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Virtual Prism Adaptation Therapy: Protocol for Validation in Healthy Adults --Manuscript Draft--

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1 TITLE:

2 Virtual Prism Adaptation Therapy: Protocol for Validation in Healthy Adults

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KEYWORDS:

visuospatial neglect, prism adaptation, virtual reality, stroke, rehabilitation, depth-sensing camera, functional near infrared spectroscopy

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SUMMARY:

This experimental protocol demonstrates the use of virtual prism adaptation therapy (VPAT) in healthy adults and the association between VPAT and functional near infrared spectroscopy to determine the effect of VPAT on cortical activation. Results suggest that VPAT may be feasible and could induce similar behavioral adaptation as conventional prism adaptation therapy.

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ABSTRACT

Hemispatial neglect is a common impairment after stroke. It is associated with poor functional and social outcomes. Therefore, an adequate intervention is imperative for the successful management of hemispatial neglect. However, the clinical use of various interventions is limited in real clinical practice. Prism adaptation therapy is one of the most evidence-based rehabilitation modalities to treat hemispatial neglect. To overcome any possible shortcoming that may occur with prism therapy, we developed a new system using immersive virtual reality and depth-sensing camera to create a virtual prism adaptation therapy (VPAT). To validate the VPAT system, we designed an experimental protocol investigating the behavioral errors and changes in cortical activation via the VPAT system. Cortical activation was measured by functional near infrared spectroscopy (fNIRS). The experiment consisted of four phases. All four included clicking, pointing or rest applied to right-handed healthy people. Clicking versus pointing was used for investigating

the cortical region related with the gross motor task, and pointing with VPAT versus pointing without VPAT was used for investigating the cortical region associated with visuospatial perception. The preliminary results from four healthy participants showed that pointing errors by the VPAT system was similar to the conventional prism adaptation therapy. Further analysis with more participants and fNIRS data, as well as a study in patients with stroke may be required.

INTRODUCTION:

Hemispatial neglect, which affects the ability to perceive the contralateral hemispatial visual field, is a common impairment after stroke^{1,2}. Although rehabilitation after hemispatial neglect is important, due to its association with poor functional and social outcomes, rehabilitation is often underutilized in real clinical practice^{3,4}.

Among the various existing rehabilitation approaches suggested for hemispatial neglect, prism adaptation (PA) therapy has proven effective for recovery and improvement in hemispatial neglect in patients with subacute or chronic stroke⁵⁻⁸. However, conventional PA is underutilized due to several drawbacks^{9,10}. These include 1) high cost and time requirement due to the prism lens needing to be changed to adjust to the degree of deviation; 2) the need to set up additional materials to be pointed at and to mask the hand trajectory; and 3) PA can only be used by patients who can sit and control their head position.

A recent study reproducing the adaptation effects in the virtual reality (VR) environment reported that it may be possible for the virtual prism adaptation therapy (VPAT) to have different effects depending on the subtypes of neglect¹¹. It was also suggested that cortical activation for PA may vary according to brain lesions¹². However, little is known about the cortical activation pattern seen in VR-induced PA.

To overcome these obstacles and promote the use of PA in a clinical setting, we developed a new PA therapy system using an immersive VR technology called virtual prism adaptation therapy (VPAT), via the use of a depth-sensing camera. We designed an immersive VR system with the ability to provide visual feedback about the position of a virtual limb to promote spatial realignment¹³. Using this immersive VR technology, which mimicked the effect of conventional PA, we designed an experiment to validate the VPAT system in healthy participants.

By conducting our visualized experimental protocol, we investigated whether the new VPAT system can induce behavioral adaptation, similar to conventional PA. Additionally, we would like to explore whether the VPAT system can induce the activation in the cortical regions associated with visuospatial perception or recovery of hemispatial neglect after stroke.

PROTOCOL:

All procedures were reviewed and approved by the Seoul National University Bundang Hospital Institutional Review Board (IRB). To recruit healthy participants, posters were used to advertise around the hospital.

