32nd Annual International Conference of the IEEE EMBS
Buenos Aires, Argentina, August 31 - September 4, 2010

Clinical study of neurorehabilitation in stroke using EEG-based motor imagery brain-computer interface with robotic feedback

Kai Keng Ang, Cuntai Guan, Karen Sui Geok Chua, Beng Ti Ang, Christopher Kuah, Chuanchu Wang, Kok Soon Phua, Zheng Yang Chin, and Haihong Zhang

Abstract—**This clinical study investigates the ability of hemiparetic stroke patients in operating EEG-based motor imagery brain-computer interface (MI-BCI). It also assesses the efficacy in motor improvements on the stroke-affected upper limb using EEG-based MI-BCI with robotic feedback neurorehabilitation compared to robotic rehabilitation that delivers movement therapy. 54 hemiparetic stroke patients with mean age of 51.8 and baseline Fugl-Meyer Assessment (FMA) 14.9 (out of 66, higher = better) were recruited. Results showed that 48 subjects (89%) operated EEG-based MI-BCI better than at chance level, and their ability to operate EEG-based MI-BCI is not correlated to their baseline FMA (r=0.358). Those subjects who gave consent are randomly assigned to each group (N=11 and 14) for 12 1-hour rehabilitation sessions for 4 weeks. Significant gains in FMA scores were observed in both groups at post-rehabilitation (4.5, 6.2; p=0.032, 0.003) and 2-month post-rehabilitation (5.3, 7.3; p=0.020, 0.013), but no significant differences were observed between groups (p=0.512, 0.550). Hence, this study showed evidences that a majority of hemiparetic stroke patients can operate EEG-based MI-BCI, and that EEG-based MI-BCI with robotic feedback neurorehabilitation is effective in restoring upper extremities motor function in stroke.**

I. INTRODUCTION

Brain–computer interface (BCI) provides a channel for the use of brain signals to communicate or control external devices without using the normal output pathways of peripheral nerves [1]. BCI technology can substantially improve the lives of people with devastating neurological disorders such as advanced amyotrophic lateral sclerosis, restore more effective motor control to people after stroke or other traumatic brain disorders by guiding activity-dependent brain plasticity by using brain signals to indicate the state of brain activity [2]. This technology can also be used to supplement impaired muscle control, or to increase the efficacy of a rehabilitation protocol to improve muscle control of the patient.

This work was supported by the Science and Engineering Research Council of A*STAR (Agency for Science, Technology and Research), and The Enterprise Challenge, Prime Minister's Office, Singapore.

K. K. Ang, C. Guan, C. Wang, K. S. Phua, Z. Y. Chin and H. Zhang are with Institute for Infocomm Research, Agency for Science, Technology and Research (A*STAR), 21 Heng Mui Keng Terrace, Singapore 119613. (email: {kkang, ctguan, ccwang, ksphua, zychin, hhzhang, ctguan}@i2r.a-star.edu.sg).

K. S. G. Chua and C. Kuah are with Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433. (email: {Karen_Chua, Christopher_Kuah}@ttsh.com.sg).

B. T. Ang is with National Neuroscience Institute, 11 Jalan Tan Tock Seng, Singapore 308433. (email: Beng_Ti_Ang@nni.com.sg).

BCI technology has been translated from laboratory research to applications that are useful in everyday life [3-9]. BCI applications can be widely classified into clinical applications such as direct control of assistive technologies or neurorehabilitation, and nonclinical applications such as computer games. However, clinical applications of BCI in neurorehabilitation have just begun to be explored [10]. Neurorehabilitation is performed on patients who suffered neurological disabilities that include stroke, spinal cord injury, traumatic brain injury, neuromuscular disease, and other neurological disorders. Among these neurological disabilities, stroke is the leading cause of severe disabilities in the developed world [11]. Stroke often results in hemiparesis or hemiplegia that is contralateral to the affected side of the brain. Motor imagery is appealing for stroke patients because they can perform imagined movements or even attempt to move their plegic hand in the absence of any motor function. Furthermore, motor imagery holds promise to recruit the motor system for stroke recovery [12], and recent clinical study using fMRI have shown that the motor network activation is detected in 20 hemiparetic subcortical stroke patients during motor imagery despite the lesion [13]. The first BCI application for neurorehabilitation in stroke was evaluated with non-invasive MEG-based motor imagery BCI (MI-BCI) in [14]. The results showed that successful BCI control was attained in 6 out of 8 stroke patients in performing motor imagery, but the clinical scales used to rate the hand motor function showed no significant improvement.

