EEG-based neuroimaging study for motor rehabilitation using a robotic system
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by

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Wanjoo Park (Signature)
朴完周의 工學 博士學位論文 審査를
完了함.

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Love without courage and wisdom is sentimentality, as with the ordinary church member.

Courage without love and wisdom is foolhardiness, as with the ordinary solder.

Wisdom without love and courage is cowardice, as the ordinary intellectual.

But the one who has love, courage and wisdom moves the world.

Ammon Hennacy
감사의 글 (Acknowledgments)

저에게 큰 뜻을 주시고 태초부터 지금까지, 또 앞으로도 이끌어주시고 기다려 주시며 사랑해주시는 성 삼위 하나님께 가장 먼저 감사를 드립니다. 지금까지 저에게 주어진 좋은 환경과 기회가 있었기에 박사학위까지 받게 되었습니다. 뒤돌아 보면, 너무도 큰 사랑과 은혜 속에서 풍족함을 누리며 살아온 것 같습니다. 그러나 안타깝게도, 그런 기회를 얻기 힘든 지역과 사람들은 굉장히 많다는 것을 알게 되었습니다. 그래서 이제는 지금까지 받은 사랑과 깊은 전리를 나누는 삶을 살고자 합니다. 또한 연구자로서 끊임없는 탐구의 자세로 하나님께서 창조하신 인간과 세상을 알아가는 즐거움을 누리며 살아가겠습니다.

나의 삶의 동반자, 사랑하는 아내 송자연에게 감사를 드립니다. 항상 믿어주고 격려해주고 지지해주었기에 학위과정을 잘 마칠 수 있었습니다. 앞으로의 길 또한 알 수 없지만, 함께 인도하심을 구하며 또 우리에게 선물해 주신 귀한 아들 이삭(태명)을 양육하며, 그 길을 함께해요.

변함없는 사랑으로 저를 양육해 주시고 신앙의 유산을 물려주신 아버지, 어머니께 감사를 드립니다. 그리고 사랑하는 동생 국주와 제수씨, 하은, 하린에게 감사를 전합니다. 저를 항상 믿어주시고 지지해주신 아버님, 어머님, 그리고 처남, 처남댁, 예은에게도 감사를 전합니다. 아빠가 되려고 하니 첫이 드는지 가족들 생각이 많이 남습니다. 가족들 앞에서 부끄러움이 없는 가정이 되도록 노력하겠습니다.

한국과학기술연구원(KIST)에 2008 년 12 월 입원하여 지금까지 오랜 시간, 30 대의 대부분을 보내고 있습니다. 이곳에서 저를 지도해주신 박범수의학기술연구원 김대현 박사님께 감사를 드립니다. 또한, 바이오닉스연구단 Medical IT 팀의 박세형박사님, 박영우박사님, 이정희박사님, 손영태박사님, 김영준박사님, 김제관연구원님, 현철씨, Dr.신상균, Dr.황상철, Dr.김성희, Dr.Charton, 단철씨, 두찬, 육진, 다혜, 규예, 장호, 지현, 주희, Lisa, Kinde, Cuong, Vania, 지금은 한양대에 개신권유현교수님께 감사를 드립니다. 그리고 지능인터넷센터 시절에서 함께 했던 승재, 하길, 교현, 건희씨, 만철씨에게 감사를 전합니다. 그때 그 시절이 참 재미있었어요.

고려대학교 뇌과학과에서 입학하여 폭넓은 연구로 시야를 넓힐 수 있었습니다. 지도교수 김성현교수님과 이종환교수님께 감사를 드립니다. 고대 BSPL 의 동율씨, 현철씨 좋은 논문 많이 쓰시기 바랍니다. 나를 항상 따뜻하게 맞아주는
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본 학위논문이 나오기까지 뇌졸중환자를 대상으로 한 임상실험을 할 수 있도록 도와주신 삼성서울병원 재활의학과 김연희교수님과 장원혁교수님께 감사를 드립니다. 또한, 이마의신생님, 이민지신생님이 도움으로 실험이 잘 진행될 수 있었습니다.

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아내가 진도사로 사역할 수 있도록 길을 열어주신 생명의빛 광성교회 이준태목사님과 청소년부, 청년부에 감사를 드립니다. 박찬군목사님, 이재현목사님, 안경혁목사님, 설성호전도사님, 서평화전도사님의 행정실에서의 원로와 기도의부에 즐거운 시간을 보냈습니다. 저희 받아주신 사모님들, 어설픈 오라인 사역님, 그리고 저희 반겨주셨던 많은 성도님들의 성함을 모두 기록하지 못해 죄송합니다.

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EEG-based neuroimaging study for motor rehabilitation using a robotic system

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Abstract

Stroke is one of the leading causes of morbidity and mortality; the people with motor impairments resulting from a stroke experience difficulties in their daily activities. In this thesis, an electroencephalogram (EEG)-based robotic motor rehabilitation system was proposed. This system measures EEG signals of subjects using robotic devices while the subjects perform motor tasks. Here, this system was used to measure the signals of patients with chronic stroke and those of healthy controls. In the first study, two robotic hand rehabilitation devices were developed. A novel patient-driven strategy was used based on the patient’s movement intention as detected by pressure sensors in the grasp device. This strategy may encourage patients with stroke to participate in rehabilitation training to recover their hand grasp function and may also enhance neural plasticity. A one-degree of freedom haptic rehabilitation system for supination hand function was also developed. The system was designed to improve hand strength and movement and to provide haptic feedback by incorporating visual games. The haptic interface enhances the clinical effect and makes it more fun than previous systems; various haptic effects were programmed to correspond to game scenarios.

In the second study, a novel method for monitoring cognitive engagement during motor rehabilitation was proposed. Active engagement reflects implicit motivation and can enhance motor recovery. In this study, EEG was used to assess cognitive engagement in 11 patients with chronic stroke while they executed active and passive motor tasks involving grasping and supination hand movements. The active motor task induced larger event-related desynchronization (ERD) in the bilateral motor cortex and supplementary motor area than the passive task. Differences in ERD between tasks were observed during both initial and post-movement periods. EEG
data were used to help classify each trial as involving active or passive motor tasks. Average classification accuracy was 80.7 ± 0.1% for grasping movement and 82.8 ± 0.1% for supination movement. Classification accuracy was higher when using a combination of movement and post-movement periods than in other cases. Our results support using EEG during motor rehabilitation to assess cognitive engagement in patients with stroke.

In the third study, differences in EEG signals due to lesion location were investigated. Twelve patients with chronic stroke were divided into three subgroups according to lesion location: supratentorial lesions that included M1 (SM1+), supratentorial lesions that excluded M1 (SM1-), and infratentorial (INF) lesions. Participants performed three motor tasks (active, passive, and motor imagery) with grasping and supination movements. We compared the hemispheric asymmetric indexes, which were calculated with laterality coefficients (LCs), the temporal changes in ERD patterns in the bilateral motor cortex, and the topographical distributions in the 28-channel EEG patterns around the supplementary motor areas and bilateral motor cortex of the three participant subgroups and the 12 age-matched healthy controls. The SM1+ group exhibited negative LC values in the active and motor imagery tasks, while the other patient subgroups exhibited positive LC values. Negative LC values indicate that the ERD/ERS intensity of the ipsilateral hemisphere is higher than that of the contralateral hemisphere, whereas positive LC values indicate that the ERD/ERS intensity of the contralateral hemisphere is higher than that of the ipsilateral hemisphere. The LC values of SM1+ and healthy controls differed significantly in both the grasping and supination movements during the active task. The three patient subgroups differed distinctly from each other in the topography analysis. The hemispheric asymmetry and topographic characteristics of the beta band power patterns in the patients with stroke differed according to the location of the lesion, which suggests that EEG analyses during neurorehabilitation should be implemented according to lesion location. Taken together, these findings provide novel insights into patient-driven and adapted brain-computer interface-based motor rehabilitation paradigms.
EEG-based neuroimaging study for motor rehabilitation using a robotic system

박완주
뇌공학과
지도교수: 이종환, 김래현

개요

뇌졸중은 사망과 질환의 주요 원인이며 많은 사람들이 뇌졸중 후 편마비로 인한 일상생활의 어려움 겪고 있다. 본 논문에서는 뇌파(EEG) 기반의 로봇 재활 장치를 제안하였고, 이를 이용하여 만성 뇌졸중 환자와 건강한 대조군의 상지 운동시 뇌파를 측정하여 비교 분석 하였다.

첫 번째 연구에서는 헨틱(haptic) 기반의 파지(grasp)와 외전(supination) 재활 장치가 개발하였다. 본 장치는 손을 잘 움직이지 못하는 환자가 스스로 움직이기 위해 하는 순간을 감지하여 로봇 디바이스에서 환자의 손을 정상적인 동작으로 움직일 수 있도록 보조하는 장치를 제안한다. 이는 뇌졸중 환자에게 재활 훈련에 참여하게 하고, 신경 기능의 향상으로 인한 손 기능의 회복을 촉진 시킬 수 있다. 특히, 작업치료사들은 환자 주도형 기능조 제활 훈련 시에 발생할 수 있는 보상적 움직임을 억제하는 효과가 있을 것으로 평가하였다. 손의 외전 기능을 위한 자유도 1의 헨틱 재활 장치에서는 손의 헨과 움직임을 개선하고자 하는 것뿐만 아니라 기능성 게임과 연동된 헨틱 피드백을 제공한다. 헨틱 인터페이스는 다양한 헨틱 효과들이 게임 시나리오에 따라 프로그램되어 의료 효과를 높이고 환자들이 좀 더 재미있게 훈련할 수 있도록 해준다. 뇌졸중 환자뿐만 아니라, 노인들 또한 본 디바이스를 통하여 인지 능력 훈련과 근력 운동을 할 수 있을 것으로 기대한다.

두 번째 연구로, 뇌졸중 환자들이 상지 재활을 하는 동안 인지적 참여도를 측정할 수 있는 방법을 제안하였다. 능동적 참여도는 동기를 반영하기 때문에 손상된 기능의 회복을 향상시키는데 중요한 요소이다. 본 연구에서 11 명의 만성 뇌졸중 환자가 능동 및 수동으로 파지와 외전 움직임을 수행하는 동안 뇌파를 측정하여 인지적 참여도를 평가하고자 하였다. 능동적 움직임은 수동적 움직임보다 더 큰 ERD(Event Related Desynchronization) 특성이 뇌의 운동피질(motor cortex)과 보조운동영역(supplementary motor

x
area)에서 감지되었다. 이러한 ERD 특징은 초기 움직임 시점뿐만 아니라 움직임 후에도 통계적으로 유의한 차이를 보였으며, 특히 베타 밴드의 차이가 알파 밴드 보다 큰 차이를 보였다. 본 특징을 활용하여 농동 및 수동적 움직임을 구별하였고, 평균적으로 과지운동에 대하여 80.7 ± 0.1%, 외전 운동에 대하여 82.8 ± 0.1%의 정확도를 보였다. 구별의 정확도에서는 움직임 동안과 움직임 후의 뇌과 정보를 모두 사용하였을 때 더 높은 구별 정확도를 보였다. 본 결과는 뇌파를 통하여 뇌졸중 환자가 상지 재활을 하는 동안 인지적 참여도를 평가할 수 있음을 보여준다.

마지막 연구는 반성 뇌졸중 환자의 손상(lesion) 위치에 따라 뇌파가 어떻게 달라지는지에 대한 연구이다. 기능 자기공명영상(fMRI)에서는 논의 손상 위치에 따라 측정되는 영상이 다르게 알려졌으나 뇌파에 대해서는 분명하였다. 12 명의 반성 뇌졸중 환자를 운동피질을 포함한 천막상 (supratentorial)의 손상, 운동피질을 포함하지 않는 천막하의 손상, 천막하(infratentorial)의 손상으로 3 종의 소그룹으로 분류하여 과지와 외전 운동에 대하여 농동, 수동, 운동상상의 3 가지 과제를 수행하도록 하였다. 뇌의 좌우 대칭에 대한 관계, 편측성 계수(laterality coefficients)와 ERD 와의 시간적 변화를 좌우 운동피질과 운동보조영역을 포함한 주변 28 개의 뇌파 채널에서 측정하여 12 명의 건강한 대조군과 비교 분석하였다. 운동피질을 포함한 천막상 손상 그룹에서 농동과 운동상상 과제 수행 시 음의 편측성 계수가 측정된 반면, 다른 그룹에서는 양의 편측성 계수가 측정되었다. 음의 편측성 계수는 움직임의 동측 반구의 ERD 특성이 반측 반구보다 크다는 것을 나타내고, 양의 편측성 계수는 그 반대를 나타낸다. 통계적 분석에서는 운동피질을 포함한 천막상 손상 그룹과 건강한 대조군이 과지와 외전 운동시 농동 과제에서 편측성 계수의 유의한 차이를 보였다. 또한 3개의 그룹들은 28 채널의 지형적 분석에서 베타 밴드의 파워 분포가 상호간의 차이를 보였는데, 천막하 손상 그룹이 건강한 대조군의 뇌파와 가장 유사하였다. 뇌졸중 환자의 뇌파는 편측성 계수와 지형적 분포가 손상 위치에 따라 달라짐으로 뇌-컴퓨터 인터페이스 기반의 재활 훈련 시스템에서 이를 고려하여야 할 것이다. 이러한 연구들을 통하여 얻은 발견들은 뇌-컴퓨터 인터페이스 기반의 환자 주도형 및 맞춤형 재활의 새로운 패러다임을 제시해 줄 것으로 보다 효과적인 재활이 이루어 질 수 있기를 기대한다.
List of Publications

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.


