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Mirror Therapy Promotes Recovery From Severe Hemiparesis: A Randomized Controlled Trial

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Background. Rehabilitation of the severely affected paretic arm after stroke represents a major challenge, especially in the presence of sensory impairment. *Objective*. To evaluate the effect of a therapy that includes use of a mirror to simulate the affected upper extremity with the unaffected upper extremity early after stroke. *Methods*. Thirty-six patients with severe hemiparesis because of a first-ever ischemic stroke in the territory of the middle cerebral artery were enrolled, no more than 8 weeks after the stroke. They completed a protocol of 6 weeks of additional therapy (30 minutes a day, 5 days a week), with random assignment to either mirror therapy (MT) or an equivalent control therapy (CT). The main outcome measures were the Fugl-Meyer subscores for the upper extremity, evaluated by independent raters through videotape. Patients also underwent functional and neuropsychological testing. *Results*. In the subgroup of 25 patients with distal plegia at the beginning of the therapy, MT patients regained more distal function than CT patients. Furthermore, across all patients, MT improved recovery of surface sensibility. Neither of these effects depended on the side of the lesioned hemisphere. MT stimulated recovery from hemineglect. *Conclusions*. MT early after stroke is a promising method to improve sensory and attentional deficits and to support motor recovery in a distal plegic limb.

Keywords: *Stroke rehabilitation; Arm; Mirror therapy; Randomized clinical trial; Motor recovery; Hemineglect*

Among the different syndromes following stroke, the severely paretic arm is one of the most devastating.[1] For its alleviation, few effective therapeutic options exist. Basic research demonstrated that the functional deficits after stroke are determined by factors that include the extent of structural damage and the level of cortical stimulation during active or passive movement of the affected limb.[2] This mechanism doubly disadvantages patients with severe hemiparesis. First, the motor impairment regularly prevents active use of the arm for functionally relevant activities, leading to a reduction of its cortical representation. Second, severe hemiparesis is often accompanied by sensory deficits.[3] Thus, even when limb usage is increased (eg, during therapies), the resulting cortical activation is limited.

As an alternative, mirror therapy (MT) has been proposed as potentially beneficial. For this approach, a mirror is placed in the participant's midsagittal plane, presenting the patient the mirror image of his or her nonaffected arm as if it were the affected one (Figure 1). This approach was first introduced by Ramachandran and coworkers for arm amputees, where the mirror image of the intact arm was used to simulate its amputated counterpart. By this procedure, illusory perceptions were induced and phantom pain in the "virtual" limb was often relieved.[4] MT was also postulated to alleviate chronic hemiparesis after stroke.[5] In their pilot study in 9 chronic stroke patients, Altschuler and colleagues reported effects of this treatment on "patients' movement ability in terms of range of motion, speed, and accuracy," especially for patients with severe hemiparesis.[6] Unfortunately, the effects of the therapy were not described in detail, which makes it difficult to understand the specific improvements achieved. Subsequently, mainly small scale case studies have been published, employing MT in combination with various other therapy approaches.[7-9] In a randomized controlled study on chronic stroke patients, Rothgangel and coworkers reported functional improvement during MT, but the 2 therapy groups differed at baseline.[10] Recently, the benefit of MT for the recovery of lower limb movements in subacute and chronic stroke patients was demonstrated in a high-quality randomized controlled trial design.[11]

The concept of MT has been further substantiated neurophysiologically. An imaging experiment demonstrated that inversion of the visual image of a hand can elicit lateralized cortical activations.[12] In other words, when a right hand is used, but perceived as a left hand, this leads to an additional activation of the right hemisphere (and vice versa). As recovery

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Figure 1
Setup for Mirror Therapy

Note: The patient's affected arm is hidden behind the mirror. While she is moving her unaffected arm, she is watching its mirror image as if it were the affected one.

