35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

The precise adjustment of coil location for transcranial magnetic stimulation during dynamic motion

Taku Kitamura, *Student Member, IEEE*, Katsutoshi Yaeshima,
Shin-Ichiro Yamamoto, *Senior Member, IEEE*, and Noritaka Kawashima, *Senior Member, IEEE*

Abstract— **Transcranial magnetic stimulation (TMS) to the cerebral cortex is a major *in vitro* technique that is used in the field of neurophysiology. The magnitude of the motor-evoked potentials (MEP) that are elicited by TMS to the primary motor cortex reflect the excitability of the corticospinal pathway. MEPs are very sensitive to the scalp location of the stimulus coil, especially when corticospinal excitability is recorded during walking or other dynamic motions. In this study, we created a coil navigational system that consisted of three-dimensional motion analysis cameras, rigid bodies on the head and coil, and programming software. In order to evaluate the feasibility of the use of our system, pseudo TMS was applied during treadmill walking with or without the navigational system. As a result, we found that the variances due to coil location and/or distance from the target site were reduced with our system. This technique enabled us to realize high precision and accuracy in coil placement, even during dynamic motion.**

I. Introduction

Transcranial magnetic stimulation (TMS) is an *in vitro* technique that is used to stimulate the central nervous system (CNS). When a TMS stimulus coil is placed above the primary motor cortex (M1) and electrical current is applied, a rapid change is generated in the magnetic field. This change induces an eddy current in M1 just below the coil. Therefore, pyramidal neurons just below the coil are activated. We then obtain a motor-evoked potential (MEP) in the muscle from the activated pyramidal neurons.

In neurophysiological research, TMS is often used to investigate corticospinal excitability from the motor cortex to target muscles [1],[2]. In a TMS study, it is necessary to pay close attention to the location on the scalp where the coil is placed during the measurement because the pyramidal neurons that activate a specific muscle are heterogeneously distributed in M1 [3]. Therefore, the stimulus coil causes a change in MEP amplitude [4],[5],[6].

Recently, many researchers have investigated the corticospinal or intracortical contributions during dynamic motion, such as walking [7],[8], cycling [9],[10], or drop jumping [11]. In these studies, the most difficult technical problem to solve was how to maintain the coil location. To date, several attempts have been made to solve this problem. Barthelemy and Nielsen (2010) investigated the corticospinal and intracortical contributions to arm muscle activation during walking, and they used a specially designed harness to maintain the coil location [8]. Sidhu et al. used a chin rest that was attached to the front of a cycle ergometer to keep the head stable in their study that investigated cortical contribution to leg muscle activation during leg cycling movement [10]. Although many approaches have been used for the stereotaxis of the stimulus coil, it is unclear if the stereotaxis of the stimulus coil was accomplished because of the absence of subjective data for coil location. Therefore, systems that can help with coil positioning and the recording of the coil location on the head are needed.

In this study, we attempted to utilize a three-dimensional motion analysis camera and passive infrared markers to objectively evaluate the coil location for TMS. With this system, the experimenter may be able to accurately adjust coil location to the same position on the subject's scalp, even during dynamic motion. The purpose of this study was therefore to establish a TMS coil navigational system that enables the experimenter to acquire the precise coil location during the experiment.

II. System Configuration

The navigational system consisted of 4 three-dimensional motion analysis cameras (OptiTrack, NaturalPoint, Inc., Corvallis, OR, USA), 2 rigid bodies that were fixed on the subject head and stimulus coil, and a computer that was used to run the system software (Figure 1). Each rigid body had 3 infrared reflection markers. The rigid body on the head was used to create the coordinate system that moved according to head motion. The x-, y-, and z-axes of the head and coil frame were defined as left to right, posterior to anterior, and bottom to top, respectively. In order to make the frame, we defined the x-axis from 2 of the 3 marker coordinates on the head rigid body. Then, the y- and z-axes were defined with the cross product. The online marker coordinates on the head and coil rigid body were transferred to the computer with 200 Hz. With the custom LabVIEW program, the coil location in the moving frame was calculated according to head motion. Because of the ease with which the experimenter could see the picture, the online coil location was displayed on the interface with a

*Research supported by KAKENHI: Grant-in-Aid for Scientific Research (B) 21300202.