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Chapter 1. General Introduction

1. Haptic interface

The term “haptic,” derived from the Greek verb “haptesthai,” is an adjective meaning “touch” [1]. In conventional computer interface technology, audio and visual information provides information exchange between human and computer. However, a virtual reality can be created to provide the user with more specific and immersive sensations. Recent developments allow the combination of this technology with haptic technology to allow the use of touch stimuli in these virtual environments. A haptic simulator requires haptic devices and rendering technology [2]. The haptic device is a mechanical device, such as a robot arm, designed to allow people to interact with the virtual environment. There are two current areas of haptic technology: force and tactile feedback [3]. The user is able to manipulate the virtual environment via a haptic device where they are able to feel a force or tactile response from the virtual environment.

Figure 1.1.1 shows our haptic system for force feedback [4]. The user feels a sense of movement or reaction force via a mechanical interface, in this case from an interface using force feedback technology. This technology is already being deployed in order to improve efficiency in industrial and military applications. Haptic technology, such as in Figure 1.1.2 [5], is widely used in medical applications, such as for medical simulators and cell manipulators [6, 7]. Doctors are often trained in the performance of a medical procedure, such as an operation, using medical simulation. This allows them to practice in a virtual, secure environment. Recently, a training simulator for intravenous injection was developed that incorporated both visual and
tactile feedback [8]. It simulates the feeling of needle insertion into the blood vessel while simultaneously showing the needle being inserted into the arm.

The introduction of haptic technology allows a number of virtual environments to be incorporated into rehabilitation engineering [9]. Sensory functions are concentrated in the cases of visual and auditory sensation. Thus, visual or auditory

Figure 1.1.1. Haptic system for force feedback [4]
nerve damage is likely to result in loss of sensory functions. Since tactile nerves are widely distributed, damage to neural centers associated with touch sensation is less likely to result in widespread loss of sensation throughout the body. Since there is less loss of tactile response, many researchers have begun to develop haptic rehabilitation systems to assist with functional motor recovery after paralysis due to stroke [10, 11].

Figure 1.1.2. Haptic system for tactile feedback [5]
2. Brain-Computer Interface

Brain-computer interface (BCI) is a technology that provides the brain with new, non-muscular communication and control channels [12, 13]. In other words, by directly measuring brain activity via a computer, this technology allows users to communicate with or control devices without the need for input devices such as a mouse or keyboard. This is a very useful technology for patients with impaired motor function. Figure 1.2.1 shows the BCI system paradigm [14]. By acquiring signals from the brain and analyzing their features, BCI allows the user to communicate with or control external devices. The three images on the right of Figure 1.2.1 show potential applications for BCI. The first, a monitor, indicates communication, wherein the user can type the desired letter by looking at the monitor [15]. The second image, a wheelchair, represents technology that allows the user to control the movement of a wheelchair using motor imagery of left and right hand movement [16]. Finally, the image of a hand holding a bottle represents a neuroprosthetic approach wherein a damaged limb can be moved by detecting movement intention signals from the brain [17]. Studies measuring activity in a specific area of the brain, analyzing brain signals, and developing protocols to interpret signals between the brain and the computer are in progress to realize these applications of BCI.

Invasive and non-invasive methods exist to measure neuronal activity in the brain (Figure 1.2.2) [14]. Electroencephalography (EEG) measures cortical neuro-activation through electrodes placed on the scalp; therefore, EEG signals represent the activity of a large number of neurons. EEG is frequently used in BCI experimentation, since the process is non-invasive and can detect millisecond-level changes in the electrical activity in the brain. It is one of the few techniques available with high temporal resolution. Electrocorticography (ECoG) recordings are also used; ECoG has characteristics that make it more suited for basic neuroscience research that to
clinical research, since this method requires surgery to implant the necessary sensors. Invasive recording techniques combine excellent signal quality and high spatial resolution. The combination of spiking activity and local field potential (LPF) also involves invasive recording techniques that can measure single-unit neuro-activation. This approach has the advantage of high spatial resolution and the ability to provide a control signal with multiple degrees of freedom; however, recording single units over a long period of time can be difficult. Encapsulation by glial tissue increases

Figure 1.2.1. Design and operation of a BCI system [14].
electrical impedance around the electrode tips, essentially eliminating single-unit isolation over time [18].
3. Neural Engineering and NeuroRehabilitation

Neural engineering is an interdisciplinary research area incorporating neuroscience and electrical engineering to analyze neuro-signal and neurological functions [19]. The main goal of neural engineering is to provide rehabilitative solutions and enhanced care for patients with impairment. The goal of neurorehabilitation is the restoration and maximization of functions compromised or lost due to impairment caused by injury to or disease of the nervous system [20]. This would allow a patient to perform at his maximum capacity, allowing greater participation in society. Neurorehabilitation is based on the concept of neuroplasticity, the capacity for continuous alteration of the neural pathways and synapses of the living brain and nervous system in response to experience or injury. Neuroplasticity involves the formation of new pathways and synapses and the elimination or modification of existing ones [21]; however, the mechanisms of plasticity are not completely understood [22].

Neurorehabilitation therapy has the advantage of stimulating the plasticity of the central nervous system through functional training. It has effects on cellular and molecular functions involved in plasticity. While beneficial, physical therapy involves considerable effort on the part of both the patient and the therapist, which may lead to injuries. The duration of the therapy session is often limited by the therapist’s endurance; therefore, robotic rehabilitation was introduced. Robotic rehabilitation aims to reduce the workload and the physical effort of the therapists, allowing for more intensive and repetitive motions while also providing researchers the ability to quantitatively assess motor recovery by measuring variables such as force and movement patterns [23].

Despite the advantages of robotic therapy, there are limitations. Robotic therapy simply guides movement without a patient's motor intention. Knowledge of motor
intention is, however, a key factor in effective rehabilitation training [24]. To overcome this, BCI-based rehabilitation has been introduced, such as that shown in Figure 1.3.1 [25]. The BCI system determines motor intention through the recognition of EEG signal patterns that occur during motor imagery tasks. The user’s intention is then translated into a desired output that is not dependent on the normal pathways of peripheral nerves and muscles. The detection of movement intention, the key technology of this system, is possible through the detection of changes in sensorimotor rhythms (SMRs) in the motor cortex. Movement-related activation of the sensorimotor cortex is associated with two oscillatory patterns: event-related desynchronization (ERD) and event-related synchronization (ERS) [26]. ERD is a power decrease of rhythmic activity occurring during motor preparation and execution. It is dominant in the alpha (~8–12 Hz) and beta (~12–30 Hz) frequency bands. ERS is a power increase found in the alpha and beta bands; it is present after movement. ERD/ERS patterns also can be volitionally produced by motor imagery.

Figure 1.3.1 Motor imagery-based brain-computer interface for upper limb robotic rehabilitation [25].
Chapter 2. Haptic systems for upper limb rehabilitation

1. Haptic rehabilitation system for grasping movement

1.1. Introduction

Every year, according to the World Health Organization (WHO), 15 million people suffer from strokes [27]. People with motor impairments resulting from a stroke have numerous difficulties in their activities of daily living (ADL). At least 30% of stroke victims cannot recover to their pre-stroke condition and abilities.

Fortunately, the brain structures related to stroke injuries can be reorganized and motor functions can be restored via neural plasticity. This has led to the development of various methods of rehabilitative training [28]. Numerous studies have demonstrated that active, repetitive, intentional, and functional training has a significant impact on the recovery of impaired motor functions after brain injuries or strokes [29, 30]. Therefore, conventional therapists assist patients to overcome their motor deficits and improve their motor patterns with repetitive movement practice [31]. This approach is effective for stroke therapy, but it is extremely labor intensive and sometimes requires a long training period, which can lead to financial issues [32].

Recently, in order to solve these problems, robot-assisted physical therapy has been proposed. Robots that perform autonomous and repetitive movements can alleviate the labor intensive physical work by therapists and can be easily customized through varying the velocity and intensity values. Liao demonstrated that the effect of
robot-assisted physical therapy for stroke patients is similar to that of conventional physical therapy [33].

Hand functions are essential for ADL, such as grasping a spoon or a fork. However, these functions are difficult to completely recover or rehabilitate. Furthermore, hand impairment causes significant discomfort to stroke patients. Thus, there have been numerous studies on the development of robotic hand rehabilitation devices. Park et al. proposed a haptic upper limb rehabilitation device for pronation and supination therapy; patients use this device to play games that are controlled using various haptic effects that provide more enjoyment to the patients [34]. In a study involving interworking with serious games, Sietsema et al. demonstrated that an activity involving game interworking improves arm reach results [35]. Weinberg et al. made a 2-degree of freedom (2-DOF) hand device using a fluid damper and interworked it into a game scenario for hand rehabilitation [36]. This system has already been applied in hospital therapy; however, it is difficult to use it at home because the fluid device requires a large and heavy control system.

For a grasp rehabilitation system, Lambercy et al. proposed haptic knob rehabilitation device for opening/closing and pronation/supination function [37]. They demonstrated the positive effects of standard clinical assessments with their proposed rehabilitation device. The Amadeo system and its effectiveness have been reported [38, 39]; however, the high cost of the Amadeo system limits the application. Exoskeleton rehabilitation devices have also been designed: Ho et al. proposed a hand rehabilitation device to detect the intention of opening/closing movements using electromyography (EMG) [40]. Furthermore, they demonstrated the significant improvement in patients’ motor tests through rehabilitation training using the proposed exoskeleton device. In addition to these innovations, Riener et al. presented the concept of patient-driven motion reinforcement (PDMR) control for the control of a functional electrical stimulation (FES)-supported system [41, 42]. In this approach,
it is hypothesized that patient-driven training can improve therapeutic outcomes compared with classical rehabilitation strategies.

Recently, brain computer interface (BCI) technology has begun to be applied to rehabilitation applications. This technology has surmounted an insufficient patients’ participation found in conventional robot-assisted training. For example, if a patient cannot voluntarily move, the robot assists the patient to move their upper limb after detecting the patient’s intention based on motor imagery [43-45]. Although this technology is useful in directly using neuroplasticity, it requires technical assistance from experts in order to measure the patient’s intention. Also, patients experience discomfort while the electrodes are attached to their head in order to record electroencephalography (EEG) signals.

In this chapter, a hand grasp rehabilitation device is proposed that allows a patient to train the grasping behavior based on their intention and that is easy to use at home as well as in medical contexts. The patient’s intention is detected using the press sensors in the device handle when the patient attempts the movement. In addition, the affordable cost and portable size are also advantages of the proposed system.
1.2. Structure

The proposed system consists of a control unit, two actuators, an infrared (IR) sensor, and pressure sensors in the grasping handle as shown in Figure 2.1.1. The main processor of the control unit is a TMS320F2801 digital signal processor (DSP) and it communicates with a PC through a USB channel. The model of actuators is LSA-3024SM by PoteNit. Its stroke length is 24 mm and the maximum force is 30 N. These actuators assist the grasping, closing a hand movement, in both passive and patient-driven modes. The model of the IR sensor module is GP2Y0A41SK0F by Sharp. The distance range of the IR sensor is 30 to 50 mm, and it measures the distance that the handle is pulled. The model of pressure sensor is FSR-402 by Interlink. The pressure range of the pressure sensor is 0 to 175 psi, and it measures the pressure of the grasping area. A scenario, such as ‘squeeze a lemon’, is incorporated into the rehabilitation
device; hence, it is expected that patients will be more immersed in and more encouraged to participate in the rehabilitation therapy.