mechanisms are known to be most prominent within the first 3 months after stroke,[13] it is reasonable to assume that MT might be most effective when applied within this time window. In summary, there is increasing evidence that MT might be an effective method to support recovery from severe hemiparesis beyond more established rehabilitation procedures based on active or passive movement execution. However, it remains unclear which symptoms can be improved. Thus, the following single-blinded randomized trial was designed to evaluate the potential beneficial effect of viewing the mirror image of the unaffected upper limb on recovery in patients with severe hemiparesis early after stroke. As previous data indicated different degrees of lateralization for proximal and distal motor function,[14-16] these aspects were analyzed separately. Preliminary data have been reported in abstract form.[17]

Methods

Patients

Patients were recruited from all inpatient admissions at the Godeshöhe Rehabilitation Center between October 2004 and April 2006. Our study was restricted to patients with severe hemiparesis because of a first-ever ischemic stroke confined to the territory of middle cerebral artery, occurring no more than 8 weeks prior to study inclusion. Patients had to be between 25 and 80 years of age, able to follow the therapy instructions, and capable of participating in 30-minute daily therapy sessions. Patients were excluded if they had experienced previous strokes, major hemorrhagic changes, increased intracranial pressure, hemicraniectomy or orthopedic, rheumatologic, or other diseases interfering with their ability to sit or to move either upper limb. Lesion localization (cortical/subcortical) was assessed on the basis of the brain scans available (CT or MRI). Handedness, prior to the stroke, was assessed by self-report, or report of the family for aphasic patients.

As usual in Germany, the patients' individual health insurance had the final decision about the duration of inpatient rehabilitation. Thus, some study patients (see Results section) could not finish the study intervention because of early discharge. The study was approved by the local ethics committee and registered at Current Controlled Trials Ltd (ISRCTN31849226). All patients or their legal representatives gave written informed consent prior to the study. Consent was given separately for participation and videotaping.

Intervention Protocol

In addition to the standard therapy delivered at the rehabilitation center, all patients underwent 6 weeks of study intervention (30 minutes a day, 5 days a week) administered by one of the authors (A. Nakaten or J. Püllen). A standardized therapy protocol was designed, requiring the execution of arm, hand, and finger postures in response to verbal instructions. By variation of the number of different configurations required simultaneously, this protocol could be scaled according to the patients' actual level of performance (shaping). During MT, patients watched the mirror image of the unaffected arm as if it were the affected one. During control therapy (CT), no mirror was present, so patients had direct view of the affected arm. During both therapy interventions, patients were reminded to move their affected limb "as well as possible," in accordance with the initial protocol of Altschuler and coworkers.[18] Thus, the therapy protocol of both therapy groups did not differ in motor performance, but only in the type of visual feedback. Patients were informed about the existence of 2 therapy groups, but not about the study hypothesis. Thus, they were not aware about their allocation to the experimental group (MT) or control group (CT). To control for differences in motivation and cooperation during the therapy sessions, each treatment session included an estimation of the patients' vigilance (1-3; 2 representing normal) and alertness (1-3; 1 representing fully alert). The resulting estimates were averaged across sessions for each patient. Patients were excluded from the study if they missed more than 4 therapy sessions for any reason. Standard therapy at the hospital was applied without any restrictions. The amount of treatment with regular occupational therapy (OT), physiotherapy (PT), and activities of daily living (ADL) training, as well as the duration of antidepressant medication, was extracted from the patients' clinical documentation after discharge.

Therapy Allocation

One of the authors (C. Rietz) created sealed, numbered envelopes with the randomization sequence, allocating patients either to MT or CT. Others (C. Dohle, J. Püllen, A. Nakaten) selected subjects based on the inclusion and exclusion criteria. The seal was broken after study inclusion and completion of the initial testing procedures (see below).

