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碩士論文

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中風後執行上肢近端與遠端功能性動作任務之大腦活化情形：近紅外光頻譜儀研究

Brain Activation during Proximal and Distal Upper Limb Functional Tasks in Subacute Stroke: A Functional Near-Infrared Spectroscopy Study

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中文摘要

肢體動作受損為常見的中風後遺症之一，其嚴重影響個案之自主生活功能及社會參與度。先前影像實驗使用功能性磁振造影或正子斷層造影探討肢體動作時之腦部活化情形；研究結果指出，患側大腦活化程度低下與上肢動作表現嚴重度呈現正相關性。然而，因造影儀器對於個案之姿勢限制，相關文章僅探討上肢遠端動作時之功能性腦部活化，尚未釐清上肢近端功能性動作與腦部活化之相關性。因此，本實驗為一橫斷面研究，使用較無姿勢限制之穿戴式近紅外光頻譜儀，探討中風患者在執行遠端及近端上肢功能性動作時之大腦皮質活化情形，並與健康成年人之腦部活化情形比較。本實驗共收取 31 位中風患者及 9 位健康受試者，請受試者執行右側及左側上肢的近端與遠端動作，包含近端之前伸任務（手臂往前伸碰到前方物品），及遠端之抓握任務（手抓握再放開）動作。上肢有嚴重癱瘓或無力情形之中風受試者則以動作心像 (motor imagery) 模式進行此實驗。執行任務中同時使用近紅外光頻譜儀探討大腦雙側前運動皮質區(premotor cortex, PMC)、主要動作皮質 (primary motor cortex, M1) 及主要感覺皮質區 (primary sensory cortex, S1) 執行各項動作任務時之活化情形。本研究使用二因子變異數分析與重複量數 (Two-way ANOVA with repeated measures) 搭配 Tukey 事後檢定，探討大腦活化皮質區域執行前伸任務及抓握任務時族群與任務之間是否有顯著相互作用 ($p < 0.05$)；此外，使用皮爾森相關分析法 (Pearson's correlation)，探討腦部活化與中風後動作損傷之關係。研究結果顯示，與健康受試者相比，中風受試者執行上肢功能性任務時的大腦活化程度整體較高。動作恢復較差之中風受試者（動作心像）相較於動作恢復較好之中風受試者(實際執行)及健康受試者在執行患側遠端動作時，其健側大腦之 PMC 及 M1 活化更高。此外，近端和遠端上肢任務

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之大腦活化沒有顯著差異，但執行近端與遠端任務時，大腦活化皆呈現顯著的側化現象。最後，本研究也發現執行近遠端上肢功能性動作時之腦部活化與中風後動作恢復呈現顯著相關性。

關鍵字: 中風，上肢功能，近紅外光頻譜儀，大腦活化

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Abstract

Background and Purpose: Impairment of upper limb function is a significant cause of disability following stroke. Studies revealed that brain reorganization post-stroke shows increased overactivation of the contralesional cortex, which was associated with poor upper limb motor recovery. Previous investigations under functional magnetic resonance imaging and positron emission tomography have sought to characterize the differences in cortical activity between stroke and healthy individuals during upper limb movement, but cortical activity during distal movements were mainly assessed, and little is known about the cortical activity associated with proximal upper limb movements following stroke. The purpose of this cross-sectional study was to investigate the cortical activation patterns in stroke individuals during functional tasks of the proximal and distal upper limb and compare activation of stroke survivors with that of healthy individuals.

Methods: Thirty-one participants with stroke and 9 healthy individuals were recruited for this cross-sectional study. After initial screening for eligibility, all participants were instructed to perform four upper limb functional tasks: forward reaching of the non-affected/right arm, forward reaching of the affected/left arm, grasping of the non-affected/right hand, and grasping of the affected/left hand. Stroke participants with severe paralysis or weakness performed motor imagery in place of actual movement execution. Functional near-infrared spectroscopy (fNIRS) was used to record brain activation patterns in the bilateral premotor cortices (PMC), primary motor cortices (M1), and primary somatosensory cortices (S1). Two-way analysis of variance (ANOVA) with Tukey post hoc test was used to assess significant differences in cortical activation between groups (healthy, stroke motor execution, and stroke motor imagery) and the tasks. Pearson's correlation analysis was used to assess the relationship between cortical activation of each channel and stroke characteristics.

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Results: Significant differences in cortical activation were found between groups and between tasks. Overall, greater brain activation was seen in the stroke participants compared to healthy participants. Stroke participants with poorer motor recovery, when engaging in motor imagery, exhibit higher activation in the non-affected hemisphere's PMC and M1compared to stroke participants with better motor recovery (actual execution) and healthy participants during the execution of affected-side distal movements. No significant activation pattern differences were found between proximal and distal upper limb tasks, but rather, significant differences were observed between tasks of the non-affected and affected limbs. Stroke individuals in the motor execution group showed lateralization index patterns similar to that of the healthy participants. In other words, Stroke individuals in the motor imagery group tend to exhibit ipsilateral activation. Significant correlation was also found between cortical activation during the upper limb tasks and upper limb motor outcome and stroke characteristics.

Conclusion: Cortical activation patterns differ between subacute stroke participants depending on their stage of recovery. Significantly higher, bilateral cortical activation was observed in subacute stroke as compared to healthy participants, and stroke participants using motor imagery showed greater contra-lesional activation patterns as compared to stroke participants using motor execution. Cortical activation during proximal and distal upper limb tasks was significantly correlated with upper limb motor outcomes and stroke characteristics, thus making it an important marker for movement recovery.

Key words: Stroke, upper limb function, functional near-infrared spectroscopy, brain activation

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Chapter 1: Introduction

This dissertation was developed to determine the differences in cortical activation between stroke and healthy participants during different upper limb functional tasks. Specifically, cortical activation in the bilateral premotor cortices (PMC), motor cortices (M1), and somatosensory cortices (S1) were assessed using functional near-infrared spectroscopy (fNIRS) during four functional upper limb movements: forward reaching of the non-affected/right arm, forward reaching of the affected/left arm, grasping of the non-affected/right hand, and grasping of the affected/left hand. The first chapter details the current knowledge gaps and introduces the research question and hypotheses of the study. Lastly, the clinical significance of this study is discussed.

1.1 Statement of the Problem and Current Knowledge Gaps

Upper limb motor impairment is a significant cause of disability following stroke, leading to decreased independence in daily activities and reduced quality of life. Previous studies have revealed that brain reorganization occurs after stroke, and that overactivation of the non-lesioned cortex was associated with poor motor recovery of the upper limb. Studies conducted under functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have sought to characterize the differences in cortical activity between stroke and healthy individuals during upper limb movement; however, due to the confining nature of the instruments, cortical activity during distal finger movements, such as pinching and tapping, were mainly assessed.

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Cortical activity during distal upper limb movements were mainly assessed, and little is known about the cortical activity associated with proximal upper limb movements following stroke Furthermore, studies typically detail cortical activity of healthy participants or of stroke participants, but no study to date have compared the differences in cortical activation patterns between these two populations. The following details the current knowledge gaps:

1) **Little understanding of differences in cortical activation between proximal and distal upper limb movements:** Investigations on the neural association with proximal upper limb movements (shoulder movements) is an area of little research due to the nature of the instruments used. Furthermore, there are few studies that have compared cortical activation differences during proximal and distal limb movements, respectively.
2) **Little understanding of cortical activation associated with proximal upper limb tasks in subacute stroke individuals:** Post-stroke individuals with hemiparesis typically present with a sequence of recovery starting from the proximal extremity to the distal.[1-3] Early studies investigating the cortical activation patterns associated with upper limb motor function were observed mainly under functional MRI and PET, and mainly assessed hand-grasping, pinching, or opposition tasks due to the confining nature of these neuroimaging instruments,. While functional, these tasks do not reveal the entirety of upper limb impairments. Furthermore, most studies utilizing fNIRS focused mainly chronic stroke individuals or on stroke individuals executing tasks of the distal hand. For post-stroke individuals in the subacute stage, where brain reorganization is occurring at a rapid pace, it is important to

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understand how changes in cortical activation correspond with upper limb proximal and distal movements and recovery.