1. Experimental set-up

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90 1.1. Participant recruitment

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1.1.1. Perform the subject screening process using the following inclusion criteria: 1) healthy, between 18 and 50 years old; 2) right-handed, assessed by Edinburgh handedness inventory¹⁴; 3) able to wear the head mount display for VR and to detect objects within VR; and 4) no history of diseases affecting the brain, such as stroke, Parkinson's disease, or traumatic brain injury.

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NOTE: These criteria were designed to screen participants with the ability to participate in the experiment and regulate factors affecting the results.

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100 1.1.2. Recruit participants and provide a detailed explanation of the entire study and expected clinical issues. Consent must be obtained prior to inclusion.

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1.2. Experimental system

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NOTE: A customized VPAT system using an immersive VR system and depth-sensing camera was used. Functional infrared spectroscopy (fNIRS) was simultaneously used to investigate the cortical activation. VPAT and fNIRS were linked together for the experiment (**Figure 1**).

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109 **1.2.1. VPAT system**

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NOTE: The VPAT system consists of a head mount display for VR implementation, a hand tracking sensor that can recognize hand gestures for intuitive input by the user, and a hardware push button. The overall composition is shown in **Figure 1**.

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1.2.1.1. Make sure that the hand tracking sensor is not tilted in front of the head mount display.

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117 1.2.1.2. Check that the reference camera for the VR system is properly installed on top of the front monitor.

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120 **1.2.1.3.** Secure the push button in a location near the hand to be used by the participant for the experiment.

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123 1.2.1.4. Run the software to make sure there are no errors.

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NOTE: The virtual environment was implemented to match the actual environment as close as possible. The task was performed through hand pointing within the virtual environment and button input through the push button.

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129 **1.2.2. fNIRS**

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1.2.2.1. Use a commercial fNIRS system including a personal computer (PC), 31 optodes (15 light

sources and 16 detectors), textile EEG caps, and data recording software.

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1.2.3. Linkage between VPAT system and fNIRS (**Figure 1**).

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136 1.2.3.1. Use the remote keyboard control software using TCP/IP communication to synchronize the starting event in the VPAT system with the timing of recording in the fNIRS system.

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1.2.3.2. Use the remote command key in the computer to start fNIRS recording.

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141 2. Experimental set-up (Figure 2)

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143 2.1. fNIRS measurement setting

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2.1.1. Place the participant in a chair with his/her back in a straight posture, about fifteen centimeters away from the table. Confirm that the participant's hand does not hit the table when reaching out.

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2.1.2. For fNIRS cap setting, select the cap size according to the participant's head circumference.
Place the cap so that the vertex (Cz) is located at the intersection of the midpoint between the inion and nasion and the midpoint between the left preauricular and right preauricular areas.
Display the montage on the screen and connect 15 sources and 24 detectors to the montage. If necessary to improve the gain from the light source, use conductive gel after hair preparation and insert the optode. Have the participant wear a retaining cap.

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NOTE: The study used three different sizes of textile EEG caps with circumferences of 54, 56, and 58 cm.

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2.1.3. For software setting (calibration, etc.), run the fNIRS system software and load the neglect
 montage.

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162 2.1.4. Let the montage be displayed on the screen and set 15 sources and 24 detectors according to the montage (**Figure 3**).

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2.1.5. Press the calibrate button. If "**Lost**" is displayed on the screen, repeat the hair preparation, and then recalibrate.

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168 2.2. VPAT system setting

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2.2.1. Connect the HMD, reference camera, and Leap motion camera, and push the button connecting the computer to set up the VPAT system.

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2.2.2. Mount the virtual reality head-mounted display (VR HMD) on the participant's head over the cap for fNIRS. Make sure to avoid movement of the cap.

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2.2.3. Run the VPAT software. Enter the participant's information (name abbreviation, age, handedness) and press the "**Start**" button.

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2.2.4. Confirm the visualization of the virtual hand in the display. Proceed with a two-step calibration (i.e., screen calibration and target distance calibration).

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182 2.2.5. Instruct the participant to watch the red cross mark (+) in the center, then press the "r" key to calibrate the screen.

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NOTE: Screen calibration places the virtual space in front of the user's visual range by recentering the coordinate system.

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2.2.6. Instruct the participant to point to the target (i.e., ball) with his or her right hand, then press the "O" key to calibrate the hand position.