Assessment

The primary outcome measures were improvements in the 7 upper limb subscores (see below) of the Fugl-Meyer test.[18] For patients with neglect symptoms, the results of the neglect testing served as secondary outcome measure. Additionally, the Action Research Arm test[19] and the motor part (first 13 items) of the Functional Independence Measure (FIM)[20] were recorded. The entire assessment was performed before (t1) and after the intervention (t2) and evaluated by independent raters. The Fugl-Meyer test and the Action Research Arm test were videotaped by one of the investigators (either A. Nakaten or J. Püllen) and assessed at the end of the study by 2 out of 3 independent raters who were not involved in the study. For each single item rating, the average value of the 2 raters' results was used for analysis. Motor FIM and neuropsychological testing were assessed by independent raters, who were not aware of the patients' group assignment, from the sections of OT and cognitive therapy. Prior to assessment, all raters received specific training on the tests used.

The Fugl-Meyer upper extremity test consists of a total of 63 items grouped into 9 parts (A to J), scoring all major neurological symptoms on an ordinal scale from 0 to 2, with 2 representing no deficit.[18] The total upper extremity motor score has been used and evaluated in a number of clinical studies.[21] Subdivisions of this score for proximal and distal function have been employed[22] and successfully correlated with electrophysiological measures.[23,24] For this study, 57 items were utilized, grouped for motor assessment and nonmotor assessment. For motor assessment, subscores for proximal arm (part A without reflex assessment = 15 items), hand (part B = 5 items), and finger function (part C = 7 items) were used. For assessment of nonmotor signs, the upper extremity subscores for surface sensibility (light touch, part Ha = 2 items), proprioception (movement mirroring, part Hb = 4 items), joint pain during passive movement (part J = 12 items), and range of motion (part J = 12 items) were employed. Interrater correlations served to validate this division. The Action Research Arm test consists of the 4 subscales grasp, grip, pinch, and gross movement. The test contains 19 movement tasks, with each task graded on a 4-point scale (total score ranging from 0-57). The motor part of the FIM contains 11 items, measuring performance in self-caring and mobility on a 7-point scale (total score ranging from 7-77).

Patients were classified as aphasic when their Token test t value was below 60. For assessment of hemineglect, several subtests of the Behavioral Inattention test (BIT)[25] (line cancellation, star cancellation, letter cancellation, figure and shape copying, line bisection, representational drawing, and article reading) as well as the omissions and reaction times in each visual hemifield in the tests of attentional performance (TAP) by Zimmermann and Fimm were employed. These tests have floor and ceiling effects at different neglect severities.[26,27] Thus, a 5-point neglect score was defined as follows:

(0) BIT = impaired (including drawing and copying), TAP = clearly impaired, many omissions, complete hemifield

(1) BIT = deficits in cancellation and bisection subtests, TAP = some omissions, not complete hemifield

(2) BIT = normal performance, TAP = single omissions, differences between sides

(3) BIT = normal performance, TAP = reaction time differences

(4) No signs of visual hemineglect

For any given patient and time, this rating was always unambiguous. For study purposes, it was applied independently by 2 blinded raters who discussed divergent judgments until they agreed on a common score.

Data Analysis

Data analysis was performed using SPSS for Windows, version 12.0.1. Only patients who completed the entire therapy course were included in the analysis. Patients who dropped out were lost to follow-up, thus an intention-to-treat analysis was not possible. Demographic variables were compared by unpaired *t* tests or *U* tests, depending on the results of the Kolmogorov-Smirnov test for normality of distributions. For Fugl-Meyer and Action Research Arm test scoring, Spearman correlation coefficients for each possible pairing of the 3 raters served as measures of interrater reliability.

Assessment of the therapy effect, on improvement in the different neurological modalities, was confounded by spontaneous recovery. Especially, it had to be considered that patients scoring better at the time of the initial testing were likely to reach higher final scores than those with worse initial scores. Thus, an analysis of covariance (ANCOVA) approach was used[28]: final values (measured at t2) in the different scores were subjected to an analysis of variance (ANOVA) with the therapy protocol (MT, CT) as the factor and the initial score (measured at t1) as the covariate.