3) **No comparative studies of cortical activation during functional upper limb movements between healthy and subacute stroke individuals:** Previous studies focused mainly on either healthy or stroke individuals during functional tasks. Most studies assessing cortical activation in stroke individuals have focused on stroke individuals in the chronic stage. To date, no study has compared cortical activation between healthy and subacute stroke individuals.

1.2 Research Question

The purpose of this study is to determine the differences in cortical activation between proximal and distal upper limb functional tasks and differences in brain lateralization between healthy and stroke participants.

1.3 Hypotheses

Null hypothesis (H_0): There is no difference in cortical activation between proximal and distal functional tasks or between brain lateralization between healthy and stroke individuals

Alternative Hypothesis (H_1): There is a difference in cortical activation between proximal and distal functional tasks and between brain lateralization between healthy and stroke individuals

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1.4 Clinical Significance

Investigating the brain activation associated with upper limb functional movements in subacute stroke individuals is important to deepen the current understanding of spontaneous and rehabilitation-related recovery processes following stroke. While most studies focused on brain activation patterns after training, it is important for clinicians to have a more comprehensive picture of brain activity following stroke. Furthermore, understanding how brain activity differs between individuals with stroke and healthy individuals is critical in future development of rehabilitation strategies and the added application of other treatment techniques that may significantly affect recovery outcomes.

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Chapter 2: Review of the Literature

Upper limb motor impairment is one of the main functional disabilities following stroke that significantly impact the stroke individual's independence during daily activities and overall quality of life. In subacute stroke, large variability in motor recovery of the upper limb is often observed, but little is known about the underlying cortical processes associated with upper limb recovery. A deeper understanding of cortical activity associated with upper limb movements, and differences between proximal and distal movements, is necessary to understand the course of upper limb motor recovery in subacute stroke.

This chapter provides an overview of the research literature, including the current knowledge regarding upper limb impairment and recovery following stroke, changes in cortical activity following stroke, the cortical activity changes associated with post-stroke upper limb movement, and the various instrumentation used for these investigations and their findings.

2.1 Upper Limb Impairment and Recovery in Stroke

Stroke is a neurological disease caused by impaired perfusion to the brain, typically due to underlying cardiac or cerebrovascular conditions, and is one of the leading causes of long-term disability.[4] One of the main sequelae after stroke is impairment in upper limb function, which is known to affect approximately 80% of survivors.[4] In the acute phase of stroke, the prevalence of upper limb impairment is approximately 50-80% of survivors, and about 40-50% of individuals with stroke sustain upper limb impairments into the chronic phase.[5-7] Upper limb impairments in

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stroke patients are complex, and may present as paresis, muscle weakness, spasticity, reduced sensation, loss of dexterity, among others.[8,9] Further, these impairments are not static.[9] As motor recovery proceeds, the nature and type of impairment changes, leading to the resolution of certain dysfunctions but also the presentation of new ones.[9] Impairments of the upper limb can cause significant disability and increased dependency in activities of daily living.[9] Recovery of the upper limb has also been reported to be slower than that of the lower limb in stroke patients, which has been attributed to differences in lesion size or volume, the anatomic location of the lesion, greater attention given to the lower limb during physical therapy, and individual variations that occur during spontaneous recovery.[10-12] Furthermore, patients typically present with multiple impairments, such as weakness of the shoulder and hand immediately after onset, and spasticity in addition to weakness weeks or months later.[9] Recovery of the upper limb has also been reported to be much slower than that of the lower limb in stroke patients.[10-12] Thus, tracking motor recovery of the upper limbs and proper adjustment of treatment methods are crucial to achieve optimal outcomes for individuals with stroke.[6,7]

From a functional perspective, impairments in the upper limb post-stroke can be attributed to three main phenomena: learned nonuse, learned bad-use, and forgetting of behavioral tasks.[6] Learned nonuse can be traced back to the work of Sherrington and colleagues who discovered reduced used of the upper limbs in monkeys after surgical de-afferentation.[13] The motor deficits result not just from the neural damage, but also from a learned suppression of movement.[14,15] Learned “bad-use” develops as the stroke patient begins to move the paretic limb. Prevailing weakness, sensory impairment, stiffness due to immobility, and developing muscle tone may

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prevent normal movement patterns.[9] Thus, stroke individuals use compensatory strategies to execute movement.[9] As the nature of the impairments change throughout the poststroke recovery period, stroke individuals become accustomed to using compensatory strategies, and thus forget how to execute normal movement.[9] These functional consequences of the upper limbs may eventually restrict the individual's independence in everyday activities and reduce their quality of life.

2.2 Predictors of upper limb motor outcomes in stroke

The heterogeneity of stroke makes prediction of upper limb motor outcomes in patients difficult. While Twitchell and Brunnstrom previously described the progression of upper limb recovery, allowing clinicians to assess to track motor function at different stages post-stroke, more recent studies focused on determining functional indications that may predict stroke prognosis.[3,16] Identifying predictors of motor recovery in the early phases of stroke is vital for managing rehabilitation and for tailoring therapies for each individual.

A previous study found that stroke individuals who demonstrate voluntary finger extension and shoulder abduction within the first 72 hours after onset had higher probability of regaining good arm function at 6 months.[17] The ability to extend paretic fingers has been thought to be a sign of an intact corticospinal tract system (CST), indicating the potential to achieve dexterity.[17] Although these two simple bedside tests are often used in the clinical setting to predict motor prognosis in stroke, these clinical biomarkers may reflect compensational strategies rather than actual neuronal repair.[18]. Numerous longitudinal tests have also revealed significant

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inter-individual variation in upper limb recovery in post-stroke individuals who initially sustained severe motor impairments.[18] A number of recent studies have shown that neurologic biomarkers are more predictive of motor recovery than clinical biomarkers.[19-22] Characterization of the stroke lesion, the integrity of non-lesioned neuronal structures, and overall functional cortical activity were investigated as potential biomarkers to inform stroke prognosis.[23] Previous studies have found that upper limb motor outcomes at 3 months can be predicted in the early subacute stages by measuring transcranial magnetic stimulation (TMS) and magnetic resonance imaging (MRI) biomarkers, such as the presence of a motor evoked potential (MEP) by TMS, and assessment of levels of cortical activation of both hemispheres by fMRI.[23] Integrity of the CST by diffusion tensor imaging (DTI) have also been indicated to predict motor outcome of the upper limb at 12 months post-stroke.[23] Level of functional connectivity between cortical areas has also been found to reflect recovery, with initial overactivation of the non-lesioned hemisphere and its gradual decrease associated with better outcomes and enhanced recovery, whereas continued overactivation is associated with poorer prognosis.[23,24] Assessment of cortical activation in the initial stages of stroke is important not only for its predictive value, but also for understanding the changes in cortical activity associated with the recovery of motor function.