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NOTE: In our study, the object that the participant had to target was a white ball on a pink stick that came down from the top of the view. Target distance calibration places the target within the reach of the user. This is used to correctly position the target during the experiment.

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2.2.7. After calibration, press the "w" key to begin the experiment.

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2.3. VPAT and fNIRS linkage setting

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2.3.1. Use the event synchronization software to enter the trigger for analysis into fNIRS and connect VPAT to fNIRS.

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202 2.3.2. For time synchronization between VPAT and fNIRS, connect the computers with the two systems to the same network, and then synchronize them through the self-produced key transferring program.

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2.3.3. After connecting through the IP and Port inputs of both computers, start the experiment session via the "w" key in the VPAT program. The event synchronization software is executed automatically, and triggers during execution are automatically transferred to fNIRS and saved.

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2.3.4. After the experiment, obtain the software auto-termination and VPAT data. Then stop the VPAT and fNIRS system software.

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NOTE: The participants must return their hands to their original position after pointing during the VPAT experiment.

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3. Experiment to validate VPAT system

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3.1. Block designed experiment with fNIRS recording (**Figure 4**)

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220 3.1.1. After completing the set-up process in step 2, confirm the participant's readiness to start the experiment.

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223 3.1.2. Start the VPAT system without the prism mode and instruct the participant to point to the target in the VR system immediately for familiarization with the procedure.

225

226 3.1.3. Each phase consists of blocks for pointing, clicking, or resting (**Figure 4**). Again, instruct the participant to click on the button or point to the target in the VR system with their right index finger as quickly as possible.

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230 3.1.4. Start the experiment with four phases simultaneously with fNIRS recording by clicking the start key.

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NOTE: During the pointing task, the white ball had to be touched within a fixed time.

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235 3.1.4.1. Instruct the participants to point, click, or rest when the appropriate icon appears.

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NOTE: During the task, pointing and clicking were indicated by an icon directly above the white ball and right side of the timer bar. The time to perform the task was indicated by the timer bar as shown in **Figure 2**.

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3.1.4.2. Tell the participant to touch the target that appears on the left or right side within 3 s. For the clicking block, instruct the participant to press the push button.

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NOTE: The target set containing the white ball was located at a distance of -10° or 10° from the participant's center, obtained by calibration. The target set appeared randomly on the right or left side. According to the experimental design, the target appeared for 3 s, then disappeared, and then regenerated to a new position.

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3.1.4.3. Ensure that the participant performs the same way when the phase is switched.

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NOTE: In the pointing task, Virtual Prism Adaptation Mode showed a deviation of 10° or 20° to the left side of the imaginary hand in the VR space relative to the participant's head. Zero degrees indicated that the positions of the virtual hand and the actual hand coincided.

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NOTE: The experiment (**Figure 4**) consists of a total of four phases, with each phase consisting of pointing and clicking or rest alternately (Phase 1 and 4 were pointing and clicking, and phase 2 and 3 were pointing and resting).

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4. Data analysis

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4.1. Pointing error analysis

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NOTE: The data were stored from the moment the experimenter pressed the start button "w".

The data were automatically stored at about 60 Hz every frame through the VPAT software. The phase name, elapsed time, and virtual index finger position were stored over time. The pointing error was the angle value between the target and index finger, centered on the participant's head position.

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4.1.1. Classify the pointing task data by phases (pre-VPAT, VPAT 10°, VPAT 20°, post-VPAT).

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4.1.2. Classify the data of the pointing task and the clicking task in the data of each phase (phase 1 and 4).

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4.1.3. Classify the data by sub-phase in units of 30 s according to each phase and each type of task.

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4.1.4. Extract the median value of 10 trial error (pointing error) values from the index finger position data for median pointing error analysis.

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280 4.1.5. Use the repeated measures analysis of variance test (ANOVA) to analyze the difference between each phase.

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NOTE: In the case of hand tracking using the Leap motion sensor, outliers were due to occlusion or false detection of the hand posture. With the exception of false hand position data, the median value was used to find the representative pointing error value in the sub-phase.

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4.2. fNIRS data processing

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4.2.1. Launch the fNIRS analysis software and load the raw data file and probe information.