The illusory experience during MT (ie, the divergence between the visual impression and the actually performed movement) is strongest when patients are not able to move their limb at all. This might lead to a greater therapeutic effect in this patient group.[6] Thus, the analysis for the 3 motor scores was performed separately for the subgroups of patients who obtained scores of zero at initial testing, ie, those that had no motor function at all (initial plegia). For ancillary analysis, the side of the lesioned hemisphere and the latency between stroke occurrence and study inclusion were included as cofactors and covariates. As hypotheses were prespecified, no adjustments were made to the reported *P* values. Effect sizes were calculated manually, implementing established formulas[29] into Microsoft Excel 2000.

Table 1
Demographic Data and Characteristics of Standard and Intervention Treatment

		Mean (SD) or Numbers		
Parameter	Normal Distribution	CT	MT	Level of Significance
Age (years)	+	58.0 (14.0)	54.9 (13.8)	ns
Men/women	–	13/5	13/5	ns
Right handed/left handed	–	18/0	16/2	ns
CT/MRI	–	13/5	14/4	ns
Cortical/subcortical lesion	–	15/14	15/14	ns
Lesion of the dominant/nondominant hemisphere	–	7/11	4/14	ns
Aphasia	–	6	4	ns
Latency between stroke and study inclusion (days)	+	27.8 (12.1)	26.2 (8.3)	ns
Amount of standard treatment				
Occupational therapy (hours)	+	12.3 (5.0)	14.7 (3.4)	ns
Physical therapy (hours)	+	23.8 (5.5)	24.7 (5.4)	ns
ADL training (45-minute units)	+	11.4 (6.5)	5.9 (6.2)	0.024
Antidepressive treatment (days)	–	21.1 (23.5)	25.0 (23.7)	ns
Intervention				
Duration (days)	+	47.0 (4.7)	45.8 (2.8)	ns
Number of sessions	–	29.0 (1.4)	28.6 (1.4)	ns
Mean vigilance	+	1.89 (0.21)	1.92 (0.23)	ns
Mean alertness	+	1.15 (0.21)	1.16 (0.15)	ns

Abbreviations: SD, standard deviation; CT, control therapy; MT, mirror therapy.

Power Calculation

Power calculation is dependent on the type of score that is employed (eg, neurological function or ADL capacity). Previous studies suggested that a specific intervention could result in increases on the basic sensorimotor level (such as that captured with the Fugl-Meyer subscores) with an effect size of about 0.4.[30] For severely affected limbs, effect sizes seem to be even higher.[31] Thus, supposing an effect size of 0.6, $\alpha = 0.05$, $1\text{-}\beta = 0.8$ and including the increase of power attained by use of the ANCOVA,[32] a total number of 36 patients was calculated to be necessary. Assuming a dropout rate of 33% and considering a further safety margin, we initially prepared to include 60 patients during the recruitment period. The study was not powered to detect differences on the Action Research Arm test or FIM scale, thus these values were not analyzed by means of the ANCOVA. During the recruitment period, it turned out that both the recruitment rate and the dropout rate were below expectations. Thus, the recruitment period was prolonged based on the observed figures, until the targeted figures were attained. No analysis was performed before finishing the entire intervention and assessment.

Results

Patient Characteristics

During the recruitment period a total of 48 patients met the inclusion and exclusion criteria, agreed to participate in the study, and were randomized. During the course of the study, 12 patients (6 in each group = 25%) dropped out. Reasons for patients dropping out were: transfers to acute hospital (CT = 2, MT = 1); medical worsening (CT = 1, MT = 0); lack of cost approval by the health insurance (see methods section; CT = 1, MT = 4); or withdrawal of patients' consent (CT = 2, MT = 1). Thirty-six patients finished 1 of the 2 therapy protocols. There were 18 in each group. Their demographic data and details of their treatment course are depicted in Table 1.

The only statistically significant imbalance between both groups was the amount of ADL treatment, disadvantaging the MT group. No significant differences could be established for any other demographic parameter, either in the entire group or in any of the subgroups described below. Patients' attention and vigilance during study performance (as markers for patient cooperation and potential treatment bias by the nonblinded therapists) were similar in both groups.

