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Original Article

Changes in cerebral blood flow before, during, and after forward and backward walking in stroke patients trained using virtual reality walking videos with deliberately induced inaccuracies in walking speed estimations

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Abstract. [Purpose] The aim of this study was to examine the effects of virtual reality (VR) training, with deliberately induced inaccuracies in walking speed estimations, on brain activity. [Participants and Methods] The study participants were 21 stroke patients, and the walking tasks involved forward and backward walking. While the VR walking speed was set at 3 km/h, estimation errors were induced by using an actual walking speed of 1 km/h during the walking tasks. Cerebral blood flow was measured using two functional near-infrared spectroscopy (fNIRS) channels located over the left and right prefrontal cortices, to determine changes in oxyhemoglobin levels from the resting state. Cerebral hemodynamics were compared during and after the VR training. [Results] The backward walking task induced a significant increase in cerebral blood flow in the right prefrontal cortex during and after the VR training. No significant changes were observed during the forward walking task. [Conclusion] In the backward walking condition, greater activation of the right prefrontal cortex was observed during and immediately after the VR training. Watching VR may have led to inaccurate walking-speed estimations, necessitating postural control (which may be attributed to the activation of the prefrontal cortex) during walking.

Key words: Stroke, Virtual reality, Inaccurate speed estimation of walking

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INTRODUCTION

Virtual reality (VR) has rapidly gained popularity in entertainment, education, medical treatment, and motor learning. A meta-analysis by Laver et al.[1] found that VR therapy had a greater effect than standard physical therapy on the activities of daily living of stroke patients. However, the results for the effects of VR-based therapies on walking speed and postural balance ability have remained inconclusive due to insufficient evidence. Nevertheless, a systematic review and meta-analysis by Ilona et al. showed improved gait and balance function[2], and consistent findings indicating improved function have also been reported in many previous studies[3–6].

Backward-walking exercise has been found to show some rehabilitative effects in stroke patients in comparison with normal walking exercise. We had previously reported that backward-walking training on a body weight-supported treadmill has significant intervention effects on the walking ability of patients with acute stroke[7]. Nevertheless, to our knowledge, no studies have examined whether VR backward-walking videos improve the physical performance of stroke patients. The

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literature contains multiple findings on the intervention effects of backward-walking training on stroke patients. However, to our knowledge, no previous studies have evaluated the effects of backward-walking training, such as increased brain activity or so-called brain activation, in terms of improvements in the overall physical performance of stroke patients.

Thus, the aim of this study was to examine the effects of training with a previously prepared VR walking video that intentionally led to inaccurate speed estimation of walking on brain activity during forward and backward walking on a treadmill.

PARTICIPANTS AND METHODS

The study participants were 21 right-handed stroke patients who underwent physical therapy (Table 1). The inclusion criteria were the ability to perform forward and backward treadmill walking while holding onto handrails and fixating on a target. Three of the participants were using ankle foot orthoses. The exclusion criteria were as follows: presence of higher cerebral dysfunction, dementia, visual disorders such as hemianopsia, orthopedic diseases, or a reduced exercise capacity due to heart disease.

We investigated basic characteristics such as age, gender, and handedness. During the training with the VR walking video, the participants used smart glasses weighing 69 g (Moverio BT-300; Epson, Suwa, Japan). The walking videos were recorded using the built-in camera of the smart glasses and a walker. The walking speed during the video recording was set at 3.0 km/h. During the video recording, the lens of the video camera was set at the approximate height of the eyes (150 cm) of the participants. The VR videos were recorded during a walk on a 35-m walking track with a 3-m width.

Brain activity was measured using functional near-infrared spectroscopy (fNIRS; sampling frequency, 0.76 Hz; distance between the transmitting and receiving probes, 3 cm; OEG-16; Spectratech Inc., Tokyo, Japan). In accordance with the method described by Nakata et al., the probes were placed in the midline of the forehead as a reference, and the measurements were performed using all 16 channels (Ch) of the fNIRS device[8]. At the start of the walking experiment, once the hemodynamics in all channels had stabilized in the measurement area, the recording was started. For the fNIRS signals, oxyhemoglobin (hereinafter, oxy-Hb) has been reported to show the highest correlation with changes in regional cerebral blood flow, and changes in oxy-Hb levels have been reported to accurately reflect brain activity. Therefore, oxy-Hb levels (unit: mM/mm) as measured by fNIRS were used as the hemodynamic index of the prefrontal cortex.

Walking was measured using a treadmill (BDX-T400; SAKAI Medical. Co. Ltd., Tokyo, Japan). The actual treadmill speed was set to 1 km/h. This treadmill speed was chosen to ensure the safety of stroke patients during walking, considering the backward walking condition.

