Thieme H, Mehrholz J, et al. Mirror therapy for improving motor function after stroke. Cochrane Database of Systematic Reviews 2012, Issue 3, Art # CD008449.

Design: Meta-analysis of randomized clinical trials

PICOS:

- **P**atient population: Adults with paresis of an upper or lower limb or both, caused by any type or severity of stroke
- **I**nterventions: Mirror therapy, defined as an intervention in which a mirror creates a reflection of a non-paretic upper or lower limb to give the patient visual feedback of normal movement of the paretic limb
- **C**omparison intervention: Usual or standard practice, placebo treatment, or any other control treatment exclusive of different mirror therapy regimens
- **O**utcomes: Motor function of upper or lower limb, measured on scales which permitted quantitative pooling; any measurement that evaluated motor function was eligible for inclusion
- **S**tudy types: Randomized parallel group and crossover trials; when crossover trials were included, only data analyzed in the first treatment period was analyzed

Study selection:

- Databases included MEDLINE, EMBASE, the Cochrane Stroke Group Trial Register, and other electronic databases through June 2011
- Hand searches were also done for German and other European conference proceedings
- Additional ongoing trials were searched for in existing search registers
- Two review authors worked independently to extract trial data and assess which articles met inclusion criteria
    - Risk of bias assessment emphasized randomization methods, concealment of allocation, intention-to-treat analysis, and blinding of outcome assessment
- Disagreements between authors were resolved through discussion, with attempts to contact the authors of the studies in order to clarify missing information

Pertinent results:

- Because motor function was reported with different measurement scales in different studies, the pooled estimates were done in terms of standardized mean differences, in which differences between mirror therapy and control are presented in terms of how many standard differences there are between groups
    - Conventional interpretation of this scale is that a difference of 0.8 SD or more is a “large” effect: 0.5 SD is “moderate,” and 0.2 SD is a “small” effect
    - Because of differences in populations and clinical features of mirror therapy, many pooled estimates showed considerable heterogeneity between studies

- A total of 13 studies with 506 participants were included in various analyses, depending on the outcome being measured and on the adequacy of the data
- For motor function at the end of treatment, 11 studies with 481 participants showed a significant effect size of 0.61 SD in favor of mirror therapy
    - Two studies which enrolled patients with Complex Regional Pain Syndrome (CRPS) contributed disproportionately to this pooled effect size; when these two studies were removed from the analysis, the pooled effect size was 0.31 instead of 0.61
    - Removing these two studies of CRPS patients also eliminated the heterogeneity of the pooled results
- For motor function after 6 months of follow-up, 4 studies with 157 participants had a significant effect size of 1.09 SD in favor of mirror therapy
- For activities of daily living at the end of treatment, data from 4 studies with 217 participants showed a significant effect size of 0.33 SD in favor of mirror therapy
- Sensitivity analyses were carried out on several outcome variables, in which studies which clearly met criteria for control of bias (such as blinded assessment, intention-to-treat analysis, adequate concealed allocation) were analyzed separately, in order to determine whether effect sizes remained significant when these biases were clearly controlled
    - Motor function at the end of treatment remained significantly in favor of mirror therapy for each of the risk-of-bias and quality analyses

Authors' conclusions:

- There is evidence for the effectiveness of mirror therapy for improving motor function after stroke
- Mirror therapy could be applied as an additional intervention in the rehabilitation of stroke patients, but no clear conclusion could be reached if mirror therapy replaced other interventions
- Results in favor of mirror therapy for activities of daily living are based on only 4 studies, and should be interpreted with caution
- The results in favor of mirror therapy were robust when factors such as control of bias and overall study quality were taken into account
- A single study showing a favorable effect of mirror therapy on spatial neglect should not be used to draw conclusions about this outcome

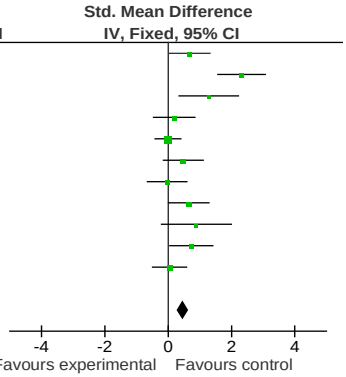
Comments:

- Both studies of CRPS were done in the same setting in Rome; for both studies, pain was the principal outcome measure and motor function was a secondary outcome (one of these studies was cited in the DOWC CRPS guideline)
- The effect size was inflated by the inclusion of the two CRPS studies for two reasons: first, the estimated effects of mirror therapy in terms of standard deviations were greater than for any of the other studies; second, these two studies were relatively small, and small studies contribute more weight in meta-analyses when a random effects model is chosen

- To illustrate this, the same pooled analysis which yielded an effect size of 0.61 SD in the random effects model produces an effect size of only 0.46 under a fixed effect model

	Experimental			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Acerra 2007	3.65	1.3	20	2.75	1.3	20	8.7%	0.68 [0.04, 1.32]
Cacchio 2009a	-1.5	0.7	24	-3.4	0.9	24	6.4%	2.32 [1.57, 3.06]
Cacchio 2009b	-2.2	0.7	8	-3.65	1.23	16	4.1%	1.28 [0.35, 2.22]
Dohle 2009	13.36	3.16	18	12.72	3.33	18	8.3%	0.19 [-0.46, 0.85]
Ietswaart 2011	31.51	20.68	39	31.61	20.63	63	22.4%	-0.00 [-0.40, 0.39]
Michielsen 2011	43.5	14	20	36.6	14.2	20	9.0%	0.48 [-0.15, 1.11]
Seok 2010	17.6	10.5	19	17.9	8.9	21	9.3%	-0.03 [-0.65, 0.59]
Stbeyaz 2007	3.5	0.8	20	3	0.7	20	8.8%	0.65 [0.01, 1.29]
Tezuka 2006	11.89	6.23	9	6.33	5.2	6	3.0%	0.89 [-0.20, 1.99]
Yavuzer 2008	3.62	1.23	17	2.79	0.99	19	7.7%	0.73 [0.05, 1.41]
Yun 2010	16.47	6.83	40	16.2	4.1	20	12.4%	0.04 [-0.49, 0.58]
Total (95% CI)			**234**			**247**	**100.0%**	**0.46 [0.27, 0.65]**

Heterogeneity: Chi² = 39.46, df = 10 (P < 0.0001); I² = 75%
Test for overall effect: Z = 4.79 (P < 0.00001)



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- Although the conclusion that mirror therapy increases motor strength in the stroke setting is not changed, the magnitude of that effect is more modest when only non-CRPS patients are analyzed
- The sensitivity analyses are helpful in illustrating that an effect of mirror therapy remains when bias is controlled and quality of reporting is adequate
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Assessment: High quality meta-analysis supporting evidence that mirror therapy may improve motor therapy following a stroke