Interrater Reliability

The interrater correlation coefficients for each possible pairing of the 2 raters are shown in Table 2. All correlations were significant at $P < .0001$, thus even higher than those reported previously,[33,34] and further justifying the use of the different Fugl-Meyer subscores in the study.

Therapy Effects

The mean values of the different Fugl-Meyer subscores are displayed in Figures 2 and 3. As apparent in the figures, the mean values of the motor subscores, surface sensibility, and proprioception improved in both therapy groups because of the spontaneous recovery and the standard therapy delivered at the

Table 2
Interrater Correlations of Fugl-Meyer Subscores and Action Research Arm Test (Based on Videotaped Observations)

	Interrater Spearman Correlation Coefficients		
	Rater 1 and 2 (n = 42)	Rater 2 and 3 (n = 5)	Rater 1 and 3 (n = 25)
Fugl-Meyer subscores			
Motor arm	0.997	1.000	1.000
Motor hand	0.991	1.000	0.977
Motor finger	0.996	1.000	0.996
Touch	0.947	1.000	1.000
Proprioception	0.995	1.000	1.000
Range of motion	0.985	1.000	1.000
Pain	0.974	1.000	0.979
Action Research Arm test	0.998	1.000	0.998

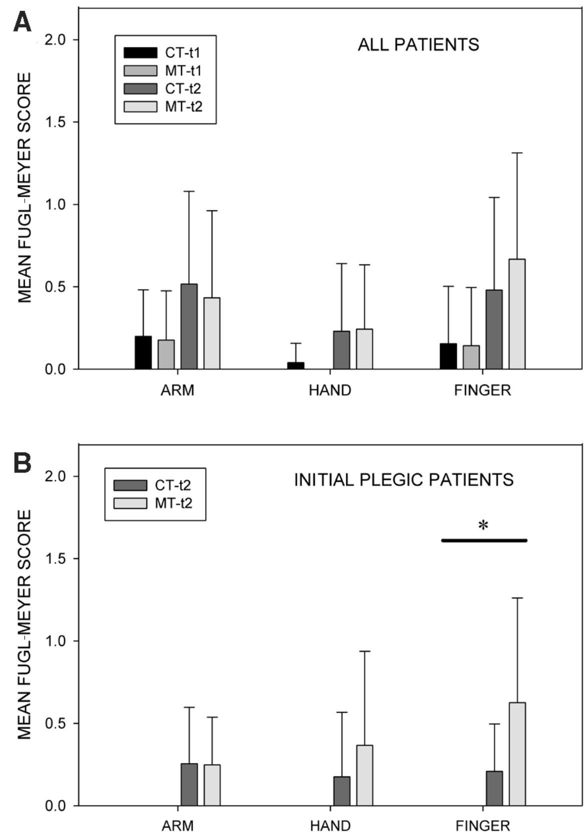
hospital. Subscores for range of motion and pain showed a slight decrease from nearly normal values at t1, suggesting that these symptoms only occur in the subacute and chronic stage after stroke. All significant therapy effects reported below were in favor of the MT group. No adverse events or side effects were noted in any of the 2 therapy groups.

Regarding motor function, there was no significant therapy effect in any of the 3 motor subscores across all patients (Figure 2A). Only the finger motor score revealed a tendency that failed to reach significance (F [1, 35] = 0.9, ns). This tendency was because of a significant difference in the subgroup of those 25 patients who were initially distal plegic (Figure 2B; F [1, 24] = 4.4, *P* = .048, effect size ε = 0.78). In absolute terms, mean improvement of the MT group was 4.4 (95% CI = 2.4-6.4) on the 14-point Fugl-Meyer subscale compared to a mean improvement of 1.5 (95% CI = –0.6-3.6) in the CT group. For the patient subgroups with initially plegic hand (n = 34) and arm (n = 18), no difference between the 2 therapy groups could be established.