Presently, an effective rehabilitation that is widely used for stroke involves human therapists to assist the stroke patients in recovering their stroke-affected side of the body [15]. One such therapy is the constraint-induced movement therapy (CIMT) [16], which encourages goal-directed movement with the stroke-affected upper limb while constraining the unaffected limb. Recent rehabilitation using robots alleviates the labor-intensive aspects of physical rehabilitation by human therapists [17], and a study has shown that robots deliver effective movement therapy [18].

This paper presents the clinical study to investigate the ability of hemiparetic stroke patients in operating non-invasive EEG-based MI-BCI on the stroke-affected upper extremity, and presents clinical scales on the motor improvements the patients using EEG-based MI-BCI with robotic feedback neurorehabilitation compared to robotic rehabilitation that delivers movement therapy.

978-1-4244-4124-2/10/$25.00 ©2010 IEEE

II. EEG-BASED MI-BCI WITH ROBOTIC FEEDBACK

Motor recovery after stroke is known to be influenced by enhanced activity of the ipsilesional primary motor cortex induced by motor training [19], and studies have shown that effective movement therapy can be delivered from robots [18]. Stroke rehabilitation using the MIT-MANUS robot delivers movement therapy that involves performing goal-directed, planar reaching tasks to emphasize shoulder and elbow movements with the stroke-affected upper limb [20]. When a patient cannot move, deviates from the goal or is unable to reach the goal; the robot provides guidance and assistance to the patient in reaching the goal.

On the other hand, motor imagery shares many cognitive aspects of movement without involving movement execution. A recent study using fMRI has shown that the ipsilesional primary motor cortex is activated in hemiparetic patients with subcortical stroke while performing motor imagery [13]. Thus motor imagery provides a substitute for executed movement as a means to activate the primary motor cortex.

Recent advances in machine learning and signal processing for EEG-based MI-BCI [21] facilitate the translation of motor imagery brain signals for neurorehabilitation. This motivated the development of a EEG-based MI-BCI with robotic feedback neurorehabilitation in stroke shown in Fig. 1, which synergizes MI-BCI with the clinically-proven MIT-Manus robot [22]. This clinical application of MI-BCI directly translates the motor imagery on the stroke-affected upper limb by the patient to a robot assisted movement feedback to the patient. This MI-BCI approach differs from the robotic rehabilitation approach as the former relies on the activation of ipsilesional motor cortex in performing motor imagery while the latter relies on the activation of ipsilesional motor cortex induced by motor execution. The former employs the MIT-Manus robot to provide a motor feedback to the patient whereas the latter employs the MIT-Manus robot to deliver movement therapy.

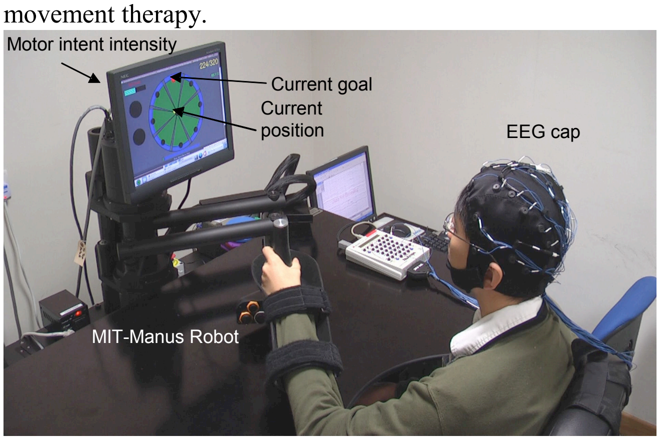

Fig. 1 Setup of Motor Imagery-based Brain-Computer Interface (MI-BCI) with robotic feedback neurorehabilitation in stroke in a local hospital.

III. EXPERIMENTAL STUDY

This section describes the clinical study performed to investigate the ability of hemiparetic stroke patients in operating EEG-based MI-BCI, and the efficacy in motor improvements of using EEG-based MI-BCI with robotic feedback neurorehabilitation.