1.3. Rehabilitation Protocol

A. Passive Mode and Active Mode

In the passive training mode, the proposed device guides the grasping movement for patients who do not have voluntary hand and finger movements. At this time, the patient’s hand must be fixed to the grasping device; thus, a fixation bandage is included as shown in Figure 2.1.1.

In Figure 2.1.2, distance is the normalized distance of the handle movement and it is measured using the IR sensor. Pressure indicates the normalized value of the pressure sensor; $\Delta P/\Delta t$ is the difference value of pressure. Min-Max normalization method is used for data normalization. The minimum and maximum values of distance and IR sensor are measured by previous test operation. As shown in Figure 2.1.2(a), in the passive mode, the grasping movement is performed regularly. However, the pressure value is too small for the patient’s voluntary movement. This demonstrates that the patient does not participate in the grasping movement or participates very little in the grasping task. Even if movement does not occur in the section, there is a baseline pressure. This is the reason for the hand being fixed to the handle of the device as shown in Figure 2.1.1.
(a) Passive mode.

(b) Active mode.

(c) Patient-driven mode when a patient can barely grasp.

(d) Patient-driven mode with a half range of movement.

**Figure 2.1.2.** The normalized value of pressure and IR pressure sensor and the differential value of pressure for each task mode. The vertical line of the patient-driven mode is the detention of a point to need assistance.
The active training mode is operated when the proposed device does not need to assist the patient’s movement. Stroke patients who have mild effects and almost recovered can train for the grasping movement in this mode. Figure 2.1.2(b) shows the active mode. While the patient attempts to grasp, the value of the pressure sensor increases. However, the distance measured by the IR sensor does not reach the maximum value. This indicates that the user could not complete the grasping task. The distance values of the second and third trials are shorter than that of the first trial. It is inferred that in these situations, the patient is becoming exhausted.

**B. Patient-Driven (Active Assisted) Mode**

Patient-driven (active assisted) mode can be operated using the movement intention for patients with minimal voluntary hand and finger movements. When a patient attempts to move the handle for grasp training, the device detects the patient’s attempt through the pressure sensors between the patient’s hand and the handle. Figure 2.1.2(c) shows the pressure value and device position of the patient-driven mode when a patient can barely grasp. In order to determine the patient’s intention, the threshold is established using Equation (2.1.1), which is a simple algorithm to determine the timing (vertical black lines in the figure) of the robot assist. At each time frame, the two actuators push the handle of the device to accomplish the grasping behavior.

\[
(P_t + \alpha) - P_{t-1} < 0
\]  

(2.1.1)

where \(P_t\) and \(P_{t-1}\) are the pressure values at times t and t-1. \(\alpha\) is the sensitivity coefficient.

Figure 2.1.2(d) demonstrates when a patient can perform the grasping movement to some extent, but they cannot finish the grasping movement completely as a result.
of their small range of movement (ROM), even though they attempt it. The vertical line in Figure 2.1.2(d) shows the time taken to detect the decrease in the patient’s grasping force using Equation (2.1.1). After that time, the device assists the patient to complete the grasping movement. In this way, the device can detect the patient’s movement intention based on the pressure changes without requiring additional bio-signal devices.

This patient-driven approach can encourage patient participation in training, improve the rehabilitation effect, and result in greater use of neuroplasticity. Meanwhile, conventional robot-assisted rehabilitation is undertaken by moving the patient’s impaired limbs passively without considering the patient’s intention.

1.4. User Study

A. Interview Questions

A small scale, semi-structured interview of two rehabilitation therapists and one stroke patient was conducted. The interview questions focused on usability, acceptability, satisfaction, suggestions for improvement, and general comments. The interview questions and their categories are presented in Table 2.1.1. The interview data was analyzed as presented below according to the question categories.
Table 2.1.1. Interview Categories and Questions

<table>
<thead>
<tr>
<th>Category</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Convenience(^a)</td>
<td>Do you think the proposed device is convenient for patients? (^a) Questions for usability.</td>
</tr>
<tr>
<td>Independence(^a)</td>
<td>Do you think patients can use the proposed device on their own without specialists? (^a) Questions for usability.</td>
</tr>
<tr>
<td>Effectiveness(^a)</td>
<td>How much does the proposed device assist in rehabilitation training? (^a) Questions for usability.</td>
</tr>
<tr>
<td>Effectiveness(^a, b)</td>
<td>Do you think the patient-driven mode assists in rehabilitation training compared with the passive mode and active mode in this device? (^b) Questions for the patient-driven mode.</td>
</tr>
<tr>
<td>Acceptability</td>
<td>If this proposed device is commercialized, do you think that patients can purchase it and train at home?</td>
</tr>
<tr>
<td>Satisfaction</td>
<td>How satisfied are you with the proposed device?</td>
</tr>
<tr>
<td>Suggestions for improvement &amp; Comments</td>
<td>What are the factors that need improvement? Do you have any other comments or suggestions?</td>
</tr>
</tbody>
</table>
B. Interview Data Analysis

In the usability category, there were three types of questions: convenience, independence, and effectiveness. The key opinion related to convenience was that the proposed device is convenient overall. There were opinions about the independent usability including that “it would be better to include a scenario related to ADL” and “patients need the assistance of therapists at the beginning of the training, but they can use this device independently once they become accustomed to it”. For the effectiveness question, there were two significant opinions: “This rehabilitation device provides assistance in training but the handle movement velocity must be adjusted according to the patient’s condition” and “the handle of the device should be more comfortable”. Furthermore, responses for the effectiveness of the patient-driven mode were obtained. The therapists stated that “it is very effective because the patient is more motivated during grasping training” and “the training in the patient-driven mode is more useful than that of a wrong trajectory or an excessively active movement”. This response stems from some stroke patients with deficits attempting excessive movements of the affected part using other physical compensation acts, e.g. whole body movements. Another therapist’s opinion was that “this devices assists patients who are not able to spontaneously grasp even thought their effort. However, just active movement training is appropriate rehabilitation for the patients who are able to do grasping movements with a half ROM”. The response to the acceptability question was that a reasonable cost would be an important issue for the diffusion of the proposed device.

However, there was an opinion from a stroke patient that he prefer therapist’s guidance more than self-training. The responses to the satisfaction question were primarily affirmative and positive. For the improvement and general comments questions, some valuable feedback was received. If the proposed device includes
grasping training and extension training functions, then it will be a better hand rehabilitation device. Furthermore, there were some opinions on the need for the ability to adjust the speed and strength so that patients can use it for adaptive training.

Taken together, the responses to the interviews indicated that a target group who will be able to effectively use the proposed device exists. Furthermore, the patient-driven mode may be useful because it helps users training with motivation and prevents a compensational strategy. However, an improvement of the handle is required in order to give more comfortable feeling to the patients, and the force and velocity must be adjustable in order to be appropriate for each patient’s needs. Moreover, it is expected that more patients will use the proposed device if an extension movement is added.

1.5. Conclusion

In this chapter, a robotic rehabilitation device that assists stroke patients for recovering their grasping functions was proposed. Also, a novel patient-driven mode based on the patient’s movement intention detected using pressure sensors was proposed in order to directly engage in neuroplasticity. In the user study conducted with therapists and a stroke patient, it was found that the proposed device with the patient-driven approach could be useful for hand rehabilitation. Our proposed device has several limitations. It is needed to adopt adaptive control strategies for each patient’s capabilities. Further research focused on investigating the rehabilitation effect of the proposed device will be undertaken through working with stroke patients and constructing solid evidence of the proposed device’s benefits using functional neuroimaging devices such as functional magnetic resonance imaging and electroencephalography.
2. Haptic rehabilitation system for supination movement

2. 1. Introduction

In our aging society, avoiding a decrease in muscular strength and cognitive function by the elderly is necessary. Particularly, a decrease in the number of hand functions after a stroke causes many elderly people to be inconvenienced in their Activities of Daily Living (ADL) and decreases their quality of life. Therefore, many devices, such as an E-Link, are used popularly for hand rehabilitation without haptic feedback [46].

Over the past several years, several studies have investigated haptic rehabilitation. Riener et al. reviewed the research on neuro-rehabilitation of the upper extremities via machines [47]. Hogan et al. studied factors regarding motor rehabilitation [48]. For hand rehabilitation, Lambercy et al. analyzed hand functions and studied a haptic knob for opening/closing activities [49]. Dovat et al. developed this research, positing wire connections for each finger [50]. Additionally, Chapuis et al. studied wrist rehabilitation [51]. In a study involving interworking with a game, Sietsema et al. showed that an activity involving game interworking improves arm reach results [52]. Weinberg et al. made a hand device using a fluid damper and interworked it into a game scenario for hand rehabilitation [53].

This research proposes a motor-based 1-DOF handle. The target subjects here are not only stroke patients but also the elderly. The purpose of this study is to improve the hand strength and to increase the Rotation of Movement (ROM) of the hands. We use a multi-modal game interface incorporating visual, aural, and haptic feedback.
2. 2. Structure

The system consists of a microprocessor, a motor, a torque sensor, and various types of handles. The main processor is a TMS320F2801 DSP and the digital to analog convertor (DAC) is a DAC0800. A DC motor is used to generate various haptic patterns. We use a RE30 DC motor, which works at 24 V and 3.44 A, with 85.0 mNm of maximum continuous torque and 1020 mNm of maximum stall torque. The torque sensor is a DR-2477 with a maximum measurable torque of 2000 mNm. Handles are installed on the torque sensor, and the motor drives the handle through the torque sensor. The encoder to measure the angular position is a MR1024 device. It measures 4096 pulses per turn. An enhanced quadrature encoder pulse (eQEP) function of DSP is used for the encoder that counts the pulses. The user can rotate the handle to feel haptic effects which are programmed along the angular position depending on the game stage. Figure 2.2.1 shows the system implementation. This mechanical structure has a table installed with a vise. It can transform into a horizontal and vertical mode, as shown in Figure 2.2.1. In the experiment, the user is asked to catch a ball by moving the goalkeeper in the visual display using the haptic handle.
2. 3. Haptic control

This section details the haptic controls. There are two types of controls: friction and barrier controls. The function of the friction control is to increase the friction to build up muscular strength as the user wins each stage of the game. The function of the barrier control is to move the barrier location to increase the ROM of the hands. When a player catches the ball, this system provides vibration to the player so that the player can feel the ball in as realistic a manner as possible. This system can also measure the user’s hand torque so as to adjust the haptic intensity.

Figure 2.2.1. System Implementation
A. Friction Control

The friction feedback is implemented via Equation (2.2.1), the friction con model [54]. The friction level $L_f$ exponentially increases with an increase in the state; however, the intensity of a player’s feeling is linear. The system induces the player to use additional power unwittingly as the level of the game increases.

Figure 2.2.2. Flash game GUI
\begin{align*}
L_f &= \exp\left(N_s(s)/s_f1\right) \\
P_{\text{curr}_f}(n) &= P_{\text{prev}}(n-1) + \left(P_{\text{now}}(n) - P_{\text{prev}}(n-1)\right) \cdot S_f^2 \\
P_{\text{diff}}(n) &= \left(P_{\text{now}}(n) - P_{\text{curr}_f}(n)\right) \cdot L_f \\
P_{\text{prev}}(n) &= P_{\text{curr}_f}(n) \\
\text{if } P_{\text{diff}}(n) > T_{f_{\text{max}}} & \text{ then } T_f(n) = T_{f_{\text{max}}} \\
\text{else if } P_{\text{diff}}(n) < T_{f_{\text{min}}} & \text{ then } T_f(n) = T_{f_{\text{min}}} \\
\text{else } T_f(n) &= P_{\text{diff}}(n)
\end{align*}

where $N_s$ is the number of stages, $P_{\text{curr}_f}$ is the current position, $P_{\text{now}}$ is the angular position of the dial knob, $P_{\text{prev}}$ is the previous position, $S_f^1$ and $S_f^2$ are the scaling factors, $P_{\text{diff}}$ is the difference in the position, $L_f$ is the friction level, and $T_f$ is the friction torque.

\textbf{B. Barrier Control}

If the ROM of hands is decreased because of stroke or old age, users experience inconvenience in their ADL. Equation (2.2.2) shows the barrier haptic feedback. Here, $b(s)$ refers to the start point of the barrier in the game state. The start point of the barrier is an edge point of the goalpost in the game GUI. The start point of the barrier can be as far away as 4.5 degrees as the stage of the game increases. A game player must continually rotate the handle more than in the previous game stage to move the goalkeeper to the edge point of the goalpost. This is expected to help users to increase the ROM of their hands unwittingly.
where $\theta$ is the rotation angle of the dial knob, $b$ is the start point of the barrier, $a$ is the amplitude of the edge function, $w$ is the range of the edge function, and $N_s$ is number of stages.