T. Kitamura is with the Department of Bioscience and Engineering, Graduate School of Engineering and Science, Shibaura Institute of Technology, Saitama, Japan (corresponding author; phone: +81-48-688-9405; e-mail: nb11103@shibaura-it.ac.jp).

K. Yaeshima is with the Department of Life Science, Graduate School of Arts and Sciences, the University of Tokyo, Tokyo, Japan and the Department of Rehabilitation for Movement Function, Research Institute, National Rehabilitation Center for persons with Disabilities, Tokorozawa, Japan (e-mail: yaeshima-katsutoshi@rehab.go.jp).

S.-I. Yamamoto is with the Department of Bioscience and Engineering, Graduate School of Engineering and Science, Shibaura Institute of Technology, Saitama, Japan (e-mail: yamashin@se.shibaura-it.ac.jp).

N. Kawashima is with the Department of Rehabilitation for Movement Function, Research Institute, National Rehabilitation Center for persons with Disabilities, Tokorozawa, Japan (e-mail: kawashima-noritaka@rehab.go.jp).

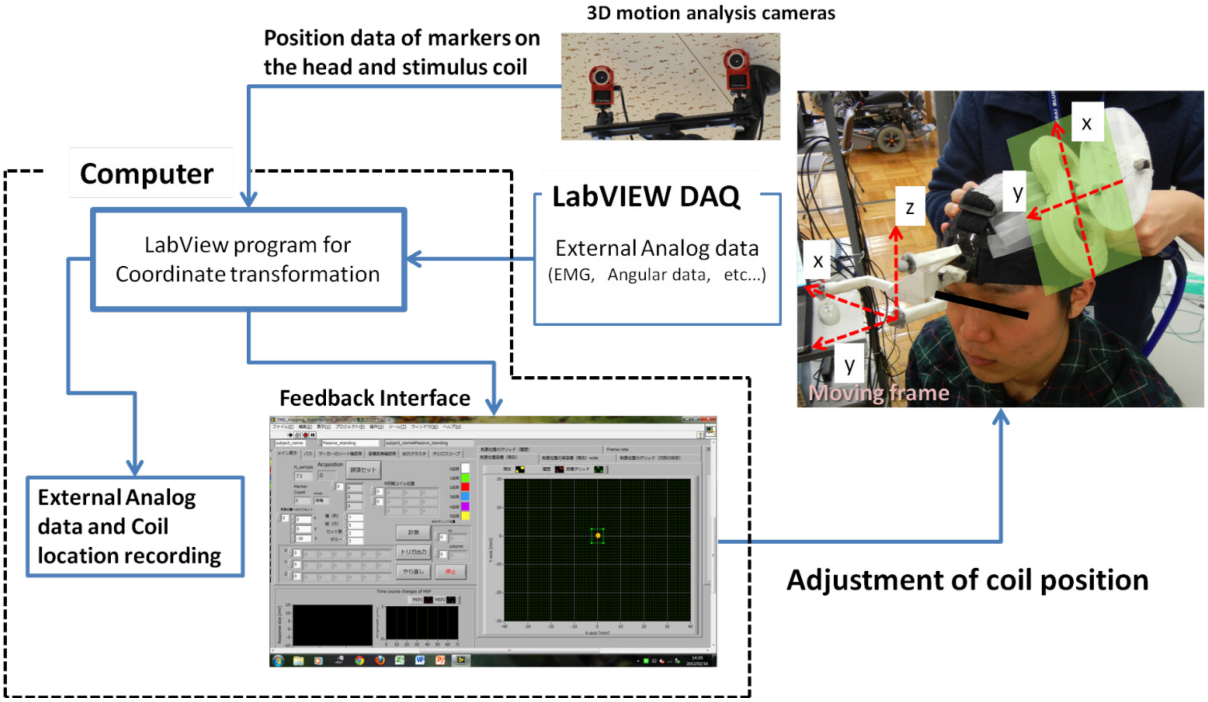

Figure 1. System configuration.