2.3 Cortical Activation Changes Associated with Upper Limb Tasks

Understanding how functional tasks relate to changes in cortical activity has been an active area of research. Neuroimaging studies under functional magnetic resonance imaging (fMRI), positron emission tomography (PET), diffusion tensor imaging (DTI), and

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electroencephalography (EEG), have been used to characterize cortical activation during movement. One of the earliest PET studies by Roland et al. found increased regional cerebral blood flow in the hand area of the primary motor (M1) and primary sensory (S1) cortices contralateral to the moving hand during a repetitive thumb and index pinching movement.[25] In addition to the contralateral M1 and S1, Ehrsson et al. found that the contralateral PMC and SMA were involved in a gripping task when observed under fMRI.[26] Involvement of the cingulate area, basal ganglia, cerebellum, prefrontal, and parietal areas were also noted in repetitive opposition tasks of the thumb and index finger.[27,28] Kinoshita et al. also found significant activation of the M1, S1, dorso-caudal PMC, caudal SMA, and cingulate motor cortices contralateral to the hand during a gripping and lifting task.[29] Other studies have also found that unilateral limb movements typically lead to activation of the contralateral M1, S1, SMA, S1, and the ipsilateral cerebellum, while inhibiting the ipsilateral hemisphere to prevent unwanted movements.[4,17,24] These neuroimaging studies reveal that the brain of the healthy individual exhibits laterality during movement.[4,26-29] Brain laterality refers to the asymmetric location of functional elements in the brain, or hemispheric dominance, during movement.[24] Brain laterality can be calculated by the laterality index (LI), which is the difference between activation of the right and left sides to assess which hemisphere is more activated during movement.[24]

These prior investigations of cortical activation in healthy individuals helped to inform the changes in connectivity in individuals who have suffered from neurological injury, such as in stroke. A PET study on 9 stroke participants found that upper-limb motor function correlated with change in regional cerebral blood flow in the SMA, bilateral cingulate, and contralesional insula,

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as well as in a small area of the ipsilesional S1.[30] Other studies assessed changes in brain activation throughout and after specific intervention methods, such as mirror visual feedback therapy or motor imagery training.[31,32] The M1, PMC, and SMA, as well as the cingulate and parietal cortical areas, basal ganglia, and cerebellum, were also found to be involved during tasks.

Although these neuroimaging studies established important findings regarding hand movement and cortical activity, due to the confining nature of the instruments (fMRI, PET), most of the studies are limited to investigations on distal finger pinching, grasping, or opposition. Previous studies have suggested that motor control of the proximal and distal joints differ. Musculature of the distal joints is controlled by the lateral corticospinal tract (CST), whereas the musculature of the proximal joints, such as the shoulder, is controlled by the corticoreticulospinal tract (CRT) and anterior CST.[33] Forward reaching is an important functional ability that requires control of multiple joints and the integration of both musculoskeletal and neural components.[34] It is also an essential ability to achieving functional independence in everyday tasks. Compared to the previously mentioned neuroimaging methods, EEG is considered to be a more portable and feasible way to measure cortical activity related to dynamic motions, such as those of the shoulder joint. However, most EEG studies focused on functional connectivity during imagining of movement rather than actual motor execution.[35] Further, many of the studies focused on establishing EEG-based brain computer interfaces (BCI) rather than to identify the cortical activity associated with upper limb tasks.[36] No previous studies have been conducted to compare activation patterns between proximal shoulder and distal hand and finger movements. Shoulder

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joint function and its association with cortical activation should be taken into important consideration when treating individuals with stroke. To date, however, there are still limited studies on proximal upper limb post-stroke conditions and recovery. There is a need to assess cortical activation during more functional movement patterns that reflect everyday activity.

2.4 Cortical Activation Pattern Changes After Stroke

After a stroke incident, typical cortical activation and brain laterality associated with unilateral movement is disrupted. Clinical studies have shown that unilateral damage to the motor system results in bilateral neuroanatomical reorganization and activation.[37] Decreased use of the affected limb was consequently found to be associated with cortical reorganization after stroke, wherein the region of the M1 that controls hand movements is invaded by areas that represent the proximal arm.[38-41] Movement of the affected limb would exhibit lowered excitability in the contralateral lesioned hemisphere, whereas increased activity or sustained overactivation in the ipsilateral non-lesioned hemisphere occurs and in turn, further inhibits the activity of the lesioned hemisphere.[24] These changes in brain laterality are further disrupted by functional compensation of the healthy limb, which has been shown to cause somatotopic reorganization in the primary sensorimotor areas in the lesioned brain hemisphere.[38,39]

After stroke, spontaneous improvement in function is seen due to the resolution of disrupted neural activity in the regions connected to and surrounding the injured brain tissue, as well as neural reorganization.[37] Animal studies have found that direct damage to the M1 results in dendritic remodeling of the remaining cortical neurons as well as reorganization of their

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functional connectivity.[37] This neural reorganization is reflected in cortical activation patterns associated in movement throughout the process of stroke recovery. Although compensatory brain reorganization occurs and helps to uphold functional performance, inhibition of the ipsilesional hemisphere has been associated with poor motor outcomes.[4,24] Previous research has indicated that post-stroke individuals with good recovery typically show a trend of relatively normal task-related brain activation, wherein initial bilateral activation shifted to greater unilateral activation of the lesioned M1 during movement of the affected hand, and those with poor recovery tend to recruit additional brain areas during tasks as compared to healthy controls.[24,42] Characterization of brain activation associated with functional motor improvement is therefore crucial to gain a deeper understanding of the cortical recovery processes following stroke.

2.5 Functional Near-Infrared Spectroscopy to Assess Upper Limb-Associated Cortical Activity

In recent years, numerous studies sought to characterize cortical activation during upper limb tasks using functional near-infrared spectroscopy.[43-45] Functional near-infrared spectroscopy (fNIRS) is a non-invasive neuroimaging technique that has the advantages of portability and real-time measurements of movements without fixation of position.[46] fNIRS has better temporal resolution compared to fMRI, and is less sensitive to motion artifacts compared to EEG.[44] Thus, the instrument can be used to record movement of proximal joints, such as the shoulder, which is limited by traditional imaging tools such as fMRI and PET.[44]

Early fNIRS studies to characterize cortical activation associated with upper limb movement were conducted mainly on healthy individuals. Movements of the hand and wrist were initially

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documented. Jalalvandi et al. found that wrist movements in four different directions (flexion, extension, radial deviation, and ulnar deviation) showed activation patterns that were spatially separated in the contralateral motor cortex.[45] Activation of the contralateral M1 and S1 were found during hand movements, which were in agreement with previous fMRI and PET studies.[47,48] Yeo et al. was one of the first to characterize cortical activation associated with movements of the proximal shoulder.[43] In their study, flexion and extension movements of the shoulder were found to induce greater activation in the contralateral prefrontal (PFC) and premotor (PMC) cortices.[43] Furthermore, additional neural recruitment was found in shoulder movements compared to movements of the hand.[43] Right shoulder movements induced activation of the left sensorimotor cortex (SM1), left PMC, and left PFC, whereas right hand movements only induced activity in the left SM1.[43] Yang et al. also conducted a study comparing differences in cortical activation between a shoulder abduction task and a finger extension task in healthy individuals.[44] Shoulder abduction done repeatedly for either 10 seconds or 20 seconds showed significant increases in oxyhemoglobin (HbO) in the contralateral PMC, contralateral supplementary motor area (SMA), contralateral primary somatosensory cortex (S1), and contralateral primary motor cortex (M1).[44]

More recently, researchers have begun using fNIRS to characterize cortical activation changes as well as cortical recovery in the stroke population.[48-50] Recovery of upper limb motor function was shown to be associated with ipsilateral compensation by the motor cortex and brain reorganization.[50] Hand movements during the early stages of stroke induced bilateral activation of the sensorimotor cortices, and gradually returned to more normal activation patterns as stroke

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recovery progressed.[50] Arun et al. found that individuals with stroke exhibited significant reduction in connectivity in the left M1 and PMC areas as compared to healthy individuals during a simple hand grasp task.[48] Furthermore, inter-hemispheric connections significantly reduced whereas contra-lesional channels exhibited increased connectivity.[48]

2.6 Summary

Upper limb impairments are a complex sequela of stroke that requires further investigation. There are currently no studies that have assessed on the cortical activity associated to with proximal joint musculature during upper limb movements, mainly due to the confining nature of most neuroimaging equipment. The studies that used fNIRS to investigate cortical activation during upper limb movement focused mainly on the activation patterns in healthy subjects, with no comparison to individuals with stroke. The limited available studies on stroke individuals typically employed grasping tasks, and there are no studies to date that have used fNIRS to investigate cortical activation during dynamic, functional tasks of the proximal upper limb. Furthermore, little is known about the differences in brain activation between functional movement of the proximal (shoulder) and distal (hand) upper limb in both healthy individuals and in individuals with stroke. Understanding the cortical activation associated with functional tasks of the shoulder and hand will be critical in understanding the recovery mechanisms following stroke, and may aid in the development of new strategies for upper limb neurorehabilitation.