2. 3. Conclusion

This chapter proposed an enhanced rehabilitation game system with an addition of a haptic interface consisting of a micro-processor, a motor, a torque sensor, and various types of handles. The system provides various types of haptic feedback corresponding to game scenarios to train users’ cognitive ability and muscular strength. It assesses user performance by measuring the muscular power and the movement angle of the hand of users.
Chapter 3. Assessment of Cognitive Engagement in Stroke Patients

1. Introduction

Stroke is one of the leading causes of death and currently ranked the second most severe disease worldwide [55]. Stroke occurs primarily as a result of blood circulation problems in the brain, which can induce injuries to motor and sensory nerve systems [56]. Rehabilitation training involving repeated movement of the upper and lower limbs can stimulate damaged brain areas and lead to partial or full motor function recovery [57]. Animal studies have shown evidence of neuroplasticity, a functional and structural reorganization of the brain, following rehabilitation training [58]. Human studies have also demonstrated that active and repetitive training foster motor function recovery following stroke [59-60].

In traditional motor rehabilitation training, patients practice repetitive limb movements aimed at improving motor function with the help of physical therapists [61]. However, this training paradigm requires extensive training periods for patients and intensive labor for therapists [62]. To address these problems, robot-assisted therapy has been developed [63, 64]. This method allows for autonomous and repetitive training without a therapist’s help. Several studies have shown that robot-assisted therapy can be effective [65]. However, there are still limitations. Robot-assisted therapy simply guides movement without knowing a patient’s motor intention, a key factor in effective rehabilitation training [24]. Previous studies highlighted the clinical importance of a sense of accomplishment in limb movement based on a patient’s motor intention during rehabilitation [66, 67].
To incorporate motor intention into rehabilitation, many studies have attempted to detect motor intention by analyzing physiological signals using electrocardiography (ECG), electromyography (EMG), and galvanic skin response (GSR) [68-71]. However, it is difficult to relate ECG and GSR findings to motor intention because the autonomic nervous system typically reacts much later. For EMG signals, measuring muscle activity is the proper method of identifying either active or passive movement in the case of gross motor control such as arm movement. Ebaugh et al. reported EMG differences during active and passive humeral elevation [72]. However, the opposite result was reported when the degree of humeral elevation was small (10-50 degrees) [73]. Less muscle activity is involved in grasping and supination movements than in humeral elevation. The participants of the former EMG study were healthy people; however, in the case of stroke patients, EMG signals may suffer from interference caused by spasticity even if participants are performing a passive task [74, 75]. Also, motor imagery tasks, rather than actual movement, are more beneficial for severe patients who have difficulties performing active movements. Motor imagery can be detected by neuroimaging methods. Thus, we turned our attention to neuroimaging approaches [13].

Neuroimaging studies directly measuring motor intention have been performed using electroencephalography (EEG), functional magnetic resonance imaging (fMRI), and functional near-infrared spectroscopy (fNIRS) to evaluate brain signals. While fMRI provides excellent spatial resolution for localizing brain activation, the method lends itself to limited training environments and has low temporal resolution. fNIRS can detect blood oxygenation level dependent (BOLD) signals without MRI, but it also has limited temporal resolution [76, 77]. Despite its low spatial resolution and sensitivity to noise, EEG is probably best suited to measuring brain activity during motor rehabilitation. Many studies have shown that imagined, planned, or executed
Limb movements produce EEG signals with high temporal resolution and that spatial and noise sensitivity are not as important [13, 78]. Additionally, compared to other methods, EEG is relatively easy to use in various clinical settings.

There have been efforts to detect motor intention using EEG for motor rehabilitation in stroke patients. Specifically, studies have investigated the effects of rehabilitation training by combining robot-assisted therapy with an EEG-based brain-computer interface (BCI) that can detect motor intention in patients [79]. Kai Keng et al. showed that the Fugl-Meyer Assessment (FMA) score, a measure of motor function, increased as a result of repetitive feedback of motor imagery (MI) to the chronic stroke patient’s affected hand [80]. Moreover, Ramos-Murguialday et al. conducted a double-blind, sham-controlled experiment to study robot-assisted rehabilitation and reported that FMA scores in the BCI-rehabilitation group were higher than the control group [81]. Gomez-Rodriguez et al. proposed a real-time rehabilitation system using motor-sensory feedback and detection of motor intent [82]. Kaiser et al. demonstrated a correlation between motor ability and event-related desynchronization/synchronization (ERD/ERS) during motor execution and MI tasks in stroke patients [83]. Kang et al. compared ERD/ERS patterns of alpha and beta oscillations between different tasks (passive, motor imagery, and passive with motor imagery) involving pronation and supination movements [84]. They showed that alpha ERD in contralateral sensorimotor areas was stronger than that in ipsilateral areas, which is typical in healthy people [85]. However, no significant difference in the pattern of beta oscillations was reported. In the case of stroke patients, however, activation areas in the brain are changed by neuroplasticity [28]. In addition, active and passive movements may elicit different ERD/ERS patterns from those of this previous study.
In contrast to motor intention, active engagement during rehabilitation training has rarely been studied in stroke patients. Measuring patient engagement during training is important for both refining training paradigms and tracking recovery. Motivation and feedback have been known to influence the brain’s reward system for rehabilitation training in the basal ganglia, playing an important role in recovering motor functions [86]. Thus, it is important to maintain stroke patients’ motivation throughout rehabilitation therapy and if one can provide feedback of active patient engagement in real time during rehabilitation training, it may help keep patients motivated and improve rehabilitation. Langhorn et al. showed that active patient participation is crucial for enhancing motor rehabilitation, and Takeuchi and Izumi proposed that rehabilitation training depends on the degree of volitional engagement [87, 88]. Still, how to properly monitor patient engagement during training has yet to be addressed. Therefore, development of new tools for tracking active engagement is important for stroke rehabilitation.

Measurement of force using a sensor incorporated into a rehabilitation device can extract more direct and clearer signals than EEG in general. In previous studies in our laboratory, we measured force signals using pressure and torque sensors during upper limb rehabilitation tasks [89, 90]. This system used the force to trigger a robotic device to initiate hand movements. However, it was designed to help motor initiation rather than to monitor persistent active engagement during the entire task period, similar to the study by Marchal-Crespo et al. [68]. Force sensor monitoring during motor tasks in stroke patients is of limited use because forces exerted by patients are likely to be unstable and unintentional due to motor impairment. In addition, some stroke patients are unable to exert sufficient force due to severe motor impairment [68]. Hence, active task engagement may be better detected by direct measurement of brain activity. In the present study, we aimed to build an active engagement
monitoring system based on brain activity that can be applied to various types of stroke patients.

The present study also aimed to gauge patient engagement during rehabilitation training using an EEG-based BCI. Information related to motor task engagement can be extracted from distinct neural activity patterns associated with either active or passive movement. Previous research has revealed that neural activity patterns differ when a subject actively moves a limb versus passive limb movement by an external force [91, 92]. Here, EEG patterns, specifically ERD/ERS, are evaluated during active grasping, passive grasping, and supination movements in stroke patients. These hand movements were selected based on their involvement in upper limb rehabilitation. To examine the feasibility of developing an online monitoring tool, we discriminated between EEG patterns associated with active versus passive movements on a single-trial basis. Our hypothesis was that the ERD during an active task would be greater than that during a passive task.

Two previously developed robotic devices were used to guide grasping and supination hand movements, respectively [90], [93]. The grasping device performs a 1-degree of freedom (DOF) opening/closing hand movement by controlling the grasping handle, where the hand is fastened to the handle so that it does not slip off due to motor impairment. Two parallel linear motors push or pull the grasping handle. The supination device performs a 1-DOF supination/pronation movement by rotating the supination handle, where an additional arm supporter holds the forearm and the hand is fastened to the handle in a similar manner to the grasping device.
2. Materials and Methods

2.1. Participants

Eleven chronic stroke patients participated in this study (8 males, 3 females; mean age = 55.5 ± 5.6). All participants were first-time stroke patients, exhibited unilateral motor problems in upper extremities/limbs, continued to have issues at least 3 months after stroke, were aged between 45 and 70 years old, and were categorized as moderate or mild by FMA scoring. Participants with other cognitive disorders rendering them unable to understand task instructions and/or with other orthopedic disorders that led to amputation or joint contraction were excluded. Mean FMA scores were 46.4 ± 9.2 for affected and 64.7 ± 1.4 for unaffected sides, lower scores indicating more severe impairment (Table 3.2.1). Stroke patients did not have a history of neurological illness and had not previously participated in an EEG experiment. The Institutional Review Boards of the Samsung Medical Center (SMC, Application Number: SMC 2013-02-091) and Korea Institute of Science and Technology (KIST, Application Number: KIST 2013-009) approved this study. Participants were informed about the study’s purpose, experimental procedures involved, and right to withdraw at any time. Written informed consent was obtained from all participants. All research data were collected and analyzed under IRB guidance.
2.2. Experimental protocol

We selected the two types of movement, grasping and supination, because these two movements are among the latest recovered movements during upper limb rehabilitation. Thus, in many real motor rehabilitation programs, these movements are intensively trained and were therefore selected as target movements in our study. We expected greater ERD with the supination movement than with grasping because supination is more difficult to perform in stroke patients in general.

For each movement, three motor tasks were performed: passive (P) movement of a robotic device, active (A) movement of a robotic device, and motor imagery (MI) of kinetic movement. We also included the MI task in our experimental protocol for

<table>
<thead>
<tr>
<th>No</th>
<th>Age</th>
<th>Sex</th>
<th>AH</th>
<th>Diagnosis</th>
<th>Grip Strength/Grasp</th>
<th>Purdue Pegboard Test</th>
<th>FMA</th>
<th>MAS/Elbow</th>
</tr>
</thead>
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<tr>
<td></td>
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<td>UH</td>
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<tr>
<td>1</td>
<td>58</td>
<td>M</td>
<td>Rt.</td>
<td>Lt. medially medullary infarct</td>
<td>NT</td>
<td>23.3</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>2</td>
<td>56</td>
<td>F</td>
<td>Lt.</td>
<td>Rt. CR infarction</td>
<td>0</td>
<td>2.5</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>49</td>
<td>M</td>
<td>Lt.</td>
<td>Cerebral infarction, rt. medially medulla</td>
<td>6</td>
<td>36</td>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>52</td>
<td>F</td>
<td>Lt.</td>
<td>Lt. MCA infarction, border zone</td>
<td>0</td>
<td>14.6</td>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>53</td>
<td>M</td>
<td>Lt.</td>
<td>Rt. MCA territory infarction</td>
<td>NT</td>
<td>23.3</td>
<td>13</td>
<td>32</td>
</tr>
<tr>
<td>6</td>
<td>57</td>
<td>M</td>
<td>Rt.</td>
<td>Lt. pons infarction</td>
<td>8</td>
<td>27.6</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>M</td>
<td>Lt.</td>
<td>Rt. Thalamus, IC infarction</td>
<td>8</td>
<td>26.6</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>8</td>
<td>65</td>
<td>M</td>
<td>Rt.</td>
<td>Lt. BG ICH</td>
<td>5</td>
<td>21</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>9</td>
<td>46</td>
<td>F</td>
<td>Rt.</td>
<td>Lt. BG infarction</td>
<td>1</td>
<td>16</td>
<td>7</td>
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<tr>
<td>10</td>
<td>59</td>
<td>M</td>
<td>Lt.</td>
<td>Rt. MCA infarct</td>
<td>15.3</td>
<td>35.3</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>11</td>
<td>52</td>
<td>M</td>
<td>Lt.</td>
<td>Lt. Pontine infarction</td>
<td>11.3</td>
<td>23.7</td>
<td>5</td>
<td>10</td>
</tr>
</tbody>
</table>

* AH: Affected Hand, UH: Unaffected Hand
* MAS: Modified Ashworth Scale
* CR: Corona Radiata
* MCA: Middle Cerebral Artery
* IC: Internal Capsule
* BG: Basal Ganglia
* ICH: Intracerebral Hemorrhage

Table 3.2.1. Clinical Data of Participants

- 32 -
the purpose of detecting motor intention by EEG, as performed in many previous BCI-based rehabilitation studies [79, 82]. However, since this study primarily focuses on the monitoring of active engagement in stroke patients during rehabilitation, we excluded the analysis of EEG patterns generated during the MI task.