The measurement procedure is illustrated in Fig. 1. First, the participants were instructed to rest in a standing position for 1 min and subsequently watch a 1-min VR video. Subsequently, they walked on a treadmill for one minute. They were instructed to rest in a sitting position for 3 min between forward- and backward-walking tasks administered in a randomized order. Hereafter, walking before watching VR is defined as Pre VR walking and walking after watching VR is defined as Post VR walking, and the direction of walking is indicated in parentheses as VR(F) or VR(B). During the measurement, the participants were asked to hold the handrails while fixating on a target placed in front of them.

Of the 16 fNIRS channels reflecting brain activity in the prefrontal cortex, Ch 7 (the right prefrontal cortex) and Ch 10 (the left prefrontal cortex) showing low noise and stable electrical signals were chosen as the sites for measurements[8]. Oxy-Hb levels were used as indicators of brain activity. Habituation time was defined as the quiet standing time before each walking and watching VR. Oxy-Hb levels averaged over the second 30-s period were used as baseline levels. One to four seconds of neural activity are required for the fNIRS signals to reach half of their maximum value[9]. In the present study, the treadmill required approximately 5 s to reach a constant speed after it was started. Therefore, to analyze cranial nerve activity after a constant walking speed was achieved, in accordance with the method described by Harada et al.[10], Δoxy-Hb for analyses was calculated as the difference between oxy-Hb levels averaged over the second 30-s period and the baseline levels for each task.

Normality was first confirmed by statistical analyses. Then, on the basis of the results, a paired t-test or Wilcoxon's rank-sum test was used to compare differences between the baseline and during watching VR and between pre- and post VR walking. After confirming the normality of the data, Student's t-test was used to compare Δoxy-Hb values obtained during

Table 1. Participant characteristics (N=21)

Age	66.7 ± 8.0 years
Gender	Male 19 Female 2
Height	167.5 ± 5.2 cm
Period from onset	66.8 ± 41.5 days
Infarction/hemorrhage	15/6
Hemisphere (R/L)	9/12
Brunnstrom stage (IV/V/VI)	6/4/11

Mean (± SD).

and post VR walking in forward- and backward-walking conditions. All statistical analyses were performed using R Statistical Software (version 3.6.3; Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at p<0.05.

This study was approved by the Ethics Committee of the Hirosaki Stroke and Rehabilitation Center (approval number: 19A008) and the Ethics Committee of the Hirosaki University Graduate School of Health Sciences (reference number: 2019-035). The research was fully explained to the participants verbally, and the consent form was signed before conducting the research.

RESULTS

Analysis of brain activity during watching VR(F) showed a slight increase in blood flow from the baseline as measured by the channels in the left and right prefrontal cortex, but this difference was not statistically significant (Table 2). Similarly, analysis of brain activity during walking after watching VR(F) also showed no significant difference from the measurements obtained pre- and post-watching VR(F) (Table 3).

In the analysis of brain activity during watching VR(B), after confirming the normality, the mean and median oxy-Hb levels watching VR(B) were compared with the baseline values. The oxy-Hb levels obtained at the baseline and during watching VR(B) (p=0.014) differed significantly. For the left prefrontal cortex (Ch 10), the oxy-Hb levels at the baseline and during watching VR(B) showed no significant difference (Table 4).

For the right prefrontal cortex (Ch 7) in the Post VR walking(B). The values obtained pre- and post-VR walking(B) differed significantly (p=0.037). For the left prefrontal cortex (Ch 10), no significant difference was observed between the values obtained pre- and post- VR walking(B) (p=0.34). A summary of the results is presented in Table 5.

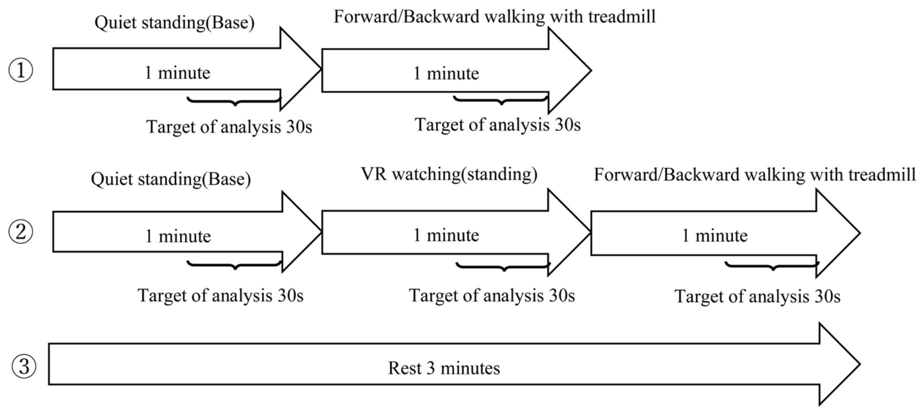

Fig. 1. Experimental procedure.
Treadmill walk speed: 1.0 km/h. VR walk speed: 3.0 km/h.
VR: virtual reality.

Table 2. Verification of brain activity during watching VR(F) (N=21)

	Base line (mM/mm)	During watching VR(F) (mM/mm)
ch7	0.13 (± 0.28)	0.24 (± 0.42)
ch10	0.16 (± 0.36)	0.28 (± 0.47)

Mean (± SD). Paired t-test. *p<0.05.
VR: virtual reality.