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Chapter 3: Methodology

The aim of this study was to assess the differences in cortical activation during four upper limb functional tasks between stroke and healthy participants. This chapter outlines the methodology used. Research design, participant recruitment, inclusion and exclusion criteria, and procedures regarding approvals, research methods, and data collection methods are presented. Lastly, methods for data analysis are explored.

3.1 Study Design

A cross-sectional design was used for this study.

3.2 Participants

Participants with stroke and healthy controls were recruited for this study. Inclusion criteria for the participants with subacute stroke were as follows: (1) aged between 20-85 years; (2) first incidence of stroke; (3) days post-stroke is within 3 months since onset; (4) medically stable; (5) can follow simple three-step instructions; and (6) presented with hemiparesis of upper limb and functional impairment (Brunnstrom Stage between stage I to V). Healthy controls must be (1) aged between 20-85 years, and (2) right-handed to be included in the study.

Participants were excluded if they (1) were medically unstable; (2) had a history of epilepsy; (3) could not follow simple three-step instructions; (4) took antidepressants, anti-anxiety, or other psychiatric drugs that may affect blood flow in the brain; (5) suffered from stroke causing bilateral hemiparesis; or (6) were diagnosed with other neurological, psychological, orthopedic,

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or other disorders that may interfere with participation in the study.

All participants provided a written informed consent of the study procedure as approved by the National Taiwan University Hospital's Institutional Review Board (IRB Registration No. 202212018RIND). The IRB approval, participant informed consent form, and other related documents, and participant recruitment poster, can be found in the appendix.

3.3 Procedures

Upon IRB approval, participants were recruited in person at the National Taiwan University Hospital stroke ward. Demographic data, including age, gender, affected side, dominant side before stroke, handedness, time of onset, duration of time after stroke incident, lesioned brain areas, medication, Fugl-Meyer Upper Extremity Score (FMA-UE) (appendix), Brunnstrom stage, and existence of other chronic or comorbid diseases, were collected for the stroke participants at baseline. For the healthy participants, demographic data including age, gender, and handedness were collected.

3.3.1 Experimental Protocol

The experimental protocol assessed functional cortical activation during four upper limb tasks: forward reaching of the non-affected/right arm, forward reaching of the affected/left arm, grasping of the non-affected/right hand, and grasping of the affected/left hand. All participants were asked to maintain a seated position and perform three repetitions of each of the tasks, for a total of 12 blocks. Each block was 30 seconds, with a

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30 second rest in between each block (Figure 1), and the entire duration of the experiment was approximately 12 minutes. The order of motor tasks was randomly assigned, and verbal instruction about which task to execute was provided before the start of each block

3.3.2 Fugl-Meyer Assessment for Upper Extremity (FMA-UE)

The Fugl-Meyer Assessment for Upper Extremity (FMA-UE) is a performance-based impairment index designed to assess motor function, sensation, and joint function in post-stroke patients with hemiparesis.[1] It is one of the gold standards for assessing upper limb function in stroke hemiparesis, and has sound psychometric properties of validity, reliability, and responsiveness.[1]

The FMA-UE contains four subsections A to D, including the shoulder-arm, wrist, hand, and coordination and speed sections, which were designed to measure impairment from proximal to distal, and from synergistic to isolated voluntary movement.[1,51] The total score of subsections A to D is 66, and all items are scored on an ordinal scale from 0 to 2, where 0 indicates absence of movement, 1 indicates partial impairment, and 2 indicates no impairment.[51] Subsections H and J measure sensation and passive joint motion/pain, respectively. Most studies focus on subsections A to D to reflect changes in upper limb motor outcomes in stroke.[51,52] In the present study we assessed subsections A to D.

3.3.3 Proximal and Distal Motor Tasks

We employed a functional forward reaching task to assess proximal shoulder

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movement and a hand grasping task to assess distal hand and finger movement, and cortical activation patterns associated with each movement sequence were recorded throughout the entire trial. For this experimental protocol, we adapted Yang et al.'s experimental design.[44]

To assess proximal shoulder movements, we used the functional forward reaching task. Participants were asked to do lift their arm from the table and reach their arm forward to touch a water bottle placed on the table in front of them with the volar side of their wrist, and then return their arm to back to the table, and repeat this movement for 30 seconds. To assess distal hand movements, we will use a hand grasping task. Participants will have their forearm resting on the table and will be asked to clench a fist around a water bottle, then relax, and repeat this movement for 30 seconds. For stroke participants with more severe paresis (i.e., unable to do shoulder flexion or reach forward, or unable to do finger flexion and extension) will be asked to perform a motor imagery task. For the forward reaching task, the stroke participants will be asked to imagine they are reaching forward and touching the object, then return their arm to the table. For the hand grasping task, stroke participants will be asked to imagine they are grasping a bottle, then release the bottle. During the forward reaching and hand grasping tasks, both healthy and stroke participants will be instructed to execute the movement under metronome guidance at a frequency of 0.5 Hz[44]. Stroke participants performing motor imagery were also instructed to follow the metronome guidance. The pace will be visually inspected by the research assistant to ensure that participants adhered to the 0.5-Hz tempo.

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Before the actual experiment, the research assistant will explain the experiment and guide the participants through a practice for all of the motor tasks. For stroke participants who are to perform motor imagery, the research assistant guided them through both execution and motor imagery of each of the tasks. The verbal instructions to start the motor tasks were “Right forward reach” or “Left forward reach” for shoulder reaching tasks, and “Right hand grasp” and “Left hand grasp” for the hand grasping tasks, respectively, and the instruction to stop the motor tasks was “Stop.” Participants will not know which motor task will be performed until the verbal instructions for initiating the motor task are given. During the testing period, participants will be instructed to not hold their breath during the movements to minimize the effects of blood pressure changes on hemodynamic responses.[44] During the rest periods, participants will be asked to relax, refrain from moving their body and head, and not think about anything in particular.[44]

3.3.4 fNIRS System and Probe Placement

Functional brain activation during the forward reaching and hand grasping tasks were assessed using fNIRS. The fNIRS instrument exports and receives the near-infrared signals in dual-wavelength of 760 and 850 nm via LED light sources and detectors. The sources and detectors are attached and secured on the fNIRS cap, which is designed to be compatible with the international 10-5 system that defines the standard surface positions for a human head with approximately 3.0 cm between any 2 adjacent probe positions.[53]

In this experiment, two multichannel wearable fNIRS imaging systems (NIRSport2

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NIRx Medical Technologies LLC, Glen Head, NY, USA) were used to detect changes in cortical hemodynamics. The dual-system set-up employed 16 sources and 16 detectors over the bilateral premotor cortices (PMC), bilateral primary motor cortices (M1), and bilateral primary sensory cortices (S1), defining a total of 44 channels.[53] The fNIRS probe placement and defined channels can be seen in Figure 2. The two fNIRS systems were linked by a connector cable, and was placed next to the participant throughout the experimental block (Figure 3). The laptop and fNIRS systems were situated so as to not interfere with the participants during the upper limb reaching and grasping tasks.