The beneficial effect of MT had also functional consequences for regaining useful reach and grasp movements, as assessed with the Action Research Arm test (Table 3). Among the initially distal plegic patients who received CT, only 1 out of 12 made improvement at the functional level (Action Research Arm test > 1) where the post-therapy score was 2.5. In the MT group, this was true for 4 out of 13 patients, where the maximum score was 21.

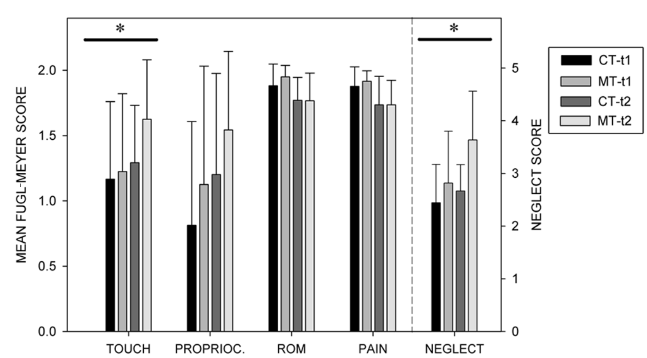
Regarding nonmotor symptoms, improvement of surface sensibility (light touch) was significantly different between the 2 treatment groups (Figure 3; F [1, 35] = 7.7, *P* = .009, effect size ε = 0.57). In absolute terms, mean improvement for MT patients was 0.8 (95% CI = 0.5-1.1) compared to 0.2 (95% CI = –0.1-0.5) for CT patients on the 4-point Fugl-Meyer subscale. For proprioception, the final difference between therapy groups was not because of an effect of therapy (F [1, 35] = 0.4,

Figure 2
Group Data of the Mean Fugl-Meyer Motor Subscores (Normalized to 0-2 Points for Each Category)



Note: Indicated are mean values and standard deviations of the patient groups receiving control therapy (CT) or mirror therapy (MT) before the intervention (t1) and after it (t2). Upper panel (A) shows group data of all patients, and lower panel (B) shows group data of the 3 subgroups of patients with no function at all at t1 in the different motor categories (see Methods/Results sections).

Figure 3
Group Data of Nonmotor Symptoms



Note: Left, shows mean Fugl-Meyer nonmotor subscores (normalized to 0-2 points for each category) of all patients; right, shows neglect scores (see Methods section) for the 20 patients with neglect symptoms at t1. Indicated are mean values and standard deviations of the patient groups receiving control therapy (CT) or mirror therapy (MT) before the intervention (t1) and after it (t2).

Table 3
Results of Functional Testing for the Entire Group and the 2 Subgroups With Statistical Significant Effects

Patient Population	Therapy Group	Mean ARAT (SD)		Mean Motor FIM (SD)	
		Initial (t1)	Final (t2)	Initial (t1)	Final (t2)
All (n = 36)	CT (n = 18)	0.8 (2.1)	3.9 (7.9)	43.9 (13.1)	60.8 (13.0)
	MT (n = 18)	0.6 (2.1)	4.7 (12.5)	48.3 (12.3)	66.6 (9.4)
Initially distal plegic (n = 25)	CT (n = 12)	0.0 (0.0)	0.4 (0.8)	42.3 (12.9)	58.4 (14.2)
	MT (n = 13)	0.0 (0.0)	2.5 (5.8)	47.5 (12.6)	65.8 (9.2)
Former right-handed patients with right hemispheric lesions and neglect (n = 20)	CT (n = 9)	1.5 (2.8)	7.4 (10.3)	36.7 (11.2)	50.1 (9.4)
	MT (n = 11)	0.8 (2.7)	6.8 (15.8)	41.3 (10.3)	54.8 (9.8)

Abbreviations: ARAT, Action Research Arm test; SD, standard deviation; FIM, Functional Independence Measure; CT, control therapy; MT, mirror therapy.

ns), but rather to differences at the baseline level. Range of motion and pain showed no therapy effect at all.