Table 3. Verification of brain activity during forward walking before and after watching VR(F) (N=21)

	Before watching VR(F) (mM/mm)	After watching VR(F) (mM/mm)
ch7	0.27 (± 0.33)	0.36 (± 0.36)
ch10	0.32 [0.11–0.43]	0.36 [0.22–0.55]

Ch7: Mean (± SD), Paired t-test. *p<0.05.
Ch10: Mean [Interquartile range], Wilcoxon signed rank sum test.
VR: virtual reality.

Table 4. Verification of brain activity during watching VR(B) (N=21)

	Base line (mM/mm)	During watching VR(B) (mM/mm)
ch7	−0.010 [−0.13–0.35]	0.19 [0.018–0.44]*
ch10	0.19 (± 0.45)	0.30 (± 0.52)

Ch7: Mean [Interquartile range], Wilcoxon signed rank sum test. *p<0.05.
Ch10: Mean (± SD), Paired t-test.
VR: virtual reality.

Table 5. Verification of brain activity during backward walking before and after watching VR(B) (N=21)

	Before watching VR(B) (mM/mm)	After watching VR(B) (mM/mm)
ch7	0.31 (± 0.37)	0.44 (± 0.33)*
ch10	0.40 (± 0.35)	0.46 (± 0.38)

Mean (± SD). Paired t-test. *p<0.05.
VR: virtual reality.

DISCUSSION

Treatment with VR has been reported to promote neuroplasticity by allowing safe and abundant implementation of task-specific functional activities[11]. The present results showed a significant increase in oxy-Hb levels from baseline during watching VR and walking after watching VR in the backward-walking condition. In the following, we will discuss the cerebral physiological effects and interhemispheric differences during watching VR, as well as differences due to differences in walking video direction. In addition, the effects on backward walking after watching VR will be mentioned with a focus on cortical activity.

One of the cerebral physiological effects of watching VR is optic flow, which is essential for visually induced kinesthesia. Many areas, including the ventral intraparietal area, have been reported to be responsible for this effect. This area has been reported to be included in the dorso-dorsal stream, a subdivision within the dorsal stream of the visual-processing network[12]. The dorso-dorsal stream has been reported to play the role of the "how–system", which induces appropriate behaviors by subconsciously processing the location and movement of the object and information on shape. Because the dorso-dorsal stream ultimately projects to the dorsolateral prefrontal cortex via the visual cortex and the superior parietal lobule, its connectivity with the prefrontal cortex cannot be ignored. Significant activation of the prefrontal cortex was observed during watching VR(B), suggesting that VR induced the motion illusion. The difference in the results depending on the walking direction may be due to the immersion in the VR. Backward walking, which does not represent walking in daily life, was a new subjective experience evoked by the video, leading to a more realistic video experience. The different results for the left and right hemispheres may be due to the laterality of the attention network. The right prefrontal cortex is involved in postural control, visuospatial ability, and spatial attention functions[13]. Therefore, brain activity in this area may have been more vigorous when watching VR in the backward walking, which is more difficult than forward walking.

During walking after watching VR, the right prefrontal cortex also showed significantly increased brain activity. This may be due to brain activation caused by the inaccurate speed estimation of actual walking after watching VR. After watching VR (walking speed in VR, 3 km/h), participants may be required to adjust their walking speed during actual walking or correct their movement due to the inaccurate speed estimation of walking. Because forward walking is a highly automatic movement, it is unlikely to induce significant activity in the cerebral cortex. On the other hand, backward walking requires the maintenance of balance with less visual information on the direction of travel. Moreover, it is a non-automatic movement that requires hip extension to swing the lower limbs, which is an unusual walking pattern. Therefore, because of the absence of automatic movement correction, the movement may require voluntary movement correction in the cerebral cortex, especially in the prefrontal and premotor areas. The 1-min walking task, particularly the second 30-s period that was included in the analysis, may have been performed during the steady-state stage. However, increased prefrontal activity in this stage that does not require control by the cerebral cortex, suggesting voluntary adjustment of movement. This supports our previous report that cerebral blood flow in the prefrontal cortex, especially in the right hemisphere, increased only during backward walking after watching VR in a study of healthy participants[14].

This study had some limitations. First, the area of measurement of brain activity was limited to the prefrontal cortex. Although our intervention using a combination of VR therapy and backward walking training resulted in increased prefrontal activity, the effects of VR therapy in the backward walking condition on the activity of other brain areas remain a matter of speculation. Second, although some studies have described cerebral hemodynamics in the premotor cortex, supplementary motor area, and parietal lobe[15–17], the present study did not measure the activity of the brain areas associated with the prefrontal cortex to examine their mutual relationships. Future studies should aim to address these limitations.

Funding and Conflict of interest

There are no conflicts of interest to disclose.

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