yellow dot on the two-dimensional surface with 50 Hz. In the interface, the target area for TMS was indicated with a green 5-mm grid because the effective field for TMS with a figure-8 coil is around a 5-mm diameter [12], and the experimenter adjusted the coil location in order to move the yellow dot into the green grid. Analog data, including electromyography or potentiometer data, were recorded with 5000 Hz with this system.

Because the motor cortex was stimulated, the coil location log was displayed in the interface. Moreover, the coil location data and the external analog data extended over 600 ms, including 300 ms before the stimulation, and this data were stored in the hard disk as a text file.

III. COORDINATE TRANSFORMATION

The orientation of an object in space relative to an absolute coordinate system can be described by the rotation from the absolute frame to the object's frame. This rotation can be expressed with mathematical tools, such as rotational matrices.

The rotational matrix of the rotation of the vector of the object's frame (v_o) to the vector of the absolute frame (v_a) can be defined with the helical angle θ and the rotational axis $[X, Y, Z]$ between v_o and v_a. The helical angle and rotational axis can be defined with the following formulas:

$$\theta = \cos^{-1}\left(\frac{v_o \cdot v_a}{\|v_o\|\,\|v_a\|}\right) \quad (1)$$

$$[X, Y, Z] = \frac{v_o \times v_a}{\|v_o \times v_a\|} \quad (2).$$

The helical angle and rotational axis can then be converted into the rotational matrix R with the following formula, with $c = \cos\theta$ and $s = \sin\theta$:

$$R = \begin{bmatrix} (1-c)X^2 + c & (1-c)XY - Zs & (1-c)XZ + Ys \\ (1-c)XZ + Zs & (1-c)Y^2 + c & (1-c)YZ - Xs \\ (1-c)XZ - Ys & (1-c)YZ + Xs & (1-c)Z^2 + c \end{bmatrix} \quad (3).$$

IV. CALCULATION OF COIL LOCATION

In our system, coil location was finally displayed as two-dimensional data in the coordinate system with the following features: 1) the origin of the coordinate system was defined as the initial coil position, and 2) the surface was aligned with the initial coil incline in the coronal plane of the head. The initial coil position and incline was determined during the calibration process before the measurement. During the calibration, the vector from the head to the coil center in the head frame (d) and the rotational matrix between the coil frame and the head frame (r) were preliminarily calculated.

The moving measurement frame can be created by 2 matrix transformations. At first, the rotational matrix for aligning the x-axis of the head frame to the x-axis of the absolute frame (R_1) was calculated with formulas (1) to (3). Then, we obtained the new frame F' with which the x-axis was aligned with the x-axis of the absolute frame with formula (4).

$$F' = F_h R_1 \quad (4)$$

Then, the rotational matrix R_2 that aligned the y-axis of frame F' to the y-axis of the absolute frame [0,1,0] was calculated. Therefore, the rotational matrix R for aligning the head coordinate system to the absolute coordinate system can be described with formula (5).