A. Ability to operate EEG-based MI-BCI

A total of 54 BCI naïve hemiparetic stroke patients were recruited from a neurorehabilitation facility linked to the local hospital with an acute stroke unit. 27 channels of EEG data were collected from each subject, with approval from the Ethics Approval Board, using Nuamps acquisition hardware (http://www.neuroscan.com) with unipolar Ag/AgCl electrodes sampled at 250 Hz. A total of 160 single trials of EEG that randomly comprised 80 motor imagery of the stroke-affected upper limb and 80 motor execution of the unaffected upper limb were collected. Each trial lasted approximately 12 s. For each trial, the subject was first prepared with a visual cue for 2 s on the screen, and another visual cue then instructed the subject to perform motor imagery or motor execution for 4 s, followed by 6 s of rest. The subjects were advised to minimize any body movement throughout the process. 10 mins of rest were given in between every 40 trials. The data from 80 trials of motor imagery on the stroke-affected upper limb and 80 trials of background rest were used without any removal of artifacts such as Electrooculogram (EOG). A preliminary study on 35 hemiparetic stroke patients were presented in [23] that used the EEG data on motor imagery and motor execution. This study used only the EEG data from motor imagery of stroke-affected upper limb and background rest condition.

Table I shows the demographic and clinical variables of these stroke subjects. The clinical variables are type of stroke (ischaemic or hemorrhagic), side of stroke (right or left) from neuroimaging, nature of the stroke (cortical or subcortical), baseline Fugl-Meyer Assessment (FMA) before rehabilitation, and the accuracy of performing MI-BCI on the stroke-affected upper limb versus the background rest condition. Fig. 2 shows the results of unbiased 10×10-fold cross-validations performed using the FBCSP algorithm [24] on the patients' EEG data. The accuracies in classifying the motor imagery brain signals from the background rest condition for each subject are sorted in ascending accuracy and a plot of the FMA of each patient is included. The results show 48 subjects (89%) operated the MI-BCI better than chance level, and the ability to operate MI-BCI is not linearly correlated to their motor ability measured using FMA (Pearson correlation coefficient $r = 0.358$).

TABLE I
DEMOGRAPHIC AND CLINICAL VARIABLES FOR STROKE SUBJECTS (N=54)

Gender M/F (%)	Handed-ness R/L (%)	Stroke Type I/H (%)	Stroke Side R/L (%)	Stroke Nature C/S (%)	Mean age (Range)	CVA to screen days (Range)	FMA (Range)
30 M (55.6)	49 R (90.7)	25 I (46.3)	30 R (55.6)	14 C (25.9)	51.8 ±9.1 (23-66)	105 ±143 (12-589)	14.9 ±11.7 (2-45)

M indicates Male; F, Female; R, Right; L, Left; N, None; I, Infarction; H, Haemorrhagic; C, Cortical; S, Subcortical; CVA, Cerebrovascular accident; FMA, Fugl-Meyer Assessment.

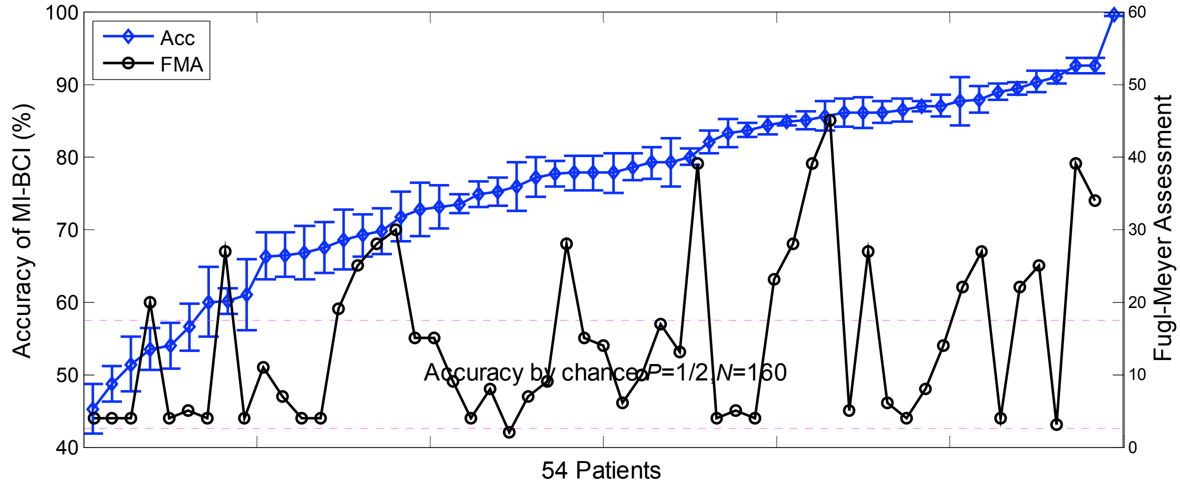

Fig. 2 Plot of the accuracies of detecting motor imagery of stroke-affected hand from background rest of 54 hemiparetic stroke patients during the screening phase with their Fugl-Meyer assessment of their upper limb motor function. The blue line with diamond markers shows the accuracies of 10×10-fold cross-validations performed using FBCSP on the EEG data of the patients whereby the blue vertical line shows the standard deviations, the black line with circle markers shows the Fugl-Meyer assessment of the patient, and the two magenta dotted lines mark the range of chance accuracies using a binomial inverse cumulative distribution function (*binoinv*) for 160 single trials.