Participants were trained on each motor task before the actual experiment (Figure 3.2.1). The main experiment involved nine runs of motor tasks separated by 10-s breaks. Motor task order was permutated (e.g., P-A-MI-A-MI-P-MI-P-A), such that the first task was chosen randomly for counterbalancing. Each motor task consisted of 14 trials and took approximately 2 min. Participants performed 42 trials of each motor task for both grasping and supination movements.

At the beginning of each run, task instructions were shown on the screen. Then, a fixation cross was displayed, and participants were instructed to stare at the cross without moving their head. In the few seconds that followed, participants waited for a task cue while gazing at the fixation cross. When the fixation cross changed to a circle paired with a beep sound, the participants performed a motor task for 2000 ms. The training device stopped for 1000 ms, and the circle changed back to the fixation cross. The training device then returned to its starting position for 2000 ms. During this return period, participants were instructed not to exert control on the device. In general clinical paradigms, upper limb motor rehabilitation treatments employ continuous action. The length of time for the hand movement task should not be too long to cope with a continuous motor control paradigm, or too short because of the difficulty in performing movements in a short period. In this regard, we empirically determined that the 2000 ms task period was not too short for patients to perform movements and that it was also not too long for the overall training task to be completed in continuous action. The 2000 ms return period was determined to be equal to the motor task period.
Figure 3.2.1. Experimental Design. The upper panel illustrates our experimental protocol, which is composed of training and main sessions. In the training session (the first box), the participants repeatedly performed passive, active, and motor imagery (MI) tasks until they were familiar with each. In the main session (the second box), a single run began with task instructions followed by 14 subsequent task trials. A 10-s rest period followed each run. Rest instructions are shown in the lower right panel. During this time, participants were able to move around freely and relax. The lower panel illustrates the task paradigm in a single run. The task instruction screen was first shown on the computer screen. A rest period followed with a random duration between 2000 and 3000 ms. A cross mark appeared on the screen during this period. Then, a 2000-ms motor task period started with auditory and visual cues, a 1000-ms stay period followed, and a 2000-ms return period followed this, in which the robotic device was reset to its original position. During the motor task period, a circle was shown on the computer screen as a visual cue for the motor task. During the stay and return periods, a cross mark was shown on the screen to indicate these periods and to guide the participants to focus their eyes on the mark.
2.3. Robotic Devices for Upper Limb Motor Tasks

The robotic devices used were designed to guide users to complete tasks that call for active and passive movement [90], [93]. Using these devices, participants performed upper limb motor tasks involving grasping and supination (Figure 3.2.2). During the experiment, participants sat in a chair that either had a board to support their arm during grasping (Figure 3.2.2(a)) or an arm supporter for supination movement (Figure 3.2.2(b)). The participant’s affected hand was fastened around the handle of the device with a bandage. A monitor that displayed instructions and visual feedback was located at eye level and 1 m away from participants. Contrast and luminosity were adjusted to optimize concentration and comfort for all participants.

During passive motor tasks, participants did not exert control, and instead, a robotic device guided performance. For active motor tasks, participants performed the task by themselves without assistance from the device. The robotic device operated differently according to task type. After completing motor tasks, the device’s handle automatically returned to its neutral position to prepare the next task. Completing the motor task within 2000 ms may be difficult for some stroke patients. Thus we did not ask patients perform a full range of movement. In the grasping movement, the initial posture was not in a fully open position but was instead half closed. The maximum distance of the grasping handle was set to 24 mm to allow a relatively short range of movement. We also asked patients to perform supination movements within a limited range between -18 and 60 degrees.
2.4. EEG Data Analysis

EEG signals were acquired using a 64-channel active electrode EEG system (sampling rate: 2048 Hz; Active-two, Biosemi, Amsterdam, Netherlands). EEG signals recorded from each channel were preprocessed through a series of steps (Fig. 3). We used EEGLAB toolbox for EEG signal processing [94]. First, EEG signals were down-sampled to 1024 Hz. And then a zero-phase finite impulse response filter was used for band pass filtering (order: 256; low cut-off frequency: 1 Hz; high cut-off frequency 80Hz). A notch filter was applied with a zero-phase digital filter to remove
line noise (order: 1024; start and end of pass band: 56, 64 Hz, first and second stop band: 58, 62 Hz). Second, the filtered EEG signal was divided into epochs corresponding to each motor task trial. A single epoch spanned from 1000 ms before the movement cue until 5000 ms after the cue. Artifacts from eye or body movement were removed after an independent component analysis (ICA) [95]. Third, trials with suspected head movement were excluded. These trials typically showed extremely large fluctuations exceeding a threshold of 100 μV and activity that was more than five standard deviations away from the mean. Finally, EEG signals were re-referenced using the common average reference (CAR) [96].

After preprocessing, a spectrogram of the EEG signal at each channel was computed via short-time Fourier transform (STFT) with a 500-ms Hamming window, sliding by 50 ms. Baseline for each epoch was determined to be 1000 ms prior to movement cues. Spectral power was normalized by subtracting the mean at baseline from every data point within an epoch and dividing by the standard deviation at baseline. This process was repeated for all EEG channels, motor tasks (active and passive), and movement types (grasping and supination). Two frequency bands were selected in our study: the mu band (8–13 Hz) and the beta band (13–32 Hz), both of which reflect sensorimotor rhythms (SMRs) [13, 78, 97].

To discriminate between active and passive movements, C3, C4, and Fz channels, the ipsilateral/contralateral motor cortex, and the supplementary motor area (SMA) were selected based on a previous finding that ERD/ERS of SMRs in these channels reflect imagined, planned, or executed arm/hand movements [85]. We extracted spectral features by dividing the period after the movement cue into six non-overlapping 500-ms segments (four segments in the motor task period and two in the stay period). Spectral power values at each frequency (1-Hz resolution) within mu and beta bands (8–32 Hz, a total of 25 frequencies in this range) were time-averaged
within each segment. This resulted in 150 \((25 \times 6)\) features for each channel. Next, a one-way ANOVA was conducted to select a subset of features that showed a significant difference between active and passive movement \((p < 0.01)\). The number of selected features differed among participants and movement types.

Using the selected features as input, we classified single-trial EEG data as involving either active or passive movement. A naïve Bayes classifier was used and classification was performed using a ten-fold cross-validation method [98, 99]. Classification was performed separately for grasping and supination in all participants. Further analysis was conducted to investigate the effect of the task type on classification using features from the motor task period (0–2000 ms after the cue), the stay period (2000–3000 ms after the cue), or both.
Figure 3.2.3. EEG preprocessing procedure. First, the recorded EEG signals were down-sampled from 2048 Hz to 1024 Hz. Signals were then filtered with a 1–80 Hz pass band and again with a 60 Hz notch filter to remove noise. Filtered signals were divided into sets of epochs, such that each epoch covered the period from 1000 ms before to 5000 ms after motor task onset. Independent component analysis (ICA) was applied to the signals to remove artifacts produced by electrooculography (EOG) and electromyography (EMG). Furthermore, epochs with signal amplitudes that exceeded a predetermined threshold or visually different waveforms were removed after visual inspection. Finally, EEG signals from all the electrodes were re-referenced using a common average reference (CAR).
3. Results

3.1. Spectral power differences between active and passive motor tasks

We investigated temporal changes in mu and beta band power in bilateral sensorimotor areas and the SMA during active and passive motor tasks. Figure 3.3.1 shows total average EEG spectrograms in bilateral sensorimotor areas and SMAs for two motor tasks and two functional movements. ERD was observed after the motor task cue and this ERD phenomenon was visible in the entire frequency range of the mu and beta bands.

For investigation of spectral power differences between active and passive movements during the motor tasks, event-related changes in mu and beta band power for every case shown in Figure 3.3.2. Overall, both active and passive grasping/supination movements induced significant decreases in mu and beta band power following the movement cue (ERD; \( p < 0.01 \)). However, there were still differences in the temporal patterns of ERD between active and passive tasks. The active task consistently induced ERD in mu and beta band power during the entire post-stimulus period in bilateral sensorimotor areas and the SMA. The passive task also induced ERD in mu and beta power during the motor tasks in all three areas. However, during the period immediately after the task, it induced ERD for most bands, areas, and movement types outside of the mu band in the SMA for both movements and the beta band in the SMA for supination. During the return period in which the training device returned to its initial position, the passive task induced ERD for everything except the mu band in the SMA during grasping. Thus, it appears that the active task induces ERD more consistently throughout the whole movement period than the passive task.
Figure 3.3.1. EEG spectrogram during active and passive motor tasks in bilateral and supplementary motor areas. Each spectrogram has time (in ms units) along the horizontal axis and frequency (in Hz) along the vertical axis. Power changes (in dB) relative to signal baseline at any given time and frequency are indicated by the color heat map. Spectrograms of active and passive motor tasks during the grasping movement are placed on the upper two rows and the other spectrograms are placed on the lower two rows. The three columns indicate the contralateral and ipsilateral motor cortex, and the SMA.
We also identified time windows in which spectral power was significantly different between active and passive tasks. Differences were observed in the beta band of all areas for grasping and supination. This difference was observed to be greatest during the stay period immediately following the motor task. We also observed differences in the mu band, but only for a few windows within this same period for supination in bilateral sensorimotor cortical areas and grasping in the SMA. Paired t-tests revealed that beta band differences between the two tasks over the entire period (0–5000 ms) were larger than mu band differences for both grasping and supination movements ($p < 0.01$) in bilateral sensorimotor areas and SMA.
Figure 3.3.2. Comparisons of event-related changes in the power of sensorimotor rhythms between the active and passive motor tasks in bilateral motor cortical and supplementary motor areas. The temporal changes in the power of sensorimotor rhythms at the mu (8–13 Hz) and beta (13–32 Hz) bands are shown for each of the three brain areas (bilateral motor cortical areas and supplementary motor area) and for grasping and supination, respectively. These time courses of spectral power, starting 1000 ms before the motor task onset (time point of 0 s in each graph) and ending 5000 ms after the onset, were obtained by averaging across all the trials of all the participants. The dashed blue lines represent the time courses of spectral power for the passive motor task and the solid red lines represent them for the active motor task. The point marks above and below the lines signify time points when spectral power showed a statistically significant change relative to baseline power ($p < 0.01$). The blue mark represents significant changes for the passive motor task, and the red mark represents them for the active motor task. The vertical lines connecting the two curves depict time points when the spectral powers of the active and passive motor tasks were significantly different ($p < 0.01$).
Figure 3.3.3 illustrates EEG spectral power topography of the grand average band power across 64 EEG channels at 553 ms and 2815 ms following the movement cue. Average ERD during the active motor task was at its maximum at 553 ms following the movement cue in bilateral sensorimotor areas and the SMA for all bands, movement types, and tasks. ERD in sensorimotor areas was also larger during the active task than the passive task ($p < 0.05$) except for the beta band with grasping movements 553 ms after movement cues. Furthermore, the associated ERD was larger in the affected hemisphere than in the unaffected hemisphere in the case of the beta band with supination movements 553 ms after movement cues ($p < 0.05$). Average spectral power during the passive motor task peaked 2815 ms after the movement cue, during the stay period that followed the motor task, in bilateral sensorimotor areas and the SMA for all bands. There was no clear ERD detected in sensorimotor areas during passive tasks.
Figure 3.3.3. EEG spectral power topography during active and passive motor tasks. The topographies of EEG spectral power patterns 553 ms after motor task onset are shown in the left two columns, and those 2815 ms after motor task onset are shown in the right two columns. EEG spectral power was calculated from the mu (8-13 Hz) and beta (13-32 Hz) bands. The left two columns represent EEG patterns during the motor task period while the right two columns represent those during the stay period. More specifically, the first and the third column show the topographies for the active motor task and the second and the fourth column show those for the passive motor task. The power representations denoted as colors are power changes relative to baseline (in dB units). AH and UH denote the affected hemisphere and unaffected hemisphere, respectively.
3.2. Single-trial classification of active and passive motor tasks

