Recovery pattern in chronic stroke post-physiotherapy : An fMRI study

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Introduction: Stroke is the leading cause of mortality and disability with a prevalence rate of 2.54 per thousand in India[1]. A number of neuroprotective and neurorestorative therapies aim to improve patient outcomes by salvaging the vulnerable tissue, or by promoting repair and restoration of function in the sub-acute or chronic phase. Physiotherapy forms the cornerstone of stroke treatment. The study is to evaluate the therapeutic effectiveness of mirror therapy, a form of virtual reality administered to stroke patients.

Methods: Six chronic ischemic stroke patients (all males, mean age = 52.1 years, SD=7.5) and six healthy controls (age matched, 4 male, 2 female, mean age 49.1years, SD=4.9) were recruited with the inclusion criteria of 2 - 3 months after the onset and within 2 years, MRC (medical research council) grade of wrist and hand muscles of at least >2; NIHSS (NIH stroke scale) of between 4 and 20, conscious and able to comprehend. The exclusion criteria were bleeding disorders, immuno-compromised subjects, any other brain lesion (tumours, infectious diseases), severe spasticity, comatose/ mechanically ventilated patients, pregnancy and contraindication to MRI. The study was approved by the Institutional Ethics Committee. Informed consent was taken from all the subjects prior to the participation in the study. They were assessed with fugel meyer, brunnstrom, barthel index and MRC grade of power of hand muscles pre and post physiotherapy. Functional MRI was performed to assess the effect of physiotherapy using block design with alternate baseline and activation task was used with a total of 80 whole brain EPI measurements (TR =4520ms, TE =44 ms, slices =31, slice thickness =4 mm).The subjects were asked to perform the motor task in the MRI scanner with paretic hand with self paced (minimum 0.5Hz) fist clenching / extension of the wrist / extension of the metacarpophalangeal (MCP) joints of the hands.

Intervention: The treatment incorporated bilateral hand exercises. The video of the unaffected hand/normal hand was captured using a web cam and the mirror image of the same was projected on the laptop screen to the subject. in such a way that the patient observed his unaffected / normal hand on the laptop screen, imagining it to be the paretic / affected hand(figure 1). The regime was administered to 5 days / week for 8 weeks which was hypothesized to result in facilitation and movement of the paretic hand as well.

Results: The Fugel Meyer scale, Barthel Index showed statistically significant improvement ($p \leq 0.001$) with treatment. The MRC and Brunnstorm showed mild improvements clinically which were statistically insignificant (t= -2.236, p=0.076 and t= -2.43, p=0.08 respectively). The laterality index for the contralateral primary (Brodmann Area 4) and premotor (BA 6) cortex also showed considerable increase post therapy (p=0.01) (table 1). A shift in the position of the coordinates of BA 4, 6 was also observed post therapy. Fractional anisotropy (FA) asymmetry index was calculated as ($FA_{unaffected} - FA_{affected}$)/ ($FA_{unaffected} + FA_{affected}$) and correlated well with the FM scores. Two of the patients (patient id 5, 6) showed an increased FA asymmetry (> 0.25) post therapy indicating that they had a lower functional potential which also correlated with the Fugel Meyer scores, suggesting that the corticospinal tract in these patients were depleted. The other four patients (id 1 - 4) showed an index of < 0.25 post physiotherapy indicating a good recovery. Infarct volume decreased marginally all the subjects after the treatment. The LI index and signal intensity of contralateral motor areas (BA 4, 6) increased consistently in all the subjects when measured post therapy.

Table 1. BOLD activation pattern and laterality index in pre, post-physiotherapy in stroke patients (showing voxel counts)

Pat ID	Location of MCA infarcts	Task	PRE TREATMENT									POST TREATMENT								
			BA 4		LI of Contr. BA 4	BA6		LI of Contr BA 6	Cerebellum		Ips CB ratio	BA4		LI of Contr. BA 4	BA6		LI of Contra. BA 6	Cerebellum		Ips CB ratio
			L	R		L	R		L	R		L	R		L	R		L	R	
1	Rt. parietal	LWE	60	112	0.30	150	343	0.39	-	-	0	-	1552	1	573	1685	0.49	1711	575	0.74
2	Lt parietal	RWE	-	-	0	141	120	0.08	280	-	0	5104	3141	0.23	5700	3361	0.25	3351	-	0
3	Rt caudate nucleus	LWE	-	237	1	-	120	1	429	313	0.57	-	303	1	-	303	1	-	-	0
4	Lt parietal	RFM	-	-	-1	623	116	0.68	106	179	0.63	509	199	0.87	1380	243	0.71	1131	186	0.14
5	Rt fronto parietal	LFM	-	-	0	416	195	-0.36	1593	-	1	20	138	0.74	554	701	0.11			0
6	Rt striato capsular	LFM	-	970	1	20	229	0.83	844	605	0.47	-	1712	1	60	1712	0.93	-	-	0

LWE: Left wrist extension; RWE: Right wrist extension; RFM: Right fist making; LFM: Left fist making; BA: Brodmann area; LI: Laterality index; C-I/C+I,
Ips CB: Ipsilateral cerebellum; ips CB/ Ips CB+ Contr. CB , BA 4: Primary motor cortex; BA 6: Supplementary/pre motor cortex; Rt: right; Lt: Left.

Discussion: Cortical reorganization depends on "recruitment" and "focusing" which is demonstrated by our results. Premotor area (BA6) takes over the function post therapy irrespective of the primary motor area (BA 4) being damaged or spared, exhibiting neural plasticity[3]. The increased activation of cerebellum also explains its role in the motor learning[4]. However, functional and clinical markers could not be very well established. Mirror therapy which is a form of observational learning leads to improvement in post stroke patients on clinical and functional markers[5].

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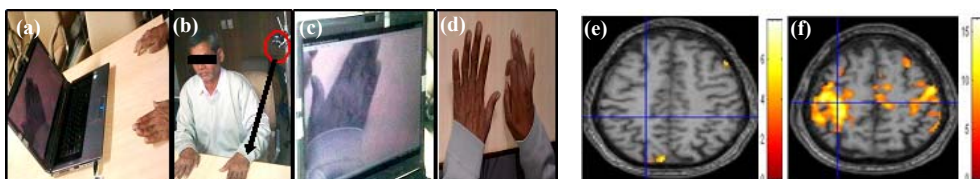
Figure 1. (a)-(d): inverted reflection for mirror therapy as captured by webcam and shown to the patient, followed by his efforts; (e) BOLD maps pretherapy (f) BOLD maps post-therapy from group average results overlaid on an anatomical image