B. Efficacy in motor improvements of EEG-based MI-BCI

26 out of the 54 recruited subjects gave further consent for this study to investigate the efficacy of EEG-based MI-BCI with robotic feedback neurorehabilitation compared to robotic rehabilitation. Each subject for this study is randomized into either group, and each group underwent 12 sessions of 1-hour neurorehabilitation on the stroke-affected upper limb for 4 weeks. The remaining 28 out of the 54 recruited subjects could not commit the time for the study and were thus not recruited. 1 subject randomized to robotic rehabilitation group dropped out after 2 weeks due to pain and was excluded from the results. The inclusion criterion for subjects randomized to the MI-BCI with robotic feedback group is the ability to operate EEG-based MI-BCI better than chance level.

Table II shows the demographic and clinical variables of 11 and 14 hemiparetic stroke patients that underwent EEG-based MI-BCI with robotic feedback neurorehabilitation and robotic rehabilitation that delivers movement therapy respectively.

For the EEG-based MI-BCI with robotic rehabilitation group, a calibration session is first performed whereby the stroke affected-limb of the subject is strapped to the MIT-Manus robot. 160 trials of EEG are collected from a total of 4 sessions that comprised 80 MI of stroke-affected upper limb and 80 rest condition. The 12-second protocol similar to section III.A is used, but the visual cue gave instruction to perform MI or rest instead. An independent test session of 40 EEG trials is also collected. For each trial in the neurorehabilitation session, the subjects performed MI for 4 s after the onset of the visual cue. If MI is detected, a movement feedback is provided by the MIT-Manus robot in moving the stroke-affected limb towards the goal displayed on the screen.

TABLE II
DEMOGRAPHIC AND CLINICAL VARIABLES FOR STROKE SUBJECTS (N=11, 14)

Gender M/F (%)	Handed ness R/L (%)	Stroke Type I/H (%)	Stroke Side R/L (%)	Stroke Nature C/S (%)	Mean age (Range)	CVA to therapy days (Range)	Week 0 FMA (Range)	MI-BCI Performance (% Range)
9 M (81.8)	10 R (90.9)	5 I (45.5)	6 R (54.5)	3 C (27.3)	47.5 ±13.5 (23-61)	383 ±291 (71-831)	26.3 ±10.3 (14-47)	77.6 ±6.4 (68.6-89.4)
7 M (50.0)	13 R (92.9)	5 I (35.7)	9 R (64.3)	4 C (28.6)	53.1± 8.6 (36-65)	250 ±184 (37-668)	26.6± 18.9 (4-57)	73.9 ±15.5 (45.3-92.6)

M indicates Male; F, Female; R, Right; L, Left; N, None; I, Infarction; H, Haemorrhagic; C, Cortical; S, Subcortical; CVA, Cerebrovascular accident; MI-BCI for Motor Imagery-based Brain-Computer Interface; FMA, Fugl-Meyer Assessment. The first row underwent MI-BCI with robotic feedback N=11, the second row underwent robotic rehabilitation N=14.

10×10-fold cross-validations on the calibration session and session-to-session transfers to the independent test session are performed using the FBCSP algorithm. Fig. 3 shows the accuracies of detecting MI of stroke-affected upper limb by 11 subjects from 54 in Fig. 2 compared with the accuracies of the calibration and independent test sessions. The results show that the accuracies of MI from the 11 patients in the calibration session (mean=75.8%) is not significantly different from the screening session (mean =77.6%, p=0.632) and the independent test session (mean =80.4%, p=0.228). All 11 subjects performed MI on stroke-affected upper limb better than chance level.

The 12-second trial protocol of the EEG-based MI-BCI with robotic feedback neurorehabilitation limits the number of trials that subject could perform within 1 hour. In addition, motor imagery was not detected in some trials. Since each session from both groups lasted 1 hour, the number of MI trials performed by subjects who underwent EEG-based MI-BCI with robotic feedback neurorehabilitation is 122 whereas the subjects who underwent robotic rehabilitation performed 960 movements.