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4.2.2. Perform a marker setting process by editing the event record to verify each condition during the experiment.

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294 4.2.3. Carry out data preprocessing by deleting the experimentally irrelevant time intervals, 295 remove artifacts, such as steps and spikes, and apply frequency filters to exclude experimentally 296 irrelevant frequency bands.

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NOTE: All data sets were filtered with a 0.01 Hz high-pass filter and a 0.2 Hz low-pass filter to remove instrumental or physiological noise contributions.

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4.2.4. Specify wavelengths by entering the value of the peak illumination wavelengths (i.e., 760 and 850 nm). Use a physical distance of 3 cm between the source and detector for channel.

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4.2.5. Select the baseline field, which refers to the time period that corresponds to a baseline wherein participants are typically resting quietly.

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NOTE: We selected the baseline field as the full-time course of the data set, which was the default

308 setting.

4.2.6. Compute the time series of hemodynamic states to finish the preprocessing from the filtered data.

REPRESENTATIVE RESULTS:

Data from four healthy participants (1 man and 3 women) were used as representative results. A pointing error is shown in **Figure 5A**, with the averages of median value of 10 trials in the subphase of each pointing task lasting 30 s. Values on average for the median pointing errors in the first block of each phase were 0.45 ± 0.92 (pre-VPAT), 4.69 ± 3.08 (VPAT 10°), 5.43 ± 2.22 (VPAT 20°), and -5.17 ± 1.60 (post-VPAT). The trend of pointing error change was statistically significant (p = 0.001) via the repeated measures ANOVA. A pointing error for each subject is presented in **Figure 5B**, illustrating the adaptation during the VPAT phase and post-prismatic adaptation (negative pointing error).

FIGURE AND TABLE LEGENDS:

Figure 1: Experimental setting with VPAT and fNIRS linkage system. VPAT = virtual prism adaptation therapy; fNIRS = functional near infrared spectroscopy. This figure was previously published by Kim et al.¹⁵

Figure 2: The subject performing the experiment with VPAT and fNIRS system. VPAT = virtual prism adaptation therapy; fNIRS = functional near infrared spectroscopy.

Figure 3: Montage containing 54 channels by arranging 15 light sources (red circles) and 24 detectors (blue circles) at intervals of 3 cm. Space between the nearest sources and the detector constituted one channel, which is represented as yellow circles with a number.

Figure 4: Experimental design. VPAT = virtual prism adaptation therapy; Pt = pointing; Cl = clicking; Re = resting.

Figure 5: Pointing errors in each block. (**A**) Average value graph of subject's median pointing error in each block. This figure was previously published by Kim et al.¹⁵ (**B**) Median pointing error in each block by each subject. The counterclockwise direction (i.e. left from the target) is the positive value.

DISCUSSION:

This study implemented the prism adaption therapy using a translated hand movement in a VR environment. It investigated whether the deviation implemented was causing angle overshooting and behavioral adaptation, as in conventional prism adaption therapy.

In the median pointing error result (**Figure 5**) and the first pointing error result, the pointing error changed significantly when the phase was switched. Although some hand-recognition errors were eliminated, there may still be false detection. The use of a median value to eliminate systematic error, such as false tracking, showed that the average pointing error results were lower than

expected. Post-prismatic adaptation was constantly shown in each subject (**Figure 5B**). These results showed similar behavioral adaptation to the conventional prism adaptation therapy.

There were some problems in the experiment. False detection of the hand occurred frequently in the pointing task. In some cases, even though the hand reached the target during pointing, the virtual hand was not tracked due to a Leap motion recognition error. In addition, because the participants were wearing HMD in the clicking task, it was difficult for them to locate the push button and the experimenter had to provide continuous assistance. The weight of the HMD and its long-term application could also cause pain in the area that comes into contact with the fNIRS optode. Therefore, there were times when the HMD was lifted or the participants themselves were holding the HMD.

If we overcome the shortcomings of the system and consolidate the results of the experiment through more data analysis, including fNIRS data, it could potentially be used in the treatment of visuospatial neglect. In addition, game-friendly contents can be applied to present an immersive and fun treatment modality. Nonetheless, further study with a more advanced VPAT system proving clinical efficacy in stroke patients with visuospatial neglect is needed.

