysiological indices of motor function (increase of ERD and coherence in the beta band). Thus, neural reorganization is facilitated by music-supported therapy. Patients in the MG group clearly outperformed those treated with conventional physiotherapy. An important next step will be to contrast music-supported therapy with one of the more established neuroscience-based rehabilitation techniques, such as CIMT. Also, the stability of the improvements needs to be assessed in further studies and the length and number of the therapy sessions might be manipulated in future research. A more general limitation of our approach is its limited applicability

in severely compromised patients, a limitation that is shared, however, with most of the other novel approaches.[16]

Conflicts of Interest

The authors declare no conflicts of interest.

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