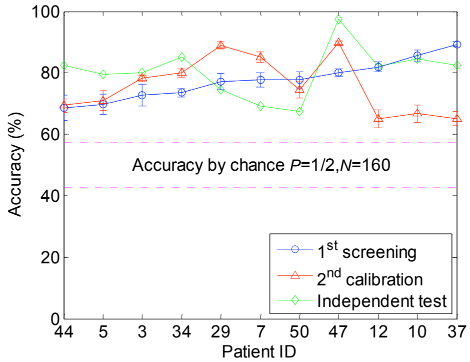

Fig. 3 Plots the accuracies of the screening session in from 11 patients who proceed with the clinical trial of MI-BCI robotic rehabilitation, accuracies of 2nd calibration session of the patient in performing motor imagery of the stroke-affected hand versus background rest, and accuracies of session-to-session transfer of the calibration to another to independent test session.

Table III shows the efficacy of 3 endpoints in terms of Fugl-Meyer motor assessment of the upper extremities of 11 and 14 subjects using MI-BCI with robotic feedback neurorehabilitation and robotic rehabilitation respectively. No significant motor improvements were attained after week 2 using the former, but significant motor improvements were attained using the latter. Nevertheless, significant motor improvements were attained at post-rehabilitation and 2-month post-rehabilitation for both groups. There were no significant difference between the improvements between two groups for all 3 endpoints (p=0.239, 0.512, 0.550).

TABLE III
IMPROVEMENTS IN FUGL-MEYER SCORE AT THE 3 ENDPOINTS FOR THE 11 HEMIPARETIC STROKE PATIENTS WHO UNDERWENT MI-BCI WITH ROBOTIC FEEDBACK REHABILITATION VERSUS 14 PATIENTS WHO UNDERWENT ROBOTIC REHABILITATION

Group	Improvements in FMA (p-value)		
	Week 2	Week 4	Week 12
MI-BCI with robotic feedback (N=11)	1.1±4.1 (0.402)	4.5±6.1 (0.032)	5.3±6.3 (0.020)
Robotic rehabilitation (N=14)	3.2±4.5 (0.020)	6.2±6.3 (0.003)	7.3±9.4 (0.013)

IV. CONCLUSION

This clinical study showed evidence that majority of BCI-naïve hemiparetic stroke patients could operate EEG-based MI-BCI on their stroke-affected upper limb better than chance level, and this ability was not correlated to their motor disability. The average motor improvement of EEG-based MI-BCI with robotic feedback neurorehabilitation was slightly less than robotic rehabilitation. The reason behind this could be due to less motor imagery trials in the former than motor executions in the latter. Nevertheless, there were no significant differences between the motor improvements from these two groups. Most importantly, significant motor improvements were observed post-rehabilitation and 2-months post-rehabilitation in both groups. Thus this study showed evidence that EEG-based MI-BCI with robotic feedback neurorehabilitation that relies on ipsilesional motor cortex activation from motor imagery is effective in restoring upper extremities motor function in stroke.