We classified EEG features from a single trial into two classes based on whether they were associated with active or passive motor tasks. For grasping, classification accuracy was at 76.4 ± 0.1% when using features extracted from the motor task period only, 76.8 ± 0.1% when using features extracted from the stay period only, and 80.7 ± 0.1% when using a combination of both (Figure 3.3.4(a)). For supination, classification accuracy was at 79.3 ± 0.1%, when using features from the motor task period only, 78.5 ± 0.1% when using features from the stay period only, and 82.8 ± 0.1% when using a combination of both (Figure 3.3.4(b)). There was no significant difference in classification accuracy between supination and grasping. Classification accuracy was significantly higher than chance level for all participants \( (p < 0.01) \) except for three (3, 6, and 9) for grasping and two (2 and 8) for supination. Classification accuracy using features from both task and stay periods was significantly higher than from each alone for grasping \( (p < 0.05) \). For supination, classification accuracy using features from a combination of both periods was significantly higher than from just using features related to the stay period \( (p < 0.05) \). This was not significant when looking at the task period only \( (p > 0.05) \).
Figure 3.3.4. Classification accuracies for grasping (a) and supination (b). Classification accuracies for the active and passive motor tasks are shown for every participant and for grasping and supination movements, respectively. In each participant, the first bar represents classification accuracy using EEG data from the task period, the second bar represents accuracy using the EEG data from the stay period, and the third bar represents accuracy using EEG data from both periods. The last bars show average classification accuracies across all the participants. The result of a pairwise statistical analysis on differences in classification accuracies between three different cases is also marked (*: \( p < 0.05 \)).
Table 3.3.1 shows the number of trials correctly or incorrectly classified for active and passive tasks across all the participants. For grasping, the rate of misclassifying active tasks as passive was reduced by 6.6% when the data from stay and task periods were combined (24.5% using the task period only → 17.9% using both periods). However, the rate of misclassifying the passive task as the active was only reduced by 2.4% (23.0% → 20.6%). Similarly, for supination, the rate of misclassifying the active task as passive was reduced by 5.0% (19.9% → 14.9%), while the rate of misclassifying the passive task as active was reduced by only 2.2% (21.3% → 19.1%). Thus, incorporating EEG data from the stay period following the motor task tended to increase classification accuracy for the active task more than the passive task.
Table 3.3.1. The Number of Correctly and Incorrectly Classified Trials for Active (a) and Passive (P) Motor Tasks across 11 Stroke Patients

### (a) Grasping movement

<table>
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<td>Estimated task</td>
<td>Estimated task</td>
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<tr>
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* Σ: the sum of each row or column.
4. Discussion

Our study used EEG signals to predict active engagement during motor tasks in stroke patients. Previous studies on determining motor intention from EEG signals have been conducted in healthy individuals [100-103]. These studies relied on ERD/ERS of SMRs to detect information related to imagined, planned, or executed movements. However, since the EEG signals of patients with brain lesions due to stroke may exhibit different neuronal characteristics, it is valuable to verify if ERD/ERS of SMRs can be directly studied in stroke patients to extract motor-related information. Our results demonstrate that we can infer information about motor task engagement using ERD/ERS of SMRs in chronic stroke patients undergoing physical therapy.

Our previous study also investigated brain oscillations in the beta and mu bands [84]. This previous study showed ERD in the alpha band during passive or motor imagery tasks but no significant changes in the beta band. This might be the result of the small sample size and the simplicity of the tasks for healthy subjects. By contrast, the present study in stroke patients revealed significant ERD in the beta and mu band for both active and passive tasks. It suggests that beta oscillations can be modulated by active or passive tasks in stroke patients. Additionally, the observation in the present study of larger differences in beta ERD between the active and passive tasks indicates that beta oscillations may serve to discriminate active engagement in stroke patients.

Our analysis revealed that larger differences are shown between active and passive tasks in beta band relative to mu band power in both bilateral sensorimotor areas and the SMA. Comparison studies between active and passive tasks have previously been reported for healthy participants. In a PET study, Weiller et al.
showed that the activation area of the SMA was larger in the active task than in the passive task, whereas the activation of bilateral areas in the depth of the sylvian fissure was smaller in the active task than the passive task [104]. By contrast, Mima et al. observed stronger activation in the active task than the passive task in the SMA, secondary somatosensory cortex, primary sensorimotor cortex, and premotor cortex areas [105]. Using EEG, Alegre et al. showed that there were no differences in ERD patterns during the active and passive tasks [106]. Previous studies describe greater ERD in the passive task than in the active task [43, 92, 107], while other studies describe greater ERD in the active task than in the passive task [108]. Therefore, even for similar upper limb movements, conflicting results for active and passive movements have been reported. A direct comparison is impossible because of the different rehabilitation devices, movements, and experimental protocols. In regard to experimental protocols, the passive task was performed separately from the other active and motor imagery tasks in the study by Kaiser et al. [43]. In the case of the passive task experiment alone, this did not include conditions of motor intention. Therefore, the task ERD was distinctly larger than baseline. The experimental protocol consisted of active and MI tasks with the same conditions; thus, the ERD may have been smaller in the active task because less motor intention existed at baseline. Ramos-Murguialday et al. used a baseline during the instruction period [92]. Therefore, the ERD of the active task was smaller than the other task because the ERD is occurred during pre-movement in the active task. However, Formagio et al. showed that the ERD of the active task was stronger than passive task, which is similar to our results [108]. We suspect that the lack of a pre-cue and the random order may have influenced these results. In other words, the presence of motor intention at baseline might lead to a reduced ERD, relative to baseline, during the motor task period.
Our results also implies that beta oscillations exhibit larger differences between active and passive upper limb movements than mu oscillations, and therefore, may be more useful for monitoring engagement in stroke patients. This is in line with previous reports that showed larger post-movement increases in beta band power relative to mu band power [109, 110]. In our study, we observed clear differences in beta and mu bands, especially during the post-movement period.

Furthermore, there were significant differences between the active and passive motor tasks during the post-movement period, even though participants were supposed to stop moving during this time. We suspect that this result is dependent upon our experimental protocol. We performed video recordings for behavior analysis and observed hand movements during the task. We confirmed that patients did not immediately stop the end of the motor task, and remained moving during active tasks. We suspect that these extra movements might be due to difficulties in motor control by stroke patients; the patients may not be able to stop moving in a timely manner as healthy individuals do. Also, we suspect that the one-second stay period in a resting position after the motor task might be too short for stroke patients to follow. Thus, the patients seemed to recognize the stay period as not a stop but instead used it to enable a smooth transition from the motor task to a return position. Therefore, ERD of SMRs associated with active movement may be sustained during the stay period following active movement (see Figure 3.3.2). On the contrary, for the passive motor task, ERD may have diminished quickly after the motor task period because patients did not have to volitionally stop movement. Instead, they did not receive proprioceptive feedback.

These observations suggest that incorporating a holding task into the design of motor tasks may lead to better assessment of patient active engagement.
There were slight changes in power during the pre-movement period especially during the passive task. As these changes occurred particularly during the more difficult supination movement, we suspect that some on-going neural activity in preparation for the supination movement may have caused these pre-movement changes in sensorimotor rhythms. However, further investigations are required to address this issue.

Our results revealed the ability to classify whether stroke patients were involved in training tasks actively or passively (average accuracy of single-trial classification was $80.7 \pm 0.1\%$ for grasping and $82.8 \pm 0.1\%$ for supination). There was no significant difference in classification results between grasping and supination. Thus, this suggests that our method can be applied to various upper limb rehabilitation tasks. However, different tie-up methods of hand impairment, movement speed, and the range of movement of the device could influence the results.

In future experiments, it would be valuable to investigate the relationship between individual differences in classification performance, motor function measures, and brain lesion characteristics. While it was beyond this study's initial scope, future investigations will take this data into account. We will also work to develop an online engagement monitoring system and investigate how one might adjust the design of rehabilitation protocols to encourage more active patient participation in rehabilitation training. The temporal resolution of this active engagement detection system will depend on the trial length of the rehabilitation protocol. From our results, for instance, a two second motor task period would be necessary to determine active engagement in real time.

Our target application is different from typical motor intention detection devices used to initiate robotic assistance [79]. The primary application of our findings is to
monitor whether stroke patients are actively participating in motor training tasks during robot-assisted therapy. In robot-assisted passive training, patients often do not pay much attention to training. This may reduce the effects of rehabilitation due to lack of motivation and feedback [14]. In clinical therapy, therefore, it is important to encourage patients to be actively engaged in a training task even though their limbs are passively moved. Monitoring active engagement may be better achieved by analyzing brain activity because active engagement is mostly a cognitive effort, making limb movements indistinguishable from passive movements. EMG or force sensing would also be unstable and inconsistent due to motor impairment. Our study focused on this point and aimed to develop an EEG-based active engagement monitoring system to provide real-time feedback of active engagement, thereby maintaining patient motivation throughout therapy.

Latent sensorimotor function can be retained through goal-directed therapy, even when a long time has passed following a stroke [86]. Rehabilitation goals may be better achieved when encouraging motivation and active engagement in stroke patients. For stroke rehabilitation therapy, an online monitoring tool that can deliver real-time feedback on performance and engagement level may lead to better rehabilitation outcomes for patients. Patient engagement may be further optimized when using an online monitoring tool with additional tools like video games and virtual reality [111, 112].

We recruited patients who were categorized as moderate or mild according to FMA scoring. However, severe stroke patients may also benefit from our proposed system. Although the present study recruited stroke patients with moderate and mild FMA scores and obtained obviously active or passive training data to determine the feasibility of active engagement monitoring with EEG, the experimental protocol can easily be modified to collect data even in the absence of physical movement, as would
be expected in severely affected patients. For instance, a training paradigm could be
developed in which active and passive movements are discriminated by visual cues to
obtain training data for these two classes for further analysis. We would expect to
observe similar ERD/ERS patterns of sensorimotor rhythms to those shown in the
present study. A follow-up clinical study will investigate this possibility in severe
stroke patients.
5. Conclusions

In this chapter, we investigated whether we could assess active engagement in stroke patients during rehabilitation training using a non-invasive BCI. We observed that in bilateral sensorimotor cortical areas and the SMA, active movement induced larger ERD in the beta band than passive movement. A larger ERD associated with active movement was observed when participants executed motor tasks. We extracted spectral features of sensorimotor rhythms in the regions above and classified them into active or passive motor tasks on each trial. Classification accuracy was 80.7 ± 0.1% for grasping and 82.8 ± 0.1% for supination. Our results demonstrate the importance and feasibility of developing an online monitoring system of active engagement for stroke patients during motor rehabilitation training.
Chapter 4. Comparisons of EEG Responses Depending on Lesion Locations and Healthy controls

1. Introduction

Stroke, which is the leading cause of adult neurological disabilities in most countries [113], typically damages particular regions of a patient’s brain and results in functional impairments [114]. These impairments vary depending on the location of the lesion. For instance, motor impairments are due to damage to the motor-related cortical regions [115, 116], cognitive deficits are usually associated with infarctions in the left anterior and posterior cerebral artery territories [117], and poststroke depression is correlated more with left frontal brain injuries than with lesions located in other areas [118, 119].

The process underlying the recovery of impaired motor functions after stroke involves brain plasticity, in which motor rehabilitation therapy stimulates new neural connections and enhances cortical reorganization in order to recover normal motor function [120, 121]. As a result, the undamaged areas of the nervous system take over the functions of the damaged areas [122].

Previous studies have shown that the recovery of motor function is influenced by lesion location. In a longitudinal study, Feydy et al. have shown that motor recovery is dependent on whether M1 is included in the lesion area [123]. Schiemanck et al. reported that the recovery of hand motor function in patients with internal capsule lesions had a significantly lower probability of recovery than that in patients with the cortical, subcortical, or corona radiata lesions [124]. Shelton et al. analyzed 41 post-
stroke patients to investigate the effects of lesion location on upper limb motor recovery [116]. They found that the probability of recovery of isolated upper limb motor function decreases progressively with lesion location such as in the cortex, corona radiata, and posterior limbs of the internal capsule.

Neural stimulation studies have been beneficial to understand the reason that motor impairment and recovery are dependent on lesion location. As an example, transcranial magnetic stimulation (TMS) has been useful for exploring the neural mechanisms of motor function after stroke [125]. A TMS study reported that lesions in cortical or subcortical areas affected intracortical inhibitory properties [126].

In addition to motor recovery, brain activation is affected by lesion location. Using magnetic resonance imaging (MRI), Alexander et al. demonstrated that damage to the posterolateral putamen is associated with temporal gait asymmetry [127]. These findings suggest that damage to the inferior portion of the posterolateral putamen is associated with asymmetrical ambulation in the chronic stage of stroke recovery. Luft et al. recruited four groups (patients with cortical, subcortical, and brainstem stroke lesions and healthy volunteers), and functional MRI (fMRI) data were compared across these groups to investigate the brain activation of the participants during knee movement. They concluded that neural adaptation in brain networks was dependent on lesion location [128]. In an fMRI study of the upper limbs performed by Luft et al., the patients were divided into cortical and subcortical groups based on lesion location, and their brain activation was compared with that of healthy controls (HCs). The cortical stroke group showed less brain activation, whereas patients with subcortical lesions showed greater overall brain activation than the HCs [129].