$$R = R_1 R_2 \quad (5)$$

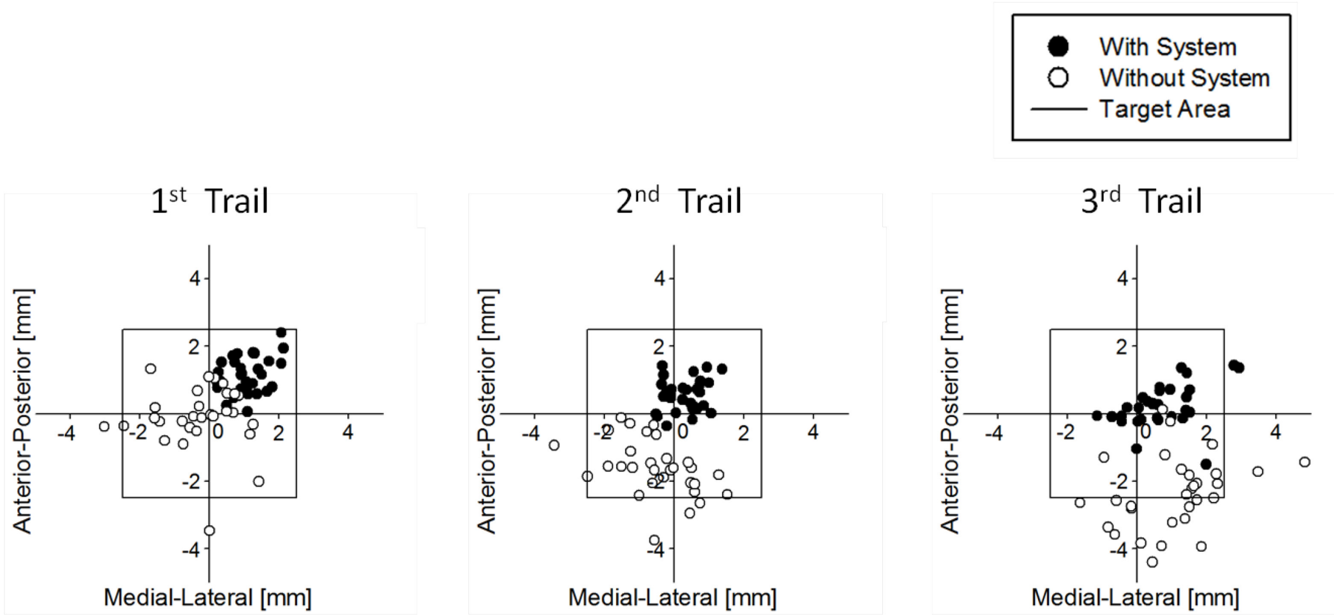

Figure 2. The location plot of the stimulus coil during treadmill walking. The open circles indicate the coil location data that were obtained with the help of the navigational system, and the closed circles indicate the data that were obtained without the navigational system. The square indicates the target area that was displayed on the interface.

Therefore, the coil marker coordinate in head frame (P) can be expressed with the following formula, with D being the vector from the absolute origin to the head frame and P_a being the marker coordinate that was measured in the absolute frame.

$$P = [(P_a - D)R - d]r \quad (6)$$

In the feedback interface, the gravity coordinates of the 3 coil markers were displayed as the stimulus coil location, but they were expressed only with the x and y components of the three-dimensional marker coordinate P.

V. Experiment

In order to evaluate the accuracy and precision of the coil placement, we applied pseudo TMS to a single subject during treadmill walking with or without the help of the navigational system.

A. Preparation

In this study, we did not stimulate the brain, and the coil was placed on C3 according to the International 10-20 methods for EEG electrode placement. Coil location was directly marked on the subject's scalp with a soft-tip pen.

In order to create the measurement frame, the subject wore a swimming cap to which the head rigid body was attached. Then, the subject stood on the treadmill, and calibration was done when the coil was placed according to the mark that was written on the head.

B. Protocols

In the experiment, the subject walked on the treadmill at 3.6 km/h. During the treadmill walking, 30 pseudo TMS were applied during which the coil was placed on the head but stimulation was not done during 2 different conditions. In the with-system condition, the experimenter could adjust the coil location while referring to the navigational system and reference markers that were written on the head. In contrast, in the without-system condition, the experimenter had to adjust the coil location by referring only to the reference marker on the head.

