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fMRI Analysis of Neural Mechanisms Underlying Rehabilitation in Virtual Reality: Activating Secondary Motor Areas

Katherine August, Member, IEEE, Jeffrey A. Lewis, Member, IEEE, Gayathri Chandar, Alma Merians, Bharat Biswal, Sergei Adamovich, Member, IEEE

Abstract— **A pilot functional MRI study on a control subject investigated the possibility of inducing increased neural activations in primary, as well as secondary motor areas through virtual reality-based exercises of the hand. These areas are known to be important in effective motor output in stroke patients with impaired corticospinal systems. We found increased activations in these brain areas during hand exercises in VR when compared to vision of non-anthropomorphic shapes. Further studies are needed to investigate the potential of virtual reality-based rehabilitation for tapping into the properties of the mirror neuron system to stimulate plasticity in sensorimotor areas.**

I. INTRODUCTION

VIRTUAL Reality (VR), a flexible computer generated environment used to develop exercise protocols for stroke rehabilitation, has been demonstrated to be effective in improving upper extremity motor function in adults with chronic stroke-related hemiparesis [1]. Underlying mechanisms of action, however, are poorly understood. Functional MRI compatible VR can be used to assess and track neural activation during exercises with somatosensory experience including manipulated or altered virtual experiences [2] modeled to stimulate 'mirror neurons' [3] associated with motor facilitation [4,5], and to determine activation of secondary motor systems important for effective motor output in stroke subjects with corticospinal system (CSS) impairment [6]. Stroke rehabilitation is moving into the realm of plasticity-mediated therapies [7] related to the ability of the adult brain to re-map functions, shifting regions of motor control to adjacent tissue [8,9,10], or the contralateral hemisphere [11,12,13] to take over functions of damaged cortical tissue. In a recent study involving patients post-stroke, a shift from primary to secondary motor networks was observed corresponding to the impairment of the CSS, with both hemispheres engaged in the generation of motor output. Secondary motor systems including ipsilesional posterior primary motor cortex, contralesional anterior primary motor cortex, bilateral premotor cortex, supplementary motor area, intraparietal sulcus, dorsolateral prefrontal cortex and contralesional superior cingulate sulcus, are important for effective motor output when there is impaired function of the CSS, although this strategy for movement is not optimal [6]. Properties of the mirror neuron system believed to exist in the human brain may explain the human ability to learn by imitation [14,15,16]. We are interested in tapping into the properties of the mirror neuron system to stimulate secondary motor systems and plasticity of motor control through our hand imitation VR rehabilitation.

Imitation exercises are more effective in activating pars opercularis of IFG during finger lifting than symbolic or spatial cues indicating importance of mirror neurons [17]. Visual guidance can reduce cognitive burden in stroke subjects compared with self-guided tasks [18]. In rehabilitation, compliance can be difficult to confirm [19]. Intelligent VR can provide imitation applications, visual guidance, and can monitor compliance, making VR an attractive choice for rehabilitation. Higher level functioning mediates motor skills learning by imitation (middle frontal gyrus for learning novel hand actions) [20]. Our hypothesis is that in the presence of VR protocols, a complex visuo-neuro stimulus can be achieved that engages mirror neurons for sensorimotor imitation, and secondary motor systems, known to be necessary for motor output in stroke patients while providing visual guidance, known to benefit stroke patients and older persons. We hypothesize that training and rehabilitation interactions in the VR environment might stimulate important cognitive networks. We believe that the training and rehabilitation in a VR environment that is matched for observation and action [21] is appropriate since it has been shown that performance improves for such task configurations. It has also been shown that presenting a first-person perspective for imitation, might stimulate more direct and stronger cognitive networks [27] than third-person perspective. Viewing virtual hand movement during VR exercises might activate hand-relevant parts of the brain

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Katherine August is a PhD Candidate with the Biomedical Engineering Department at the New Jersey Institute of Technology (phone: 732-673-1182; e-mail: ka38@njit.edu).

Jeffrey A. Lewis is with the Biomedical Engineering Department at the New Jersey Institute of Technology and with the Physical Therapy Program at the University of Medicine and Dentistry of New Jersey (e-mail: lewisje@umdnj.edu)

Gayathri Chandar is an MS student with the Biomedical Engineering Department at the New Jersey Institute of Technology (e-mail: gayathrichandar@gmail.com)

Alma Merians is with the Physical Therapy Program at the University of Medicine and Dentistry of New Jersey (e-mail: merians@umdnj.edu)