Several previous studies have reported motion sickness induced by the use of Immersive VR, or head-mounted VR sets¹⁶. Motion sickness is reported to be infrequent if VR is implemented in seated positions¹⁷. Motion mismatch can also cause motion sickness, but it can be reduced by independently configuring the background in the virtual environment^{18,19}. In this system, only the hand deviation angle caused motion mismatch, which should have less impact on motion sickness overall.

Participants in this experiment were normal adults, so there were no consistent problems. However, to be used as therapeutic treatment for stroke patients, the above issues need to be considered, and virtual prism therapy protocols need to be taken into account, such as taking breaks during treatment or the length of treatment time.

ACKNOWLEDGMENTS:

This study was supported by the Seoul National University Bundang Hospital Research Fund (14-2015-022) and by the Ministry of Trade Industry & Energy(MOTIE, Korea), Ministry of Science & ICT(MSIT, Korea), and Ministry of Health & Welfare(MOHW, Korea) under Technology Development Program for AI-Bio-Robot-Medicine Convergence (20001650).

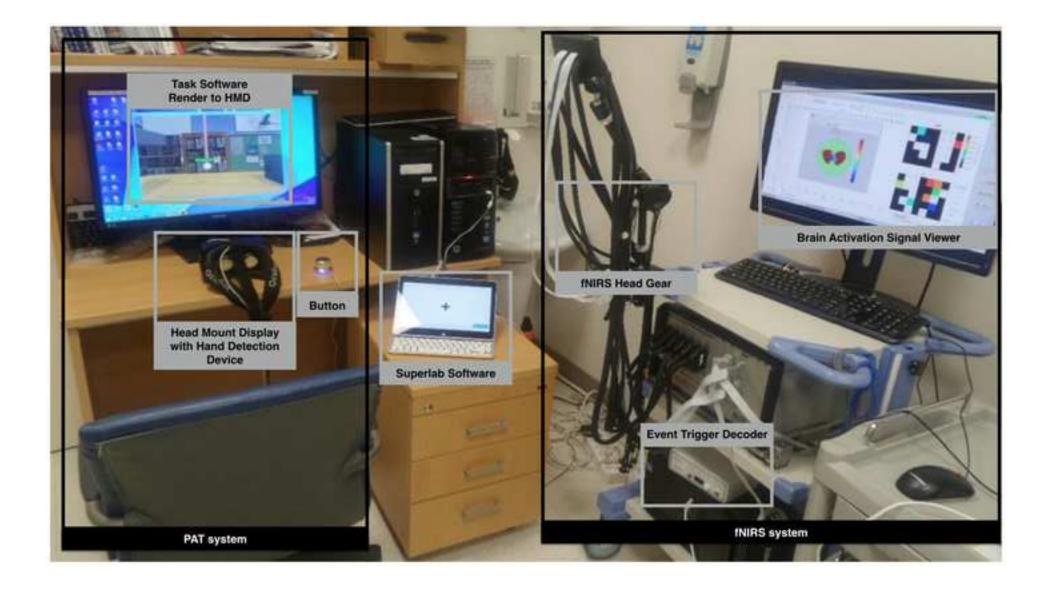
DISCLOSURES:

Won-Seok Kim, Sungmin Cho, and Nam-Jong Paik have a patent entitled "Method, system and readable recording medium of creating visual stimulation using virtual model", number 10-1907181, which is relevant to this work.