In these fMRI studies, the brain activation patterns differed according to the lesion location. However, no studies have investigated the alterations in
electroencephalography (EEG) responses according to lesion location. In light of technical advancement of EEG-based brain-computer interface (BCI) rehabilitation approaches [45, 130], a study to address this issue is urgently needed.

In our previous study, we investigated the levels of cognitive engagement of stroke patients by examining their brain activities while they performed active and passive hand movements [45]. We observed that active movement induced stronger event-related desynchronization (ERD) in the beta band compared to passive movement. These results showed that the beta band power patterns are associated with the level of motor engagement. However, in these studies, the lesion location of the patients had not been considered in the EEG data analysis.

In this study, we evaluated our hypothesis that the EEG patterns of patients with chronic stroke differed according to lesion location. The patients were divided into the three groups according to the location of their lesion: (1) patients with supratentorial lesions that included M1, (2) patients with supratentorial lesions that excluded M1, and (3) patients with infratentorial lesions. The three patients groups and HCs were compared to each other in terms of ERD power change in time, ERD topography in mu and beta bands, and the corresponding laterality coefficient (LC). The ERD and event-related synchronization (ERS) phenomenon are well known to be associated with motor movement and has been used to evaluate brain activities in BCI-based motor rehabilitation studies [13, 85, 131]. The LC of the ERD/ERS power of stroke patients is affected by brain damage. In general, healthy subjects show strong brain activation in the brain regions contralateral to the moving hand. However, when chronic stroke patients with damage to the brain regions controlling motor functions move their affected hand, they show brain activation in both hemispheres: weak activity in the ipsilesional (i.e. contralateral) regions, as expected, and strong activity in the contralesional (i.e. ipsilateral) regions. In stroke patients, neuroplasticity
influenced the contralesional regions to take over some of the motor function of the lesioned area compromised by the brain injury [28, 83, 132]. Thus, the LC may be a good metric to evaluate the brain activation according to lesion location. Therefore, we expect that using both the ERD magnitude and LC metrics will lead to a better understanding of neural activities according to lesion location in stroke patients. In a previous study, Gong et al. have shown that patients with stroke exhibit different LC patterns of event-related potentials while performing motor imagery tasks compared with those of HCs [133]. Kaiser et al. also have investigated the relationship between the LC of ERS and motor function ability [83]. However, these studies did not systematically report the changes in the EEG LC patterns depending on the distinct lesion location.
2. Materials and Methods

2.1. Subjects

Twelve patients with chronic stroke [9 males, 3 females; mean ± standard deviation (SD) age, 54.0 ± 6.6 years] participated in this study. All of the participants had a single stroke, exhibited unilateral motor problems in the upper extremities/limbs that continued for at least 3 months after their stroke, and were aged between 45 and 70 years old. Patients with cognitive disorders that rendered them unable to understand the task instructions and/or those with orthopedic disorders that led to amputation or joint contraction were excluded. The mean ± SD Fugl-Meyer Assessment scores were 47.3 ± 9.2 and 64.8 ± 9.2 for the affected and unaffected sides, respectively. Lower scores indicate more severe impairment. The patients did not have any history of neurological illness. The characteristics of these patients are provided in Table 4.2.1. Grasp strength, Purdue Pegboard Test, and Fugl-Meyer Assessment (FMA) have been used to evaluate motor functions of patients with stroke during rehabilitations phases [134-136]. More specifically, grasp strength shows the physical strength of the hand (clinical norms for the 55-59 years age group: men: right hand, 45.8; left hand, 37.7; women: right hand, 25.9, left hand 21.4 [kg]), Purdue Pegboard Test indicates the delicate control ability of the hand function (norms for the 55-59 years age group: men: right hand, 19.2; left hand, 21.0; women: right hand, 17.8, left hand 19.4), and FMA is generally used to evaluate the upper-limb functions for volitional movement ranges and reflex activities (scored on a scale of 0 and 66). Patients have significant differences
in hand function between affected and unaffected hands in Grasping strength, Purdue Pegboard Test, and FMA (rank sum test, \( p < 0.01 \)). These scores were used as exclusion criteria for patients with severe impairment (0 to 20 FMA score), and all participants in the moderate (21 to 50 score) or mild (51 to 66 score) categories, who were able to perform the motor tasks, were included [136]. A radiologist assessed and categorized lesion location based on the MRI data: (1) supratentorial lesions that included M1 (hereafter, SM1+), (2) supratentorial lesions that excluded M1 (SM1-), and (3) infratentorial (INF)

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**Supratentorial lesion excluding M1**

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**Infratentorial lesion**

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</table>

Abbreviations: FMA-UE, Fugl-Meyer Assessment Upper Extremity; AH, Affected Hand; UH, Unaffected Hand; CR, Corona Radiata; MCA, Middle Cerebral Artery; IC, Internal Capsule; BG, Basal Ganglia; ICH, Intra Cerebral Hemorrhage
lesions. SM1+ indicates a cortico-subcortical lesion and damaged M1, whereas SM1- indicates a subcortical lesion without M1 damage. The lesions of the SM1+ and SM1- groups are located in the supratentorial area while those of the INF group are in the infratentorial area. In addition to the patients with stroke, twelve age- and sex-matched HCs (8 males, 4 females; 57.8 ± 4.7 years) served as controls. No subjects had previously participated in an EEG experiment. The Institutional Review Boards of the Samsung Medical Center (Application Number: SMC 2013-02-091) and Korea Institute of Science and Technology (Application Number: KIST 2013-009) approved this study. The participants were informed about the study’s purpose, experimental procedures, and their right to withdraw at any time. Written informed consents were obtained from all of the participants. All of the research data were collected and analyzed under Institutional Review Board guidance.

2.2. Experimental protocol and EEG data processing

In this study, the subjects were asked to conduct grasping and supination movements with the affected hand; these are two basic hand functions involved in activities of daily living. They performed each movement with active, passive, and motor imagery (MI) tasks. In the active task, subjects were asked to perform a given movement with motor intention by themselves. A robotic device performed the movement in the passive task. In the MI task, each subject was asked to imagine the movement with motor intention, but he or she did not perform the physical movement. The experimental protocol consisted
of three motor tasks, each composed of three blocks (nine blocks in total). Each block consisted of 14 repeated trials, and each trial consisted of four time periods: relax, motor task, stay, and return. A fixation appeared on the screen during the relax period with a random duration between 2 and 3 s. Participants performed a motor task in the 2-s motor task period, which started with auditory and visual cues. The 1-s stay period is necessary in order to prevent the risk of a sudden movement change. Then, the robotic device was reset to its original handle position during the return period in the case of active and passive motor tasks. Therefore, each participant performed 42 sequential trials (14 trials for each of the three blocks) for each of the three motor tasks (active, passive, and MI), accounting for a total of 126 trials; EEG data were recorded during the entire experimental protocol.

EEG signals were acquired with a 64-channel EEG active electrode system (sampling rate: 2,048 Hz; Active-two, BioSemi S.V., Amsterdam, Netherlands). The acquired EEG signals were preprocessed using the following steps: downsampling, 1–80 Hz band-pass and 60 Hz notch filtering, trial epoching, independent component analysis (ICA) for electrooculographic and muscle artifacts removal [95], and common average reference (CAR) [96]. In our study, the CAR was used for re-reference with the average of whole EEG channels for each individual EEG channel. Alternatively, the Laplacian Montage method can be used when the local average surrounding a target EEG channel is adopted to adjust the bias of the target channel [137]. After preprocessing, spectral power was computed using short-time Fourier transform with a 500-ms hamming window, and sliding by 50 ms for each of
the 64 EEG channels. The baseline of each epoch was defined as the 1 s before
the motor task cues. The spectral power was normalized by subtracting the
baseline mean from each data point in an epoch and by dividing the resulting
value by the baseline SD. The ERD/ERS was defined as the spectral power
changes in the motor task period relative to the baseline. Two frequency bands
selected in our study include the mu (8–13 Hz) and beta (13–32 Hz) bands,
both of which reflect sensorimotor rhythms. Detailed information on the
experimental protocol and the EEG processing method can be found elsewhere
[131].

The quantitative analyses of the EEG data were based on the LC and
topographic mapping of the EEG spectral power. The hemispheric
asymmetries for ERD/ERS, LC was calculated as follows:

$$LC = \frac{(C - I)}{(C + I)}$$  \hspace{1cm} (4.2.1)

where $C$ denotes the ERD/ERS of the contralateral motor cortex and $I$
denotes the ERD/ERS of the ipsilateral motor cortex [83, 138].

We compared the LC values across different combinations of the
frequency bands (mu and beta bands), motor tasks (active, passive, and MI
tasks), movements (supination and grasping movements), and participants
(SM1+, SM1-, INF, all patients, and HCs). We observed the LC pattern in the
mu and beta bands because these bands are known to be associated with motor movement.

In the analysis of this study, we focused on the active and MI motor tasks because the passive motor task using a robot-guided device would lack of the subject’s motor intention, a key factor in effective rehabilitation [24, 139]. ERD/ERS patterns on the active and MI motor tasks was compared between the subgroups of patients and the HCs. More specifically, Pearson’s linear correlation analysis was performed using the ERD/ERS power changes in the bilateral motor cortex during the motor task period. For the topographical analysis, we selected 28 EEG channels around the bilateral motor cortex and supplementary motor area (SMA), both of which are associated with motor movement. For each of the 28 channels, the ERD/ERS power changes were averaged across all HCs or each of the patient subgroups. In addition, we compared the EEG topographies from all possible combinations across the two frequency (i.e., mu and beta) bands, three motor tasks (i.e., active, passive and MI tasks), two different movements (i.e., grasping and supination), and four subject groups (i.e., SM1+, SM1-, INF and HCs). A Pearson’s correlation coefficient was calculated using the ERD/ERS power changes between the HCs and each of the three patients subgroups for each of the 28 channels. Then, one-way ANOVA was performed across the three patient subgroups using the 28 correlation coefficients across the 28 channels from each subgroup.
3. Results

3.1. Comparison of the LC patterns between all patients and HCs

Figure 4.3.1 illustrates a comparison of the LC values in the beta band of patients and controls. The five bars indicate the LC values of SM1+, SM1-, INF, all patients, and HCs. In HCs, the ERD in the contralateral motor cortex was stronger than that in the ipsilateral motor cortex regardless of the movement and task types, which resulted in positive LC values.

The difference in the LC values between all patients and HCs was not significant, even though all the patients represented lower LC values compared to the controls in the active and MI tasks.

3.2. Comparison of LC patterns between patient subgroups

Figure 4.3.1 shows that the SM1+ subgroup had a negative LC value in both of the movements in the active and MI motor tasks. Especially in the active task, there were significant differences between the SM1+ subgroup and HCs (rank-sum test, p < 0.05). The SM1- and INF subgroups had positive values in the same condition. For the passive task, LC values were very small values. It indicates the brain activation in bilateral motor cortex. The SM1+ subgroup exhibited negative LC values while they performed the MI task;
Figure 4.3.1. Beta band laterality coefficients for the three motor tasks (passive, active, and MI) in supination and grasping movements. Solid bars indicate the mean value; error bars reflect standard deviation. Significant results of pairwise statistical analysis on differences in laterality coefficients are indicated (rank sum test, *p < 0.05).

Abbreviations: SM1+, supratentorial lesion including M1; SM1-, supratentorial lesion excluding M1; INF, infratentorial lesion, Patient, all patients; Healthy, healthy controls.

however, these values were not significantly different from those of the other groups.
Figure 4.3.2. Average power patterns of the beta band in the ipsilateral and contralateral motor cortex during 2 s of active and MI supination movements. The ipsilaterial motor cortex is in the unaffected hemisphere, and the contralateral motor cortex is in the affected hemisphere in patients.
3.3. Comparison of the EEG responses relative to the lesion locations in the patients

Figure 4.3.2 shows the average power patterns of the beta band of the three patient subgroups and HCs during the 2 s supination movements in the active and MI tasks. The average power patterns of the beta band showed marginal differences between the ipsilateral and contralateral sides of the motor cortex and between the active and MI tasks. The ERD in the contralateral motor cortex was generally stronger than that in the ipsilateral motor cortex. The ERD of the HCs appeared stronger than those of the patient subgroups, except in the ipsilateral motor cortex during the active task.