3.3.5 Signal Processing for Brain Activation

fNIRS data were processed using the open-source software HOMER2[54] which is implemented in MATLAB (Mathworks, Natick, MA, USA). For stroke participants who present with left-sided lesion, the fNIRS data were flipped. Visual inspection of the raw fNIRS signals was done by two physical therapists experienced with the use of fNIRS. To ensure sufficient signal-to-noise quality of the channels, serial preprocessing was applied to the acquired signals. First, the relative coefficient of variation (CV, in %) was calculated for the raw signals at each wavelength. Data rejection was based on two types of CV, CVchan and CVtrial, was used to reduce physical artifacts, such as motion-induced instabilities and blood pressure-induced hemodynamics. Criteria for rejection was set at CVchan > 15% and CVtrial > 5%.[53] Bad channels and trials were removed based on these criteria.

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The remaining fNIRS signals were bandpass-filtered at a low-cut frequency of 0.005 Hz and high-cut frequency of 0.03 Hz to eliminate the effects of heartbeat, respiration, and low-frequency signal drifts for each wavelength.[55] Wavelet filtering was used to remove motion artifacts.[56] Preprocessed signals for each channel was then converted to concentration changes in oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR) using the modified Beer-Lambert law.[57-59] Mean values were calculated for the resting period, which was a 10-second baseline collected before each forward reaching or hand-grasping trial, and trial periods (from 0 seconds to +30 seconds) for each of the 44 channels to indicate the relative changes in HbO and HbR concentrations. To improve signal-to-noise ratio, changes in HbO and HbR were averaged over the three trials for each of the upper limb tasks (non-affected/right forward reaching, affected/left forward reaching, non-affected/right hand grasp, and affected/left hand grasp).[55,59]

The HOMER2 fNIRS processing package was used for filtering, artifact removal, and conversion of the signals for further analysis.[54] Neuronal activation is typically coupled with a rapid increase in HbO and a relatively lower-amplitude reduction in HbR based on neurovascular coupling. In accordance with the latest literature and best fNIRS practices, HbO was used to evaluate cortical activation in this study.[53,60-62] Statistical analysis to compare brain activation data between trials for each of the conditions was run using a customized script developed on Matlab2017b (Matlab, The MathWorks Inc., Natick, Massachusetts).

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3.4 Measures

3.4.1 Cortical activation

fNIRS quantifies the concentration of oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR) to neuronal activity via neurovascular coupling.[63] In accordance with the latest literature and best fNIRS practices, HbO was measured (in mM/cm) to evaluate cortical activation in this study.[53,60-62]

3.4.2 Laterality Index

The laterality index (LI) represents the difference in activation between the lesioned and non-lesioned brain hemispheres. Although LI is usually calculated via results of fMRI, recent studies have used fNIRS to calculate LI for language dominance and and visuospatial attention.[64,65] Furthermore, results of LI calculated via fNIRS were in moderate accordance compared to those calculated by fMRI.[47]

In this study, the average hemodynamic response of the channels in the right M1 (10 channels) and left M1 (10 channels) was determined to calculate LI during each task. The hemodynamic response of the channels in the left M1 and the channels in the right M1 were used to determine lateralized responses per task condition (non-affected/right forward reaching, affected/left forward reaching, non-affected/right hand grasp, and affected/left hand grasp).[47, 66] The equation used to calculate LI is as follows:

$$\mathbf{LI} = \left(\frac{\mathbf{Contralateral\ hemisphere - Ipsilateral\ hemisphere}}{|\mathbf{Contralateral\ hemisphere}| + |\mathbf{Ipsilateral\ hemisphere}|}\right)$$

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Positive LI = contralateral hemispheric dominance

Negative LI = ipsilateral hemispheric dominance

3.5 Data Analysis

All data in this study were analyzed using SPSS version 19.0 for Windows (SPSS Inc., Chicago, IL, USA). Prior to data analysis, all data were screened to assess for normal distribution. Graphical representations of normality were assessed using box plots to determine the spread of the data as well as determine the presence of outliers. The outliers discovered were handled as follows: 1) the original data was reviewed to ensure no errors; 2) the outlier was discarded; 3) a value based on the series mean was input in place of the outlier. For missing data, due to the removal of bad channels/trials, the mean for that channel was used in its absence.

For all demographic data, means and standard deviations were calculated to represent baseline characteristics of the participants. Means and standard deviations were also calculated for the 44 channels for each of the four tasks (non-affected/right reaching, affected/left reaching, non-affected/right grasping, affected/left grasping).

Two-way analysis of variance (ANOVA) with Tukey post hoc test were run to analyze the effects of the independent variables, which were group (stroke motor execution, stroke motor imagery, healthy control) and task (non-affected/right reaching, affected/left reaching, non-affected/right grasping, affected/left grasping) on the dependent variable, which was brain activation of each of the 44 channels. Two-way ANOVA were also run to assess the interaction

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between the left and right sides (brain laterality) during each of the four tasks. Level of significance was set at $p < 0.05$.

A Pearson correlation was run to analyze the relationship between cortical activation and demographic data of the stroke participants. The factors input for the correlation analysis included age, gender, number of days post onset, Fugl-Meyer Assessment for Upper Extremity score, and Brunnstrom stages for the proximal and distal upper limb for the stroke participants. Level of significance was set at $p < 0.05$.

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Chapter 4: Results

The purpose of this dissertation was to determine the differences in cortical activation patterns between proximal and distal upper limb functional tasks and activation of the left and right (lesioned and non-lesioned) sides of the brain between healthy and stroke participants. In this chapter, the results from the experiment are presented.

4.1 Participants

Participants were recruited between March and November 2023 through individual recruitment at National Taiwan University Hospital. Thirty-three participants with stroke were screened for eligibility and underwent the experimental protocol. In two of the stroke participants, fNIRS signals were poor, and more than half of the channels were excluded based on CV and by visual inspection, and were thus excluded from data analysis. Ten healthy controls were initially recruited for this study; however, the age of one of the participants was much younger than the average (29 years old). This study aimed to compare cortical activation between stroke and healthy participants around the same age group, thus, one healthy participant was excluded from data analysis.

In total, 31 participants with stroke and 9 healthy controls were included in the data analysis for this study. The average age of the stroke participants was 63.58 ± 11.85 years, and the average

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age of the healthy participants was 51.10 ± 12.24 years. The average number of days after stroke onset was 32.76 ± 20.67. Of the 31 stroke participants, 21 were able to actively carry out the forward reaching and grasping task with their affected arm (motor execution), and 10 participants sustained more severe paralysis used motor imagery for the reaching and grasping task for the affected side. Table I (List of Tables) details the demographic data of all the participants, and Appendix 1 (Appendices) contains a list of the different brain lesion areas for the 31 stroke participants.

4.2 Cortical Activation Patterns between Stroke and Healthy

Cortical activation patterns in the PMC, M1, and S1 areas during the four tasks were visualized for both healthy and stroke groups (Figures 4 to 7). Stroke participants were further categorized into the motor execution group (N=21) and motor imagery group (N=10) for analyses. The results of fNIRS indicated significant cortical activation in multiple channels covering the bilateral PMC, M1, and S1 areas during each upper limb task.

During forward reaching of the right arm, healthy participants exhibited significant cortical activation in the PMC, M1, and S1 areas of the hemisphere contralateral (left) to the moving arm (Figure 4). Few channels in the outer PMC, M1 and S1 areas also showed significant activation changes compared to baseline. In stroke motor execution participants, movement of the non-affected limb showed significant activation in the areas of the PMC, M1, and S1 in the

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non-lesioned (left) hemisphere (Figure 4). During non-affected reaching by the stroke motor imagery group, only a few channels in the non-lesioned M1 and S1 were noted to show significant cortical activation compared to baseline (Figure 4).

During forward reaching of the left arm, significant bilateral activation was observed in healthy participants, with greater and more significant channels of activation in the the hemisphere contralateral (right) to the moving arm (Figure 5). In the motor execution group, affected arm reaching induced significant bilateral activation across the PMC, M1, and S1 was also observed, and greater and more significant activation was also found in the lesioned (right) hemisphere (Figure 5). During forward reaching of the affected arm by the motor imagery group, significant increases in cortical activation was found mainly in the non-lesioned (left) M1 and S1 areas (Figure 5).