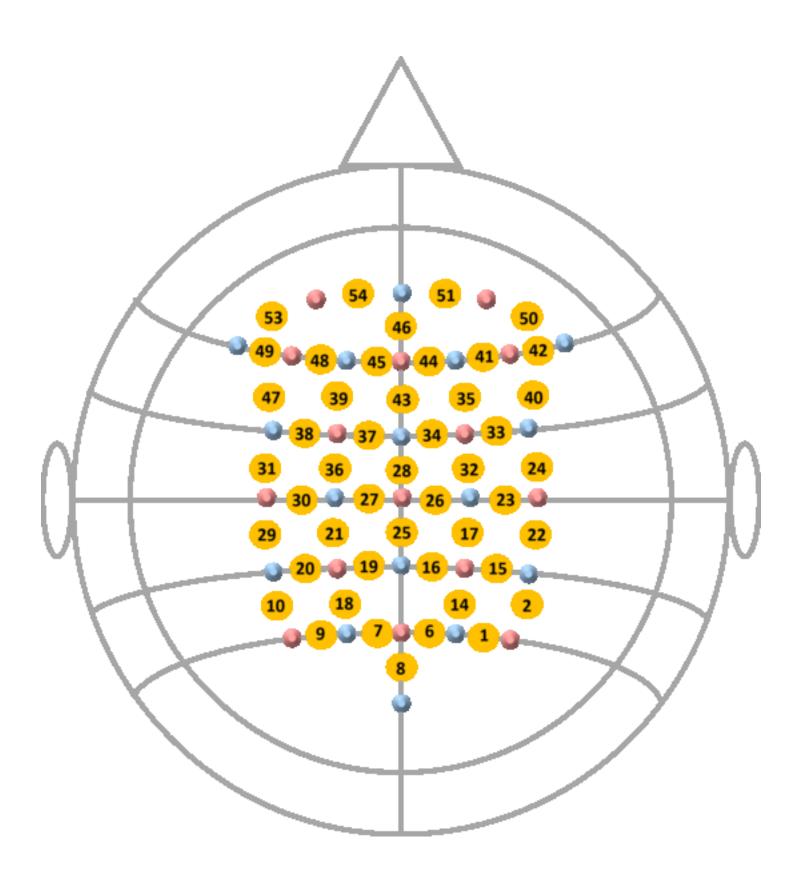
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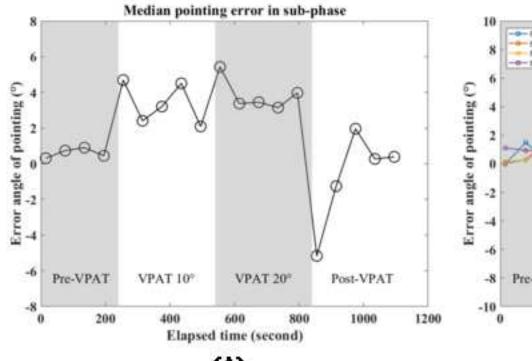
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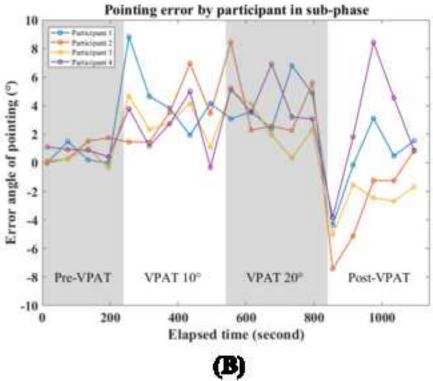






	Phase 1 (pre-VPAT, 4 min)														Phase 3 (VPAT 20°, 5 min)								Phase 4 (post-VPAT, 5 min)															
F	t	CI	Pt	CI	Pt	Cl	Pt	CI																					Pt	Cl	Pt	CI	Pt	CI	Pt	CI	Pt	Cl
	Pt Re Pt Re Pt Re Pt Re Pt Re								Pt	Re	Pt	Re	Pt	Re	Pt	Re	Pt	Re																				





Name of Material/ Equipment	Company	Catalog Number	Comments/Description
EASYCAP	Easycap	C-SAMS	Platform to accommodate fNIRS optodes
Leap Motion 3D Motion Controller Leap Motion VR Developer Mount	-	FBA_LM-C01-US	Hand detection device attached HMD
for VR Headset Matlab R2015a	Ultrahaptics mathworks Medical Technology	VR-UAZ	Programming language running with NIRStar
NIRScout	LLC Medical Technology	NSC-CORE	fNIRS system
nirsLAB v201605	LLC Medical Technology		Software for analyzing data collected with NIRScout
NIRStar 14.1	LLC		NIRScout Acquisition Software
Occulus Rift DK2 PowerMate USB Multimedia	Occulus Griffin		VR HMD
Controller	Technology	NA16029	Push Button in task
superlab 5.0	cedruc corp.		Synchronize the stimulus presentations allied to NIRScout

Editorial comments:

We greatly appreciate your thorough review and comments. We did our best to incorporate all comments as much as possible into our manuscript.