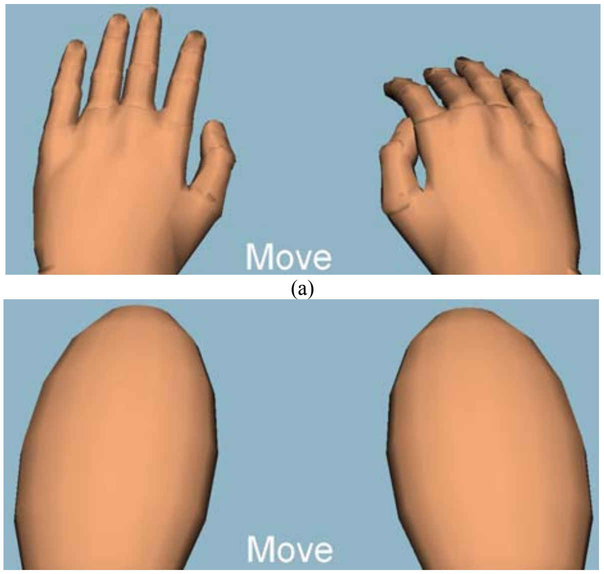
Bharat Biswal is with the Department of Radiology at University of Medicine and Dentistry of New Jersey (e-mail: biswal@umdnj.edu)

Sergei Adamovich is with the Biomedical Engineering Department at the New Jersey Institute of Technology (e-mail: adamovic@njit.edu)

(right MT/V5, left and right anterior IPS, right precentral gyrus, and right inferior frontal sulcus [21]), might promote engagement in feelings of ownership of the virtual hand [22,23], understanding goals of the observed virtual action [24], recognition of biological movement [25] of the virtual hand in the scene, and sense of self-awareness and agency [26,27]. Ultimately, this MRI compatible VR environment might enable analysis of the feedback and feed-forward realtime dynamics of the brain network associated with the interaction of visual recognition of actions and the control of actions [28]. We would like to determine whether secondary motor systems, recruited for motor control in stroke subjects with CSS injury, can be activated through engagement in hand VR training. Therefore, we conducted an initial pilot experiment in a VR environment using functional MRI.

II. METHODOLOGY

Images were obtained using a 3T Siemens Allegra imaging system. Single shot gradient echo (GE) axial EPI images (64´64, TR=1s, TE=27 ms, FOV= 22 cm x 22 cm, slice thickness = 4 mm, 32 slices) were acquired over 105 data points (210 seconds). The scan was obtained while subjects were instructed to perform hand exercises. Images were processed using AFNI software.



(a)

(b)

Figure 1. VR representation viewed by subject
a) Condition 1: Move while watching moving hand
b) Condition 2: Move while watching static oval shape

All data were tested for the presence of any head motion induced signal changes using image registration algorithm. A synthesized box-car waveform corresponding to the stimulus presentation cycle was cross-correlated with all pixels on a pixel-by-pixel basis for each data set to identify the regions activated by the task. The correlation-coefficient threshold of 0.5, after a Bonferroni correction, corresponded to a statistical significance of $p < 0.001$. All pixels that passed this threshold were considered activated and belonging to the sensorimotor and its associated cortex.

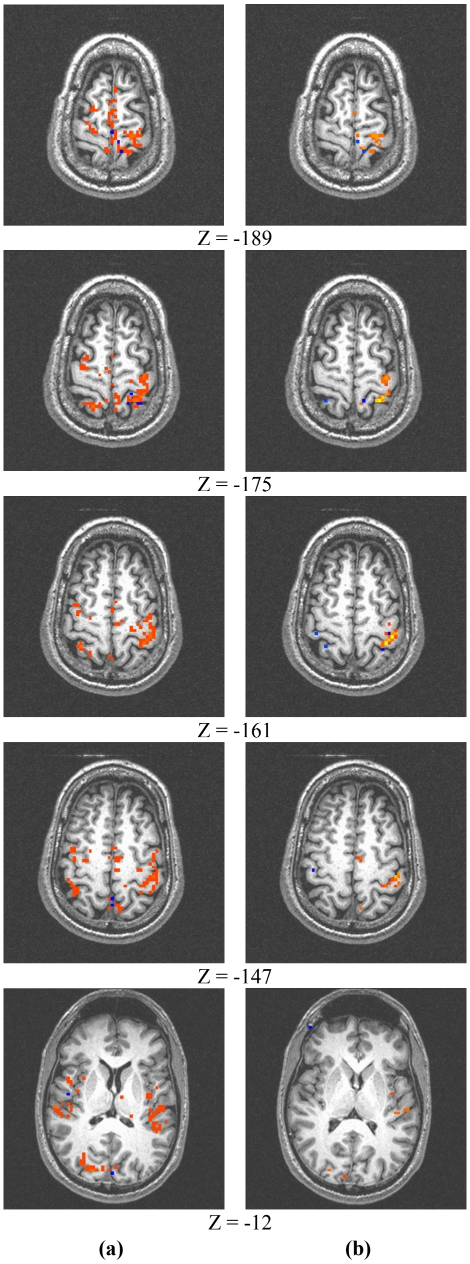


Figure 2. Slices at specified Talairach Z coordinate with highlighted significant increases in activation relative to baseline
a) Condition 1: Move while watching moving VR hand
b) Condition 2: Move while watching static oval shape
Right side of the brain is shown on the left.