During grasping of the right hand, only one channel in the contralateral (left) PMC, M1, and S1, respectively showed significant cortical activation from baseline in the healthy group (Figure 6). During grasping of the non-affected hand by the stroke motor execution group, significant bilateral activation was found in areas of the PMC, M1, and S1, with a greater increase in HbO in channels in the non-lesioned M1 and S1 areas (Figure 6). The stroke motor imagery group exhibited an increasing trend in cortical activity during non-affected grasping, but very few channels showed significant differences in activation (Figure 6).

During grasping of the left hand, significant cortical activation was found in the

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contralateral (right) M1 areas (Figure 7). In the stroke motor execution group, affected grasping induce significant bilateral cortical activation in the PMC, M1, and S1 areas, with greater significance of activation found in the lesioned (right) hemisphere (Figure 7). In the stroke motor imagery group, significant bilateral activation was also found during affected grasping, but more channels that showed significantly different activation compared to baseline was found in the non-lesioned (left hemisphere (Figure 7).

4.3 Statistical Analysis of Cortical Activation

4.3.1 Group Differences

The results of two-way ANOVA pairwise comparisons revealed statistically significant differences in cortical activation between groups. Table III and Table IV show the means and standard deviations for cortical activation of each channel according to each upper limb task for all three groups (healthy, stroke motor execution, and stroke motor imagery).

Significant cortical activation differences were found between the stroke motor execution group and healthy participants in areas of the bilateral PMC, M1, and S1. Channels of the lesioned (right) PMC (Ch. 6) showed significant group differences, with greater cortical activation seen in the motor execution group ($p = 0.009$ and Ch. 7, $p = 0.002$). Significant differences were also found to be greater in the motor execution group in the non-lesioned (left) M1 (Ch. 11, $p = 0.015$) and multiple channels of the lesioned

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(right) M1 (Ch. 21, Ch. 22, Ch. 25, Ch. 26) , wherein greater activation values were found in the motor execution group during reaching and grasping ($p = 0.001$, $p = 0.003$, $p = 0.018$, $p = 0.042$, respectively). Furthermore, significant differences in activation of areas within the non-lesioned (left) S1 (Ch. 33, $p = 0.026$; Ch. 34, $p = 0.036$; Ch. 37, $p = 0.001$) and affected (right) S1 (Ch. 38, $p = 0.047$ and Ch. 40, $p = 0.035$) were found. Compared to healthy individuals, the stroke motor execution group exhibited higher levels of cortical activation in these areas.

Significant group differences in cortical activation were also found between the stroke motor imagery group and healthy participants. Significant differences were found in the lesioned PMC (right) (Ch. 7, $p = 0.002$), where greater cortical activation was seen during both non-affected and affected arm movements by the stroke motor imagery group compared to the healthy participants. Areas of the non-lesioned (left) M1 (Ch. 12, $p = 0.020$ and Ch. 14, $p = 0.026$) also exhibited significant group differences, where the stroke motor imagery group showed greater cortical activation during the upper limb tasks compared to the healthy participants (Table II and Table III).

Lastly, significant group differences were also found between the stroke motor execution and motor imagery groups. Significant differences in cortical activation were found in the non-lesioned (left) M1 (Ch. 11, $p = 0.015$), where the motor imagery group exhibited greater activation compared to the motor execution group. Significant

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differences in the affected (right) M1 (Ch. 22, $p = 0.003$ and Ch. 24, $p = 0.026$) and left S1 (Ch. 37, $p = 0.001$) indicated greater cortical activation found in the motor execution group. (Table III).

4.3.2 Task Differences

Results of two-way ANOVA pairwise comparisons revealed statistically significant differences in cortical activation between tasks. Table III and Table IV show the means and standard deviations for cortical activation of each channel according to task for all three groups (motor execution, motor imagery, and healthy).

Significant differences in cortical activation were observed between the tasks of reaching of the non-affected arm and reaching of the affected arm. Areas of the lesioned (right) M1 (Ch. 24 and Ch. 25) indicate greater cortical activation levels during reaching of the left, or affected, arm compared to reaching of the right, or non-affected arm (Ch. 24). Significant differences were also found in the lesioned S1 (Ch. 38 and Ch. 40), where greater intensity of cortical activation was found during reaching of the left/affected arm compared to reaching of the right/non-affected arm. (Ch. 38 and Ch. 40).

Significant differences in cortical activation were also observed between grasping of the right/non-affected hand and grasping of the left/affected hand in areas of the lesioned (right) PMC (Ch. 7 and Ch. 9), lesioned (right) M1 (Ch. 24), and lesioned (right) S1 (Ch.

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38 and Ch. 40). Greater cortical activation was found during grasping of the affected hand compared to grasping of the non-affected hand.

Lastly, significant differences in cortical activation were also found between reaching of the non-affected arm and grasping of the affected hand. Greater levels of activation were observed in multiple channels in lesioned (right) PMC (Ch. 7 and Ch. 9), the lesioned (right) M1 (Ch. 24, Ch. 25, Ch. 29), and the lesioned (right) S1 (Ch. 38, Ch. 39, Ch. 40) during the grasping of the affected hand compared to reaching of the non-affected arm (Table II and Table III).

4.3.3 Group and Task Interaction

Results of two-way ANOVA found statistically significant interaction between the effects of group and task on cortical activation in the left/non- lesioned PMC (Ch. 1 [$F(6, 148) = 3.567$, $p = 0.002$]) and the left/non- lesioned M1 (Ch. 11 [$F(6, 148) = 2.373$, $p = 0.032$] and Ch. 12 [$F(6, 148) = 3.111$, $p = 0.007$]).

Simple main effects tests for Ch. 1 (non-lesioned PMC) indicated that cortical activation during affected grasping was significantly higher than in the motor imagery group compared to the motor execution group ($p < 0.001$) and healthy group ($p < 0.001$).

Simple main effects tests for Ch. 11 (non-lesioned M1) indicated that cortical activation during affected grasping was significantly higher in the motor imagery group

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compared to the motor execution group ($p = 0.001$) and the healthy group ($p < 0.001$).

Simple main effects tests for Ch. 12 (non- lesioned M1) indicated that cortical activation was significantly higher for affected grasping for the motor imagery group in comparison to the motor execution group ($p < 0.001$) and healthy group ($p < 0.001$).

4.4 Brain Lateralization

Results of two-way ANOVA showed statistically significant differences between groups and between tasks in terms of lateralization. To calculate brain laterality, the following equation was used:

$$\mathbf{LI} = \left(\frac{\mathbf{Contralateral\ hemisphere - Ipsilateral\ hemisphere}}{|\mathbf{Contralateral\ hemisphere}| + |\mathbf{Ipsilateral\ hemisphere}|}\right)$$

For the motor execution group, the difference between the summation of the HbO values obtained from ten M1 channels in the hemisphere contralateral to the moving arm, and the values from the ten M1 channels ipsilateral to the moving arm, was calculated for each task. A positive LI value indicates that contralateral hemisphere is dominant during the movement, whereas a negative LI value indicates greater activation of the hemisphere ipsilateral to the moving arm.

The stroke motor execution group showed positive LI values during both the reaching and grasping tasks of both the non-affected and affected arms. The LI value during non-affected reaching was 0.55 ± 0.44, 0.29 ± 0.51 during non-affected grasping, 0.09 ± 0.50 during affected reaching, and 0.07 ± 0.52 during affected grasping (Table IV). The positive LI values indicate a

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pattern of brain lateralization closer to that of healthy controls, who also presented with positive LI values during right reaching (LI = 0.24 ± 0.40) and right grasping (LI = 0.39 ± 0.29). For the stroke motor imagery group, positive LI values were observed during non-affected reaching (LI = 0.36 ± 0.81) and non-affected grasping (LI = 0.23 ± 0.53), however, negative LI values were observed during affected reaching (LI = -0.31 ± 0.56) and affected grasping (LI = -0.15 ± 0.30) (Table IV).