Comment 1: Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues.

Response 1:

Thank you for the kind comment. The original manuscript was edited by English editing service. We reviewed the manuscript and resolved any spelling and grammar issues as much as possible through an English correction service again.

Comment 2: Please obtain explicit copyright permission to reuse any figures from a previous publication. Explicit permission can be expressed in the form of a letter from the editor or a link to the editorial policy that allows re-prints. Please upload this information as a .doc or .docx file to your Editorial Manager account. The Figure must be cited appropriately in the Figure Legend, i.e. "This figure has been modified from [citation]."

Response 2:

Thank you for the kind comment. Figures 1 and 5 were reused. We received permission from IEEE and uploaded the license from RightsLink. This was appropriately cited in the legends of both figures.

Comment 3: JoVE cannot publish manuscripts containing commercial language. This includes company names of an instrument or reagent. Please remove all commercial language from your manuscript and use generic terms instead. All commercial products should be sufficiently referenced in the Table of Materials and Reagents.

Response 3:

Thank you for your careful review. We removed all commercial language and used generic terms instead. All commercial products were referenced in the Table of Materials and Reagents.

Comment 4: Please use h, min, s for time units.

Response 4:

Thank you for your advice. Accordingly, we made these changes in the manuscript.

Comment 5: There is a 2.75 page limit for filmable content. Please highlight 2.75 pages or less of the Protocol steps (including headings and spacing) in yellow that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol.

Response 5:

Thank you for your careful guidance. As directed, we highlighted the steps for the video.

Comment 6: Please avoid long notes/steps (more than 4 lines).

Response 6:

Thank you for your suggestion. We shortened the notes and steps.

Comment 7: Figure 3: Please add a short description of the figure in Figure Legend.

Response 7:

We added a short description of Figure 3.

Comment 8: Figure 5: Please add a title for the whole figure in Figure Legend.

Response 8:

We added a title for the whole figure in the Legend of Figure 5.

Comment 9: Please sort the items in alphabetical order according to the name of material/equipment.

Response 9:

Thank you for your suggestion. We sorted the items in alphabetical order in the Table of Material file.

Reviewer #1:

Thank you for your careful review. We tried to reflect all of your comments.

Comment 1: The sample size is quite small and unbalanced between male and female participants, a bigger sample size could improve the research conducted. **Response 1:** I agree with your opinion. This paper was written to introduce our experimental protocol in detail with video demonstration. The results are preliminary, and the data from more participants and fNIRS data will be analyzed further in future studies.

Comment 2: Possible sickness problems, caused by using VR in stroke patients should be at least introduced and discussed.

Response 2: Thank you for your comment. We agree with your opinion. To be used in patients with stroke, the experimental design with the consideration of possible sickness problems has to be considered. We briefly introduced and discussed this issue in the last part of the Discussion Section.

Comment 3: Authors claim that False detection of hand occurred frequently in the pointing task due to a Leap motion recognition error, I've used Leap motion for several experiments and it is quite stable. Is there any issue with the software or with the setup of the experiment?

Response 3:

Thank you for your kind review. As you mentioned, the leap motion is stable. However, when performing the pointing task, the index finger is sometimes obscured by different parts of the hand and could not be detected by the leap

motion attached to the front of HMD. In such situation, the hand posture is recognized as the fist posture, and the fingertips of the index finger are not recognized properly. In addition, during the quick motion of the pointing task (pointing and returning to original state), the index finger was sometimes recognized as staying in the target position for a period of time even when the hand returned to the starting position. In this case, the hand had to be positioned close to the corresponding location again to be recognized again.

Comment 4: Authors claim that because the subjects were wearing HMD in the clicking task, it was difficult for subjects to locate the push button and the experimenter had to provide continuous assistance.

To solve this issue a virtual button could be inserted into the virtual environment to give users clear feedback on the real button position.