In the trial experiment, the control subject is presented with a task to perform in the MRI environment, and in analysis, changes relative to a control state are mapped. A 41 year-old right-handed control subject participated in an imitation of hand movement protocol created in a three-dimensional VR environment. A 5DT MRI compatible VR glove was used on the subject's right hand to control the VR animated hand, to correlate brain activation with finger articulation, and to confirm subject compliance with instructions. Eight experimental runs were conducted, each beginning with a thirty second period of rest for baseline followed by four fifteen second test tasks separated by thirty second periods of rest.

The subject is first asked to watch the virtual hand animation (opening and closing of the hand at about 1 Hz), while intending to imitate the action. In Condition 1, he is asked to reproduce the observed hand motion by moving his right hand while watching the moving representation of his hand on the screen. In Condition 2, the subject moved his right hand while looking at oval shapes displayed on the screen the same color and size as the virtual hands (Fig. 1).

III. RESULTS

When we compare Condition 1 with Condition 2, we can see greater activation in a number of regions associated with the sensorimotor control of the hand in Condition 1 while the subject sees the virtual hand moving (Figure 2). In addition to increased activation in the primary motor cortex, we observed increased activation in a number of sensorimotor areas including dorsal premotor and supplementary motor areas, as well as anterior cingulate cortex, anterior intraparietal cortex and superior temporal gyrus. Analysis of the hand kinematics demonstrated that this increase in brain activation was not associated with any significant increase in the amplitude or frequency of finger motion (Figure 3).

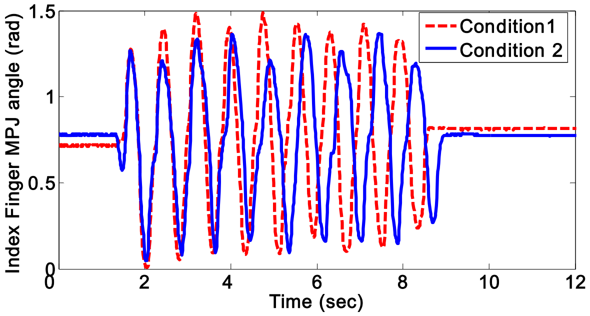


Figure 3. Representative example of angular displacements for the metacarpophalangeal joint (MPJ) of the index finger during brain imaging in Condition 1 and Condition 2.
Condition 1: Move while watching moving VR hand
Condition 2: Move while watching static oval shapes

IV. DISCUSSION

The control subject showed distinctly different activation under each condition. Relevant secondary motor systems were activated by observation of the virtual hand during exercises in the VR environment and were not activated when the subject performed the hand exercise in the absence of the virtual hand animation. The preliminary findings in this pilot study suggest that an imitation hand exercise protocol in VR might be an excellent choice for training stroke subjects since activation of secondary motor systems has been associated with successful motor skills performance in stroke subjects with CSS impairment. VR provides flexibility to manipulate visual feedback to the subject as part of the therapy, a desirable feature for stroke rehabilitation. Additionally, VR may be used to monitor compliance and to provide visual guidance for rehabilitation tasks.

Since multiple theories exist about brain plasticity and its role in motor skills recovery, we believe the computer-based intelligent VR physical therapy provides great opportunities to deliver therapy in a low-cost architecture, to study the mechanisms of human motor skills recovery, and to test these concepts through functional imaging while simultaneously measuring motor performance. It has been shown that an environment matched for observation and action improves performance [21], that first person perspective stimulates more direct cognitive networks, that viewing hands activates specific hand-relevant brain regions [22], that feelings of ownership of external objects can be developed [23,24], that a person can understand the goal of the movement in an exercise [25], that the brain can differentiate biological and linear movement through different regions [26], and that the effect of causal involvement, agency, can be experienced [26,27].

It is possible that use of the complex VR environment may expose the subject to these experiences and may therefore activate many brain regions associated with motor skills and related experiences. We also believe that complex feed forward and feedback interaction of visual processing of actions and the motor control of actions [29] may play a role in the rehabilitation of stroke subjects who are suffering from paralysis of the hand. A person may see their hand and its function more than most other parts of their body. Investigating the complex cognitive network associated with the perception and motor action of the hand might help to uncover relevant clues for rehabilitation of motor skills following stroke. Specifically, we are encouraged by the properties of mirror neurons and seek methods of accessing these properties to stimulate secondary motor systems recruited for motor movement in stroke subjects with CSS injury. VR enables development of rehabilitation systems and also investigation into this area. Future work will include extending this preliminary work to include additional control subjects, additional rehabilitation protocols, and studies including stroke subjects.

V. CONCLUSION

In our trial experiment, using functional MRI to understand underlying mechanisms of action of VR rehabilitation exercises, the subject trained in a VR environment for an imitation task resulting in desired activation of the brain regions associated with secondary motor systems. We are encouraged that through functional imaging experiments with VR, we will be able to understand underlying neural mechanisms leading to the development of rehabilitation protocols for imitation hand therapies for subjects suffering from various motor control issues such as stroke.

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