Signs of hemineglect at the beginning of the therapy were present in 20 out of the 24 right-handed patients with right hemispheric lesions (CT = 9/11, MT = 11/13). Among these patients, improvement of the neglect score was significantly greater in the MT group (mean = 0.9, 95 % CI = 0.6-1.2) than in the CT group (mean = 0.2, 95% CI = –0.2-0.5) (Figure 3; $F[1, 19] = 10.4$, $P = .005$, effect size $\varepsilon = 0.99$).

For the level of ADL capacity (as measured with the motor FIM), no difference between both therapy groups could be established either in the entire group or in the relevant subgroups (Table 3). Small differences favoring the MT group were already present at the beginning of the therapy. Even though the CT patients received significantly more ADL training, this difference persisted after treatment.

When included as a second factor in the ANCOVA, no analysis revealed a significant effect of the side of the lesioned hemisphere—whether anatomical (right/left) or functional (dominant/nondominant). Similarly, inclusion of latency between stroke occurrence and inclusion into the study as a second covariate showed no effect. Furthermore, there was no obvious effect of lesion locus (cortical or subcortical; Table 1). More detailed lesion analysis was not possible because of the lack of brain scans of equal quality (ie, MRI) for all patients.

Discussion

We demonstrated, in the present study, that application of MT in the early phase after stroke resulted in functionally relevant improvements in motor, sensory, and attentional domains. These improvements were not because of a nonspecific, global, beneficial effect. Besides, as demonstrated by the assessment of vigilance and alertness of patients in the MT and CT groups, they cannot be attributed to a treatment bias caused by insufficient blinding. The effects are in accord with basic neurophysiological findings, confirming a role of observing mirrored movement in cortical stimulation.

Regarding improvement of motor functions, it has been demonstrated that observation of mirrored distal movements enhances corticospinal excitability, similar to actual movement execution.[35,36] Apparently, this modulation of excitability contributes to motor recovery, even in an initially plegic limb. In our study, this effect is only present for distal arm muscles and not for proximal arm muscles. This is in accord with previous data, demonstrating a different contribution of both hemispheres for proximal and distal motor functions.[14-16] There is evidence that the distal component is organized strictly unilaterally,[37] whereas proximal movements rely more on bihemispheric representations.[38] Thus, we propose that movement mirroring mainly stimulates lateralized motor representations for the distal limb.

The improvement of sensory deficits further confirms the tight coupling of vision and touch. It has been shown that movement observation modulates not only motor cortex excitability, but also cortical somatosensory representations.[39] Viewing a stimulated body part enhances discrimination ability both in normal and in brain-damaged participants,[40] accompanied by changes in excitability of the primary somatosensory cortex.[41] Watching stimulation in a mirror can lead to a referral of sensation to the other hand.[42] Our results indicate that these cross-modal processes can also be employed therapeutically for long-term enhancement of somatosensory perception. This further supports the hypothesis that patients with sensory deficits benefit especially from MT.[7] However, our results on somatosensory function are only based on the surface sensibility subscore of the Fugl-Meyer test. Although less detailed than the motor subscores, these scores are still sufficiently valid.[32,33] Additional studies are required to explore the effect of MT on sensory functions more specifically.

The impact of MT on attentional processes is further illustrated by its beneficial effect on hemineglect. Interestingly, Ramachandran and coworkers originally proposed alleviation of hemineglect the other way around. They tried to stimulate awareness for the affected side by placing a mirror on the unaffected side of neglect patients.[43] In our study, the mirror was placed in the neglected hemifield. Apparently, watching a healthy moving arm and hand in the neglected hemifield provides a stronger stimulus for recovery from neglect than watching the attempted movements of a paretic side. One may assume that this improvement of hemineglect promotes recovery in the motor and sensory domain. In our study, however, similar sensorimotor improvements were observed for patients with lesions of the dominant and nondominant hemisphere. It should be pointed out that our neglect rating was based on a score that we devised and the validity has not been proven explicitly. Thus, we regard the improvement of hemineglect as a positive side effect whose independent therapeutic value remains to be proven. At the very least, we have demonstrated that MT is also successfully applicable for patients with severe hemineglect. Again, further studies are required to explore the interplay between recovery in the attentional and sensorimotor domain more specifically.