Response 4:

Thank you for your kind comment and idea. A virtual button that is visible at the location of the actual button would make it easier to assist the experiment. This will be considered in the next experimental setup. Thank you again for the valuable suggestion.

Reviewer #2:

Thank you for your thorough review. We accepted your advice and modified the manuscript to adhere to your suggestion as much as possible.

Comment 1: The literature review provided in the Introduction is insufficient. Key articles must be reviewed on this topic, in my opinion, are the following. Rossetti, Y., Rode, G., Pisella, L., Farne, A., Li, L., Boisson, D., & Perenin, M. T. (1998). Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. Nature, 395(6698), 166-169. doi:10.1038/25988 Redding, G. M., & Wallace, B. (2006). Generalization of prism adaptation. Journal of Experimental Psychology-Human Perception and Performance, 32(4), 1006-1022. doi:10.1037/0096-1523.32.4.1006 Gammeri, R., Turri, F., Ricci, R., & Ptak, R. (2018). Adaptation to virtual prisms and its relevance for neglect rehabilitation: a single-blind dose-response study

with healthy participants. Neuropsychological Rehabilitation, 1-14. doi:10.1080/09602011.2018.1502672

Saj, A., Cojan, Y., Assal, F., & Vuilleumier, P. (2019). Prism adaptation effect on neural activity and spatial neglect depend on brain lesion site. Cortex, 119, 301-311. doi:10.1016/j.cortex.2019.04.022

Among the articles I listed above, Gammeri et al. (2018) is probably the first report using VR to induce behavioral effects like prism after-effects. I may be incorrect, but your study is definitely not the first.

Response 1:

Thank you for your kind comment and idea. The above articles you listed have been added to the introduction.

Comment 2: The manuscript is poorly organized and poorly written. The Methods section is especially difficult to read with too many unnecessary detailed subsections and paragraphs labeled with "NOTE". Do you want readers to read the notes? I suggest a total revision of this section and make sure the section is written following a style that is easy to follow and conveys necessary details. Please consult with an editor who is specialized in science, English writing.

Response 2:

Thank you for your careful review. As suggested, the sections labeled with "NOTE" were shortened, removed, and/or rewritten more concisely. The whole manuscript was reedited by an English editing service.

Comment 3: Related to my previous point, I have great difficulty understanding the clicking task. What was it exactly? What was the purpose of it? How was it performed?

Response 3: Participants just clicked the button when the virtual target emerged. In the clicking task during the pre-VPAT mode, the participant just clicked the push button instead of pointing the target using their index finger. Therefore, in

the clicking task, the visual perception and attention might be the same as the reaching task but the gross motion is minimal compared to the motion during the reaching task. Therefore, we hypothesized that we might see the activation in the hand motor cortical area when the fNIRS data from the reaching task were analyzed in contrast to the data from the clicking task.

Comment 4: In Figure 5, errors were positive or negative in direction. Was left positive or negative?

Response 4:

Thank you for your careful review. Counterclockwise direction, i.e. the left, from the target, was the positive value. We added this in the legend of Figure 5.

Comment 5: Where are fNIR data? You did not analyze it or report it here. **Response 5:** Thank you for pointing this out. This paper was written to introduce our experimental protocol in detail with video demonstration. The results are preliminary, and data from more participants and fNIRS will be analyzed in future studies. Although we have the preprocessed fNIRS data from 4 participants, there is insufficient sample size to derive meaningful results from statistical analysis.

Comment 6:"Visuospatial hemispatial neglect" is unnecessary mouthful. Most of the time, you used "hemispatial neglect". Then just use this term and be consistent throughout of the manuscript.

Response 6:

Thank you for your careful review. The corresponding part was changed to "hemispatial neglect."

Comment 7: "People", "subjects", or "participants"? At one point (2.1.1) the word "patient" is used. I suggest you change the title to ".... in healthy adults" and remove the period at the end of the title. I suggest you refer your study participants as "participants" rather than "subjects".

Response 7:

Thank you for your careful review. As suggested, we used "participants" to refer to our study participants.

Comment 8: Remove the word "non-motor" in the Abstract and the Introduction. Such descriptor does not convey any information.

Response 8:

Thank you for your careful review. As recommended, we removed the word "non-motor" from both sections.



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