Table 4.3.1. Pearson’s Linear Correlation Coefficients between the Average Beta Band Power Patterns of each Subgroup and that of the Healthy Controls during Supination movement

<table>
<thead>
<tr>
<th></th>
<th>Ipsilateral motor cortex</th>
<th>Contralateral motor cortex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>INF</td>
<td>SM1-</td>
</tr>
<tr>
<td>Active</td>
<td>0.880**</td>
<td>0.676**</td>
</tr>
<tr>
<td>MI</td>
<td>0.511**</td>
<td>0.263</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01

Abbreviations: INF, infratentorial lesion; SM1-, supratentorial lesion excluding M1; SM1+, supratentorial lesion including M1;
Table 4.3.1 lists Pearson’s linear correlation coefficients of the average beta band power (shown in Figure 4.3.2) calculated between each patient subgroup and the HCs. In most cases, the correlation coefficients are statistically significant. Moreover, the correlation coefficients consistently decreased in the following order: INF > SM1- > SM1+.

### 3.4. Topographical analysis

A topographical analysis was implemented based on the 28 EEG channels around the SMA and bilateral motor cortex. Figure 4.3.3 shows the average beta band power distributions across the subjects in each group during the supination movement in the active task. The upper three rows display the topography patterns that corresponded to the three patient subgroups. For the SM1+ subgroup (first row), the ERD of the ipsilateral side was stronger than that of the contralateral side. For the SM1- subgroup (second row), the ERD of the contralateral side was stronger than that of the ipsilateral side, and it was particularly widespread. The INF subgroup (third row) showed that the ERD of the contralateral side was stronger than that on the ipsilateral side, and, in particular, the ERD distribution was focused on the motor cortex and parietal area on the contralateral side. For all of the patient subgroups in the fourth row, the ERD distribution was located in the bilateral motor cortex. In the case of the HCs in the last row, the ERD of the contralateral side was stronger than that of the ipsilateral side, and the strong ERD distribution was focused on the contralateral motor cortex.
Figure 4.3.3. Twenty-eight channel topography of the beta band during active supination movement. The horizontal axis represents 2 s of the motor task with a 0.5-s window interval. The vertical axis represents the subject groups. The upper three rows represent each subgroup of patients according to their lesion location. The fourth row represents all patients and the last row represents the healthy controls.
Figure 4.3.4. Pearson’s correlation coefficients for the beta band power changes between the HCs and each of the three patient subgroups for each of the 28 channels during the active task supination movement. Significant results of a pairwise statistical analysis on the differences in the correlation coefficients are indicated (one-way ANOVA test, \(**p < 0.01\)).

Figure 4.3.4 shows the similarities of the beta band power changes across the 28 channels between the HCs and each of the three patient subgroups. The INF group showed similar ERD/ERS power changes in comparison to HCs, whereas the SM1+ group was represented a deviated ERD/ERS power changes compared to the HCs. The correlation coefficients differed significantly between the three subgroups (one-way ANOVA test, \(**p < 0.01\))
4. Discussion

In this study, we investigated how EEG patterns differ across the stroke patient groups divided by lesion location, while they performed motor tasks, such as active, passive, and MI tasks with both supination and grasping movements. The active and MI tasks require the subject’s motor intention, whereas the passive task does not. The active and passive tasks are performed with the physical movement, but the MI task does not. Moreover, the LC values of the ERD in the left and right motor areas were statistically different between patient subgroups and the HCs in the beta band (Figure 4.3.1); however, there were no significant differences in the mu band.

The supination and grasping movements show very similar ERD/ERS patterns. Moreover, Figure 4.3.1 shows that supination and grasping movements have similar LC values. This might be because of due to the similarity of sensorimotor EEG changes and topography between the two movements. Therefore, we examined the results for sensorimotor EEG changes and topography analysis only for the supination movements.

For the SM1+ group in the active and MI tasks, the LC value was always negative in both the grasping and supination movements (Figure 4.3.1). This indicated that the ERD power in the ipsilateral motor cortex was stronger than that in the contralateral motor cortex. The contralateral motor cortex of the SM1+ patients was directly damaged, and therefore, was no longer capable of normal motor function. Instead, the unaffected ipsilateral motor cortex assumed the function of the damaged area [135].

The SM1- and INF groups showed positive LC values in the same tasks. In these groups, the motor cortex was not directly damaged; therefore, it showed a level of brain activation similar to that observed in HCs. Interestingly, in the passive task, the
SM1+ group exhibited an LC value close to zero in the supination movement and a low positive LC value in the grasping movement. These results suggested that the participant’s motor intention, which was required in the active and MI tasks, might have resulted in a strong ERD in the ipsilateral motor cortex.

For the HCs, the LC values were positive in all of the tasks. These results were similar to those of the study by Kaiser [43]. She investigated sensorimotor EEG changes during passive, active, and MI tasks in healthy elderly individuals. Interestingly, in both movement tasks and bilateral motor cortex, there is a consistent trend in the correlation coefficients between each subgroup and HCs, whose values consistently decreased in the following order: INF > SM1- > SM1+ (Table 4.3.1). In addition, we measured how the beta band power changed during the active supination movement task in the 28 EEG channels around the motor cortex that were selected for the topographical analysis. Figure 4.1.4 shows the correlation coefficients between each patient subgroup and the HCs; the statistically significant differences observed among the three coefficients pairs are also shown (one-way ANOVA, \( p < 0.01 \)). From these results, we can conclude that the similarity between the beta band power patterns is the highest between INF and HCs and the lowest between SM1+ and HCs.

In TMS studies, cortical lesion groups show properties that differ in similar ways from those of the subcortical and HCs. Shimizu et al. compared intracortical inhibition (ICI) and transcallosal inhibition (TCI) in cortical and subcortical lesion groups [140]. They demonstrated that ICI was significantly reduced in the cortical lesion group compared with the age-matched HCs. TCI was absent in the cortical lesion group, but it was observed in the subcortical lesion and HCs. Liepert et al. compared the properties of four groups (motor cortex, striatocapsular, internal capsule, and pontine lesions) and demonstrated that only the motor cortex lesion group had a loss of the ICI in the affected hemisphere [125].
As shown in Figure 4.1.3, the topography analysis showed distinct differences between the three subgroups of patients. The INF group with lesions in the deepest location showed EEG topographical maps that were similar to those of HCs. The ERD was stronger around the contralateral motor cortex than around the ipsilateral motor cortex, and the ERD distribution was focused on the motor cortex and parietal area on the contralateral side. The SM1+ and SM1- groups showed topographies that differed distinctly from the INF group and HCs. The SM1+ group had a strong and focused ERD distribution on the ipsilateral side, and the SM1- group showed a widespread ERD distribution.

We inferred that the interhemispheric inhibition (IHI) was associated with the different patterns of the topographical distributions that depended on the depth of the lesion location. IHI involves inhibitory interactions between the bilateral primary motor cortexes [141, 142].

Because the IHI in the SM1+ group decreased from the ipsilesional M1 to the contralesional M1, the ERD on the ipsilesional side may be stronger than that on contralesional side. This hypothesis is supported by the results of the study by Bütefisch et al [143]. They reported that IHI decreased abnormally from the ipsilesional M1 to the contralesional M1 in the cortical lesion group but not in the subcortical lesion group.

The SM1- and INF groups had subcortical lesions that injured the pyramidal tract [144]. Thus, the injury does not greatly affect the IHI between the bilateral M1s [143]. We inferred that this was why the SM1- and INF groups had different patterns of neural activation compared with the SM1+ group.

As far as we are aware, subcortical lesions have not been specifically segmented in most lesion studies [43, 129, 143]. However, our study divided the subcortical
lesion group into two subgroups and demonstrated that the beta band ERD distribution of the INF group was stronger and more focused in the ipsilesional hemisphere than that in the SM1- group. Nevertheless, the motor function of the INF group was more severely affected compared with the SM1- group. Because the neural mechanisms associated with the SM1- and INF lesions are not yet fully understood, additional studies investigating this issue, including ones using a simultaneous EEG-fMRI modality, are warranted [145].

Our results indicated that plasticity changes that occurred during the motor rehabilitation period differed depending on lesion location and that these changes produced different patterns of neural activation in patients with chronic stroke with different lesion locations. Our findings may be limited by the number of patients in each subgroup, and thus, a future study is warranted to investigate these findings in a large cohort.
5. Conclusions

Previous studies have reported that ERD in patients with stroke occurs bilaterally during the same task [28, 83, 132]. In our study, we observed similar results in all patient subgroups. However, in patient subgroups that were classified by their different lesion locations, we observed distinctly different beta band EEG patterns in each group. These findings indicated that EEG spectral analyses should be implemented for patients with stroke considering their lesion location. We envision that this finding will provide an important foundation for studies of BCI-based motor rehabilitation.
Chapter 5. Concluding Remarks

In this thesis, a robotic haptic rehabilitation system for measuring EEG while motor tasks are performed was proposed for use with patients with chronic stroke. Healthy controls were tested for comparison.

First, two different haptic hand rehabilitation devices were designed for grasping and supination movements. The grasping device provides active mode (patients move the device), passive mode (patients’ hand is moved by the device), and active-assist mode which provides robot-assisted function when a patient is unable to move the device themselves. Active-assist mode is designed to encourage neuroplasticity through synchronized movement assist based on patients’ movement intention. It mechanically determines the assist time point by monitoring pressure changes in the handle and changes in handle movement. This function received favorable evaluation by both patients and occupational therapists in the hand rehabilitation user-study. A serious game, which included various haptic profiles associated with game contents, was applied by the rehabilitation device at supination. The patients' hand rehabilitation training would vary depending on the game scenario in contrast to traditional, boring training without any stimulation. The haptic device could also adjust the intensity of training based on patient hand function. This approach would be applicable to cognitive rehabilitation and muscle training for the elderly as well as stroke rehabilitation; however, biological signals are needed in order to determine accurate movement intention. Therefore, we chose to measure the EEG of patients with chronic stroke during motor tasks using grasping and supination rehabilitation devices.

The patients and healthy controls performed three motor tasks: active, passive, and motor imagery (patients imagined the movement without physical movement). To determine differences in cognitive engagement during motor rehabilitation,
changes in ERD/ERS in the bilateral motor cortex and supplementary motor area during active and passive motor tasks were analyzed. We found that the ERD in the bilateral cortex and supplementary motor area was stronger during the active motor task than during the passive motor task. In addition, after the active motor task ERD was maintained during the stay period immediately following the motor task. Conversely, after the passive motor task ERD returned to baseline during the stay period. The active/passive classification accuracy was higher when using EEG data from both the motor task and stay periods then when only using the data from the motor task period. In order to improve the effectiveness of patient rehabilitation, “how much effort (intensive)” and “how to repeat” are important factors. This result may be an important factor in how patients determine how much engagement (effort) to impart during motor rehabilitation.

For the final study, we investigated differences in EEG signals based on lesion locations in patients with chronic stroke. Because cortical neural plasticity can vary depending on the depth of lesion location, the segmentation of patients is needed when measuring EEG cortical neural activity signal. The patients were divided into the three subgroups according to the location of their lesion: patients with supratentorial lesions that included M1 (SM1+), patients with supratentorial lesions that excluded M1 (SM1-), and patients with infratentorial lesions (INF). The three patient subgroups, all patients with stroke, and healthy controls were compared to each other in terms of ERD power change in time, ERD topography in mu and beta bands, and the corresponding laterality coefficient (LC). In the case of all patients with stroke, the observed bilateral ERD pattern was consistent with previous studies. However, when patient subgroups are compared, distinctly different beta band EEG patterns are observed depending on lesion location. In the case of the SM1+ subgroup, the ERD power in the ipsilateral motor cortex was stronger than that in the contralateral motor
cortex because this group has direct motor cortex damage. Moreover, the correlation coefficients for the beta band power changes between the healthy controls and each of the three patient subgroups for each of the 28 channels during the active task supination movement consistently decreased in the following order: INF > SM1- > SM1+. Many of the existing studies using brain-computer interface (BCI) only studied healthy people; those that did study patients with stroke did not include detailed classifications of the patients. The results of our study show that BCI-rehabilitation studies need to consider classification of patients with stroke based on lesion location.

This thesis contributes to the field of rehabilitation by the creation of haptic devices, improvement in the understanding of cognitive engagement in motor rehabilitation, and demonstration of the importance of classification on the depth of lesion location as well as demonstration of the differences in EEG when utilizing the proposed haptic hand rehabilitation devices. These results are expected to contribute to the establishment of new paradigms of EEG-based motor rehabilitation treatment protocols.

Throughout these experiments, I met many patients. For patients with brain diseases, the ability to translate thoughts to action (e.g. eating, speaking, moving) often becomes suddenly more difficult. After an experiment, a participant said the following words:

“Did I help? I am suffering so due to stroke.”

“I really want to be a help in this study!”

I sincerely hope that the results of these studies prove to be helpful in clinical practice and benefit patients.
References


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