A significant group difference in LI values were found between the stroke motor execution and stroke motor imagery groups ($p = 0.030$). Statistically significant differences in brain lateralization were also found between non-affected forward reaching and affected forward reaching, as well as between the non-affected forward reaching and affected grasping tasks ($p < 0.0005$). Table V presents the LI values for healthy and stroke participants.

4.5 Cortical Activation Correlates with Stroke Characteristics

Pearson's Correlation analyses were conducted to examine the relationship between brain activation of each channel during reaching and grasping of the affected and non-affected hand and the LI values, considering the following stroke characteristics: number of days post-onset, Fugl-Meyer Assessment for Upper Extremity score, Brunnstrom scores for the proximal and distal limb, age, and gender. Table V presents the outcomes that demonstrate significant correlation.

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Results showed significant correlation between several channels during the affected reaching, non-affected grasping, and affected grasping tasks and upper limb motor outcomes. During reaching of the affected arm, channels in the non-lesioned PMC (Ch. 6, $r = -0.381$, $p = 0.038$) and lesioned M1 (Ch. 32, $r = 0.499$, $p = 0.005$; and Ch. 40, $r = 0.418$, $p = 0.021$) showed significant correlation with FMA-UE outcomes. During non-affected grasping, channels that showed significant correlation with FMA-UE were in the hemisphere contralateral to the moving hand, specifically the non-lesioned PMC (Ch. 8, $r = 0.427$, $p = 0.019$), non-lesioned M1 (Ch. 10, $r = 0.468$, $p = 0.009$; Ch. 15, $r = 0.452$, $p = 0.012$; Ch. 17, $r = 0.430$, $p = 0.018$), and non-lesioned S1 (Ch. 20, $r = 0.405$, $p = 0.027$; and Ch. 22, $r = 0.462$, $p = 0.010$). During grasping of the affected hand, significant correlation was observed between channels in the ipsilateral hemisphere. The non-lesioned PMC (Ch. 1, $r = -0.446$, $p = 0.014$) and non-lesioned M1 (Ch. 2, $r = -0.440$, $p = 0.015$; and Ch. 11, $r = -0.468$, $p = 0.009$) showed significant negative correlation with FMA-UE. Pearson's correlation analysis also revealed significant correlation between non-affected reaching and the average number of days post-stroke. The non-lesioned PMC (Ch. 3, $r = 0.64$, $p = 0.044$) and lesioned M1 (Ch. 2, $r = -0.399$, $p = 0.026$) showed significant positive and negative correlation, respectively. However, the LI values were not significantly correlated with upper limb motor outcomes, and Brunnstrom stages showed no significant association with brain activation either.

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Chapter 5: Discussion

This chapter discusses the key findings of this research in relation to the current evidence. Limitations of this study and potential for future research are also discussed, and concluding remarks about this research are reported.

5.1 Discussion

The initial research question was to assess the differences in cortical activation between stroke and healthy participants during four different upper limb motor tasks. The hypothesis was that stroke and healthy participants would exhibit differences in cortical activity during the four tasks, and that significant differences would be observed between proximal and distal tasks of the upper limb.

5.1.1 Cortical Activation Differences in Subacute Stroke

The initial hypothesis of this research was that there would be significant differences in cortical activation between subacute stroke and healthy individuals. The results of two-way ANOVA with Tukey post-hoc analysis found significant group differences; specifically, both the stroke motor execution and stroke motor imagery groups respectively exhibited higher levels of cortical activation compared to healthy participants. These

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results support the initial hypothesis, and are in line with the literature. Previous studies have found that higher functional brain activity was observed in individuals post-stroke. This phenomenon was often attributed to the increased activation in the non-lesioned hemisphere as a form of compensation for the lesioned brain areas, reflecting of the processes of brain reorganization and spontaneous recovery that typically occur during the subacute phase of stroke.[38,39,50]

Furthermore, significant differences in cortical activation were also observed between stroke motor execution and stroke motor imagery groups. Higher levels of activation were found in the motor execution group in the M1 of the lesioned hemisphere. Additionally, the motor imagery group showed higher activation in the non-lesioned M1 compared to the motor execution group (Table II and Table III). These patterns of brain activation in the motor imagery and motor execution groups reflect good functional recovery processes that are in agreement with the results of previous longitudinal studies under fMRI, PET, and EEG.[67-71]

The brain activation differences between the motor execution and motor imagery groups represent a compensatory phenomenon where stroke individuals who present with more severe motor impairment and have difficulty executing active motions (motor imagery group), display higher activation in the non-lesioned M1 and less activation in the lesioned M1.

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5.1.2 Cortical Activation Between Proximal and Distal Limb Tasks

The initial hypothesis of this research was that there would be significant differences in cortical activation between proximal reaching and distal grasping tasks of the upper limb. The results of the study, however, do not support this hypothesis. No significant differences were observed between cortical activation during proximal and distal upper limb tasks of either the non-affected or affected sides in stroke participants, nor were differences seen in healthy participants.

Few studies to date have investigated the cortical activation differences between proximal and distal upper limb tasks. One of the first fNIRS studies on healthy individuals found greater PMC and prefrontal (PFC) involvement in movements of the shoulder, whereas greater sensorimotor (SM1) involvement was found in movements of the hand.[43] More recent studies on healthy individuals found that compared to a finger extension task, shoulder abduction movements demonstrated significantly higher activation in the medial part of the contralateral motor cortex, whereas activation was higher and more lateral for hand movements.[44,72] A previous EEG study found that in healthy subjects, motor imagery of shoulder movements showed greater contralateral localization compared to motor imagery of hand movements.[73] The findings of our present study, however, differ from these previous results.

One possibility may be the influence of task duration. While Yeo et al. employed a

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30-second trial length for the tasks, Yang et al. used both 10- and 20-second trial lengths, and Bonnal et al. used 10-second trial lengths to investigate differences in brain activation during shoulder abduction and finger extension.[43,44,72] While longer trials have the benefit of observing more changes in cortical activation overtime, they may also result in participant burden, especially in stroke individuals who are more easily fatigued.[44]

Further, the choice of upper limb task may be a factor. Previous studies observed neural differences between a shoulder abduction and finger extension task.[43,44,72] The present study used a forward reaching task and a hand grasping task. The absence of significant differences between these tasks may potentially be attributed to the functional similarity of the tasks. We typically reach forward with the intent of grasping an object placed in front of us. Although the participants in this study were instructed to reach forward and touch the object with the dorsal aspect of their wrist, rather than grasp the object, the intent of grasping during the functional forward reach motion may potentially influence cortical activation.

While the current available studies compared proximal and distal limb cortical activation differences in right-handed healthy individuals, our present compared cortical activation between proximal and distal tasks in both the affected and non-affected limbs in individuals with subacute stroke. Significant differences were observed during reaching and grasping tasks of the non-affected compared to the affected limbs. Reaching of the

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affected arm and grasping of the affected arm induced higher cortical activation in the lesioned hemisphere of stroke participants. Longitudinal fMRI, PET, and EEG studies have found that good motor recovery in stroke was associated with shifts in brain activation from initial recruitment of additional brain areas, to the gradual development of activation restricted to the hemisphere contralateral to the moving limb.[71,74,75] Greater activity in the lesioned hemisphere of stroke participants indicates positive functional brain recovery. During both affected reaching and affected grasping, significant cortical activation was observed in channels located in the contralateral hemisphere. These results are in accordance with the concept of brain lateralization.