REFERENCES

[1] J. R. Wolpaw, N. Birbaumer, D. J. McFarland, et al., "Brain-computer interfaces for communication and control," *Clin. Neurophysiol.,* vol. 113, no. 6, pp. 767-791, Jun. 2002.
[2] J. J. Daly and J. R. Wolpaw, "Brain-computer interfaces in neurological rehabilitation," *The Lancet Neurology,* vol. 7, no. 11, pp. 1032-1043, 2008.
[3] M. M. Moore, "Real-world applications for brain-computer interface technology," *IEEE Trans. Neural Syst. Rehabil. Eng.,* vol. 11, no. 2, pp. 162-165, Jun 2003.
[4] A. A. Karim, T. Hinterberger, J. Richter, et al., "Neural Internet: Web Surfing with Brain Potentials for the Completely Paralyzed," *Neurorehab. Neural Re.,* vol. 20, no. 4, pp. 508-515, Dec 2006.
[5] A. Kubler, V. K. Mushahwar, L. R. Hochberg, et al., "BCI meeting 2005-workshop on clinical issues and applications," *IEEE Trans. Neural Syst. Rehabil. Eng.,* vol. 14, no. 2, pp. 131-134, Jun 2006.
[6] R. Leeb, F. Lee, C. Keinrath, et al., "Brain-Computer Communication: Motivation, Aim, and Impact of Exploring a Virtual Apartment," *IEEE Trans. Neural Syst. Rehabil. Eng.,* vol. 15, no. 4, pp. 473-482, Dec 2007.
[7] D. J. McFarland and J. R. Wolpaw, "Brain-Computer Interface Operation of Robotic and Prosthetic Devices," *Computer,* vol. 41, no. 10, pp. 52-56, Oct 2008.
[8] G. Pfurtscheller, G. R. Muller-Putz, R. Scherer, et al., "Rehabilitation with Brain-Computer Interface Systems," *Computer,* vol. 41, no. 10, pp. 58-65, 2008.
[9] N. Thakor, "In the Spotlight: Neuroengineering," *IEEE Reviews in Biomedical Engineering,* vol. 2, no. pp. 18-20, 2009.
[10] J. N. Mak and J. R. Wolpaw, "Clinical Applications of Brain-Computer Interfaces: Current State and Future Prospects," *IEEE Reviews in Biomedical Engineering,* vol. 2, no. pp. 187-199, 2009.
[11] M. H. Beers and R. Berkow, "The Merck Manual of Geriatrics," 3rd ed New Jersey: Merck Research Laboratories, 2000.
[12] N. Sharma, V. M. Pomeroy, and J.-C. Baron, "Motor Imagery: A Backdoor to the Motor System After Stroke?," *Stroke,* vol. 37, no. 7, pp. 1941-1952, Jul. 2006.
[13] N. Sharma, L. H. Simmons, P. S. Jones, et al., "Motor Imagery After Subcortical Stroke: A Functional Magnetic Resonance Imaging Study," *Stroke,* vol. 40, no. 4, pp. 1315-1324, Apr 2009.
[14] E. Buch, C. Weber, L. G. Cohen, et al., "Think to Move: a Neuromagnetic Brain-Computer Interface (BCI) System for Chronic Stroke," *Stroke,* vol. 39, no. 3, pp. 910-917, Mar. 2008.
[15] A. Pollock, G. D. Baer, P. Langhorne, et al., "Physiotherapy Treatment Approaches for Stroke," *Stroke,* vol. 39, no. 2, pp. 519-520, 2008.
[16] J. C. Grotta, E. A. Noser, T. Ro, et al., "Constraint-Induced Movement Therapy," *Stroke,* vol. 35, no. 11_suppl_1, pp. 2699-2701, 2004/11/1 2004.
[17] P. S. Lum, C. G. Burgar, P. C. Shor, et al., "Robot-assisted movement training compared with conventional therapy techniques for the rehabilitation of upper-limb motor function after stroke," *Arch. Phys. Med. Rehabil.,* vol. 83, no. 7, pp. 952-959, Jul. 2002.
[18] H. I. Krebs and N. Hogan, "Therapeutic Robotics: A Technology Push," *Proc. IEEE,* vol. 94, no. 9, pp. 1727-1738, Sep. 2006.
[19] C. Calautti and J.-C. Baron, "Functional Neuroimaging Studies of Motor Recovery After Stroke in Adults: A Review," *Stroke,* vol. 34, no. 6, pp. 1553-1566, Jun. 2003.
[20] H. I. Krebs, N. Hogan, M. L. Aisen, et al., "Robot-aided neurorehabilitation," *IEEE Trans. Rehabil. Eng.,* vol. 6, no. 1, pp. 75-87, Mar. 1998.
[21] B. Blankertz, R. Tomioka, S. Lemm, et al., "Optimizing Spatial filters for Robust EEG Single-Trial Analysis," *IEEE Signal Process. Mag.,* vol. 25, no. 1, pp. 41-56, Jan. 2008.
[22] K. K. Ang, C. Guan, K. S. G. Chua, et al., "A clinical study of motor imagery-based brain-computer interface for upper limb robotic rehabilitation," in *Proc. EMBC'09*, 2009, pp. 5981-5984.
[23] K. K. Ang, C. Guan, K. S. G. Chua, et al., "A clinical evaluation of non-invasive motor imagery-based brain-computer interface in stroke," in *Proc. EMBC'08*, 2008, pp. 4178-4181.
[24] K. K. Ang, Z. Y. Chin, H. Zhang, et al., "Filter Bank Common Spatial Pattern (FBCSP) in Brain-Computer Interface," in *Proc. IJCNN'08*, 2008, pp. 2391-2398.