A pair of conditions was defined as 1 trial, and each trial was repeated 3 times. Between the conditions, there was a brief rest. The order of the experimental conditions was randomly decided. In order to minimize the fatigue of the experimenter, sufficient rests were taken between the trials. All trials were conducted by the same experimenter who was skilled in the techniques of TMS.

C. Parameters

In order to evaluate precision, the variances of the coil location for the x and y axes were calculated and compared between the conditions for each trial. Moreover, the distances between the actual coil location and the target site, which was the origin of the measurement coordinate system, were calculated as the error.

D. Statistics

For all parameters, a normality test was done with a Kolmogorov-Smirnov test. If there was normality in the variance of the coil location, a F-test was done between the conditions in each trial in order to evaluate the precision of the coil placement. For the error of the coil location, a Wilcoxon rank-sum test was applied to the data in each trial in order to evaluate the accuracy of the coil location.

VI. Results and Discussion

A Kolmogorov-Smirnov test showed that, for all conditions and trials, there was normality in the coil locations for the x- and y-axes and the distance from the target site. In the with-system condition, the coil was more precisely placed

TABLE 1. THE RESULTS OF THE VARIANCES IN THE COIL LOCATIONS AND THE DISTANCES BETWEEN COIL LOCATION AND TARGET SITE

	1st Traial			2nd Traial			3rd Traial		
	With System	Without System	p-value	With System	Without System	p-value	With System	Without System	p-value
Variance for X axis [mm]	0.31	1.19	*p<0.001	0.27	1.24	*p<0.001	0.90	1.84	p=0.058
Variance for Y axis [mm]	0.30	0.87	*p=0.005	0.23	0.69	*p=0.005	0.42	1.16	*p=0.008
Distance from the target [mm]	1.64±0.61	1.19±0.83	*p=0.004	0.85±0.41	2.05±0.75	*p<0.001	1.10±0.80	2.96±0.97	*p<0.001

* Significant differences between conditions

in the target area compared to the without-system condition. Moreover, in both conditions, the precision of placement worsened in the third trial (Figure 2). This may have been due to the fatigue of the experimenter.

Using the coil navigational system, the precision of coil placement improved in all trials, except for the data for the x-axis during the third trial (Table 1). These results suggested that the precision of coil placement improved with the use of the navigational system. For accuracy, the averages of the distances from the target site were significantly smaller in the with-system condition during the second and third trial, while that for the first-trial distance in the without-system condition was smaller. In the without-system condition, it seemed that it was difficult to adjust the coil location from the starting location when imperceptible displacement of the coil had occurred because the experimenter had to subjectively adjust the coil location with visual estimation. Moreover, the experimenter could not objectively know whether the online coil location was accurate. Therefore, in the without-system condition, it was considered that the initial coil location in the session was critical for accuracy because the error from the target was small, even when imperceptible displacement of the coil occurred. In contrast, the navigational system provided objective location data, and the experimenter could then easily move the coil to the accurate target site. Thus, with the use of the navigational system, we were able to place the coil at the accurate site from the first measurement and control the coil location with high precision.

The results of this study indicated that our system enabled us to set the coil more accurately. Because the process that was used for adjusting the coil position and target was quite easy, the system would be helpful for TMS during dynamic whole-body movements.

In the TMS technique, coil incline, as well as coil location, is important because the change in coil incline affects the induced eddy current direction in the cortex, and MEPs are sensitive to the induced current direction in M1 [13]. However, our system was able to navigate coil location but not the coil incline. Therefore, in both conditions in the experiment, the experimenter adjusted the coil incline by referring to the markers that were written on the head. If we can utilize navigation of the coil incline, it is expected that TMS measurements will have more precise and accurate coil orientations. Thus, further improvements in the navigating of coil incline are needed.