The contribution of distinct cortical areas to the processes mediating recovery, and thus the precise mechanism of MT, remain speculative. Frequently, effects of MT are attributed to "mirror neurons," ie, neurons in the premotor area of both monkeys and humans that are active during observation of meaningful movements.[44,45] However, in the only imaging experiment on inverted visual feedback, lateralized activations were not recorded in the premotor area, but in occipital and posterior parietal regions.[12] We assume that the precuneus region (area V6) plays a decisive role. This area belongs to the neural network supporting the mental representation of the self.[46] It might well be that premotor areas are activated bilaterally, without lateralization because of the observed body side.[47] Thus, the beneficial effect of MT is possibly mediated by the visual illusion that actions carried out by oneself are performed normally. It is quite probable that this illusion can prevent, or at least reduce "learned non-use" of a paretic limb.[5]

In our study, the effects were observed in the subacute phase after stroke. Within the chosen time frame of 8 weeks after stroke, we found no influence of the latency between onset of symptoms and start of the therapy. It remains speculative whether this result would also be valid for chronic stroke patients (> 3 months). Recent imaging experiments suggest differential involvement of the ipsilateral and contralateral hemisphere during different phases of recovery from stroke.[48] It is not known, however, if this implies different therapeutic strategies in different recovery phases.[49] We assume that the basic therapeutic principle of repetitive, effective stimulation of the lesioned hemisphere remains valid, irrespective of the time interval between stroke and rehabilitation. However, it should be noted that the effects in our study are quite robust, despite the great individual variability in spontaneous recovery from stroke.[50]

MT therapy is very easy to implement, even in an acute setting, and patients can be instructed to train on their own.[7] However, the optimum procedure with regard to frequency, duration, and protocol remains to be established.[51] In our study, we only investigated the effect of the inverted visual feedback, thus active movements of the affected side were those within the patients' capabilities. However, MT can also be performed with passive movement of the affected limb, thus possibly adding the therapeutic value of bilateral arm training.[52] There is clinical and neurophysiological evidence that this therapy variant is even more effective than the one we used in our study.[36,53] For methodological reasons, we restricted our study to patients early after a first-ever ischemic stroke confined to the territory of the middle cerebral artery. In principle, however, the results could be generalized to all neurological conditions with severe hemiparesis because of a unihemispheric lesion.

Taking all our results together, we found a clear, functionally relevant effect of MT on sensorimotor recovery that is in good accordance with neurophysiological findings. The effect on regaining ADL capacity was less pronounced. In our study, the ADL testing of the 2 therapy groups showed some (not significant) difference at the baseline level, slightly advantaging the MT group. This difference was not reflected at the basic sensorimotor level. As only patients with severe hemiparesis with very limited functional capacity of the affected limb were included, initial ADL scoring mainly reflected patients' greater ability to use compensatory (ie, one hand) techniques. The higher amount of ADL training that was necessary for the control group supports this interpretation. The final ADL scoring represents both contributions from regained sensorimotor function in the affected limb and acquired compensatory techniques, which are difficult to disentangle.[54]

The effect of MT on recovery of basic motor functions appears to be most prominent for those patients who have no distal function at the beginning of the therapy. The recovery process might be further supported by gains in sensory function and a possible beneficial effect on hemineglect. This fact is of major importance both clinically and economically as many modern rehabilitative concepts, such as constraint-induced movement therapy, can lead to significant functional improvements, but only when some distal motor function is already present at the beginning of the therapy.[55,56] Based on our results, systematic application of MT in densely hemiplegic patients early after stroke might support the recovery of these motor functions, allowing progress to other forms of therapy. Thus, when integrated into a modern neurorehabilitative program, the long-term effect on arm function and ADL capacity of MT, applied in the early phase after stroke, might be even greater than the immediate effect we recorded in our study.

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