VII. CONCLUSIONS

We created a navigational system that consisted of motion analysis cameras, infrared markers that were placed on the forehead, and the coil, for TMS coil location. In order to confirm the availability of the system, pseudo TMS was applied to the subject with and without the help of the navigational system during treadmill walking. The results of the experiment indicated that the navigational system provided us with more precise and accurate coil placement on the head during treadmill walking.

ACKNOWLEDGMENT

This research was supported by KAKENHI: Grant-in-Aid for Scientific Research (B) 21300202.

REFERENCES

[1] A. T. Barker, R. Jalinous, and I. L. Freeston, "Non-invasive magnetic stimulation of human motor cortex," *Lancet*, vol. 1, pp. 1106-7, 1985.

[2] V. Di Lazzaro, D. Restuccia, A. Oliviero, P. Profice, L. Ferrara, A. Insola, P. Mazzone, P. Tonali, and J. C. Rothwell, "Effects of voluntary contraction on descending volleys evoked by transcranial stimulation in conscious humans," *J Physiol*, vol. 508, pp. 625-33, 1998.

[3] H. Asanuma, "The pyramidal tract," in *Handbook of Physiology: Section 1. The Nervous System,* vol. 2, *Motor control:* Part 2, V. B. Brokks, Ed. Bethesda, MD: American Physiological Society, pp. 703-33, 1981.

[4] S. A. Wilson, G. W. Thickbroom, and F. L. Mastaglia, "Transcranial magnetic stimulation mapping of the motor cortex in normal subjects. The representation of two intrinsic hand muscles," *J Neurol Sci,* vol. 118, pp. 134-44, 1993.

[5] M. C. Ridding, B. Brouwer, T. S. Miles, J. B. Pitcher, and P. D. Thompson, "Changes in muscle responses to stimulation of the motor cortex induced by peripheral nerve stimulation in human subjects," *Exp Brain Res*, vol. 131, pp. 135-43, 2000.

[6] M. C. Ridding, D. R. McKay, P. D. Thompson, and T. S. Miles, "Changes in corticomotor representations induced by prolonged peripheral nerve stimulation in humans," *Clin Neurophysiol*, vol. 112, pp. 1461-9, 2001.

[7] N. T. Petersen, J. E. Butler, V. Marchand-Pauvert, R. Fisher, A. Ledebt, H. S. Pyndt, N. L. Hansen, and J. B. Nielsen, "Suppression of EMG activity by transcranial magnetic stimulation in human subjects during walking," *J Physiol*, vol. 537, pp. 651-6, 2001.

[8] D. Barthelemy and J. B. Nielsen, "Corticospinal contribution to arm muscle activity during human walking," *J Physiol*, vol. 588, pp. 967-79, 2010.

[9] S. K. Sidhu, B. W. Hoffman, A. G. Cresswell, and T. J. Carroll, "Corticospinal contributions to lower limb muscle activity during cycling in humans," *J Neurophysiol*, vol. 107, pp. 306-14, 2012.

[10] E. P. Zehr, M. Klimstra, E. A. Johnson, and T. J. Carroll, "Rhythmic leg cycling modulates forearm muscle H-reflex amplitude and corticospinal tract excitability," *Neurosci Lett*, vol. 419, pp. 10-4, 2007.

[11] W. Taube, C. Leukel, M. Schubert, M. Gruber, T. Rantalainen, and A. Gollhofer, "Differential modulation of spinal and corticospinal excitability during drop jumps," *J Neurophysiol*, vol. 99, pp. 1243-52, 2008.

[12] S. Ueno, T. Matsuda, and O. Hiwaki, "Localized stimulation of the human brain and spinal cord by a pair of opposing pulsed magnetic fields," *J Appl Physics*, vol. 67, pp. 5838-40, 1990.

[13] S. Ueno, T. Matsuda, and M. Fujiki, "Functional mapping of the human motor cortex obtained by focal and vectorial magnetic stimulation of the brain," *IEEE Trans Magn*, vol. 26, pp. 1539-44, 1990.