5.1.3 Group and Task Interactions in Cortical Activation

The results of this study found significant group and task interaction in three channels located in the non-affected PMC and M1 areas. In these three channels, the motor imagery group exhibited significantly higher non-lesioned hemisphere cortical activation during grasping of the affected hand, compared to both motor execution and healthy groups.

These results represent overactivation of areas of the ipsilateral, or non-lesioned, hemisphere, which is often seen in stroke individuals in the early stages of stroke. The group and task interaction was found to be significant for the stroke motor imagery group, who present with severe paresis of the arm. These results also reveal that motor imagery

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tasks of the affected limb may also induce overactivation and compensation of the non-affected brain areas.

5.1.4 Brain Lateralization

It has been well-established in the literature that in healthy individuals, movement of the unilateral limb typically induces activation of the contralateral brain.[76] Previous studies regarding brain lateralization have indicated that a positive laterality index of values between 0 to 1 indicates dominance of the hemisphere contralateral to that of the moving hand.[77] Studies have also found that in individuals with stroke, brain lateralization is altered due to the brain lesion and subsequent cortical reorganization.[78,79] The results of this research found that the stroke motor execution group exhibited dominance of the cortical hemisphere contralateral to the moving hand during tasks of both the non-affected and affected limbs. The positive LI values of the motor execution group, indicating contralateral hemispheric dominance, show a similar trend to that of the healthy controls. The motor imagery group, on the other hand, had positive LI values during movement of the non-affected hand, but negative LI values were observed during the affected arm and grasping tasks, indicating ipsilateral hemispheric dominance (Table IV).

It is also important to note the different values of LI across populations as well as between tasks. In healthy participants, a greater LI is seen for the grasping task compared

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to the reaching task. For the stroke motor execution group, although positive LI values were found during tasks of both the non-affected and affected limbs, greater LI values were observed for non-affected reaching and grasping compared to affected reaching and grasping. Although reaching and grasping of the affected hand induced greater dominance of the lesioned hemisphere, the small positive LI values indicate that bilateral activation, rather than greater dominance of the lesioned hemisphere, still occurred during affected arm movements. In the motor imagery group, movement of the affected arm induced greater non-lesioned hemispheric dominance, reflective of the early stages of stroke and compensatory brain reorganization. It is interesting to note that the LI value for affected reaching is much smaller than that of affected grasping. One explanation for this may be the variation in motor imagery methods between participants during the reaching as compared to the grasping task.

Numerous functional brain imaging studies have found increased activation of the ipsilateral brain areas during affected limb movement after stroke as a result of adaptive compensation of the intact hemisphere.[70,80,81] Severe paresis of the affected side is represented by greater ipsilateral, rather than the typical contralateral, activation.[82] Delorme et al. found that stroke individuals demonstrated a shift in cortical activation, from bilateral activation to unilateral activation, when performing simple unilateral upper limb motor tasks throughout the period of motor recovery.[82] Previous EEG studies

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demonstrated found similar results. Higher brain symmetry indices (BSI), which compares the power spectra between the two brain hemispheres during resting, found that higher BSI-theta values, which reflect asymmetry between the hemispheres, is associated with poor outcomes at six months post-stroke, and that decrease in BSIdir-delta values reflect improvement of neurological impairment.[74,83]

The LI values of our study are thus representative of the different stage of motor recovery of the stroke participants in this study. The motor imagery group, situated in the severe stage of paralysis, displays ipsilateral hemispheric dominance during tasks involving the affected arm and hand. In contrast, the motor execution group demonstrates better motor recovery compared to the motor imagery group, resulting in brain lateralization indices close to those of normal healthy individuals.

5.1.5 Correlations between Cortical Activation and Stroke Characteristics

Pearson's correlation analysis found significant correlation between the reaching and the grasping tasks of the affected limb with upper limb motor outcomes (FMA-UE). During reaching of the affected limb, an inverse correlation was found with cortical activation of the non-lesioned M1, whereas strong positive correlation was found between affected reaching and areas of the lesioned M1. The greater the activation in the

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non-lesioned M1 during reaching of the affected arm indicated a lower FMA-UE score, while the greater the activation in the lesioned M1 was associated with higher FMA-UE scores in our stroke participants. During grasping of the affected hand, significant inverse correlations were found between cortical activation in channels of the non-lesioned PMC and M1 with the FMA-UE scores. These results indicated that greater cortical activation in the PMC and M1 of the non-lesioned brain was associated with lower FMA-UE scores, and more severe motor impairment.

The results of this study are in agreement numerous previous studies that found significant correlation between functional brain activation as well as brain structural changes associated with upper limb motor ability post-stroke.[82,84] A recent study investigating the association between resting-state functional connectivity (RSFC) in subacute stroke patients and FMA-UE scores found significant association between FMA-UE and the RSFC of the dorsolateral prefrontal cortex (DLPFC) of the lesioned hemisphere.[85] Different degrees of upper extremity impairment in subacute stroke reflect different RSFC patterns between the DLPFC and bilateral M1.[85] Although the present study did not investigate areas of the PFC, the results of our correlation analysis indicate an association between the site of activation (lesioned or non-lesioned motor-associated areas) and functional upper limb motor outcomes.

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5.2 Limitations

Several limitations were recognized in this study. First, due to the large variation in upper limb motor ability in subacute stroke patients, this research initially hoped to achieve a more scoping overview of this group of stroke individuals. This, however, led to the rather large inclusion criteria (Brunnstrom Stage I to V) in this study. Although a sub-analysis was conducted for stroke participants who did motor execution and those who did motor imagery, the number of participants in each group (N=21 for motor execution; N=10 for motor imagery) did not exceed 30 participants. Considering the already large variation within subacute stroke participants, narrowing down the inclusion criteria to a specific range of upper limb ability may provide for greater clarity when conducting comparative analysis for cortical activation.

In addition to the small number of stroke participants, there was also small number of healthy controls (n=9). Furthermore, the healthy controls recruited for this study were much younger in average compared to the stroke participants. While the average age for stroke participants was 63.58 ± 11.85 years, the average age of the healthy participants was 51.10 ± 12.24 years. Studies have found that gender and age play crucial roles in deciding post-stroke outcome.[86] Comparison between age- and sex-matched controls would provide a more comprehensive understanding of cortical activation outcomes between healthy and stroke individuals.

Although the current research used a dual-system fNIRS set-up and observed 44 channels

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spanning the bilateral PMC, M1, and S1 areas, other areas that have been found to be associated with upper limb movements, including the prefrontal cortex, supplementary motor area, parietal cortex, and cerebellum, were not investigated in this study. fNIRS probes set up in these areas of the brain may provide a more comprehensive understanding of cortical activation patterns during upper limb movement in subacute stroke.

5.3 Future Research

Future studies using fNIRS should investigate other areas associated with upper limb movement, for a more comprehensive understanding of the different patterns of cortical activation related to proximal and distal arm movement. A recent study investigated the kinematic interactions between proximal and distal limb movements in stroke individuals, and found that muscle co-contraction of the distal hand muscles affected proximal shoulder and arm movements.[87] Future research may employ use of kinematic measurement tools to assess proximal and distal movement and its relation to cortical activation parameters.

5.4 Conclusion

During functional upper limb tasks, significant differences in cortical activation were observed between groups as well as the tasks. Individuals with subacute stroke showed greater intensity of cortical activation in areas of the bilateral PMC, M1, and S1 during upper limb

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movements compared to healthy controls, and within the stroke individuals, those who carried out the affected grasping task by motor imagery showed significantly higher cortical activation in the non-lesioned cortices compared to those who did motor execution. In regards to brain laterality, stroke motor execution individuals demonstrated cortical lateralization more similar to that of healthy controls, with greater contralateral dominance during unilateral upper limb movement. The motor imagery group, however, demonstrated ipsilateral dominance during movement of the affected limb. Lastly, cortical activation during the tasks was significantly correlated with upper limb motor outcomes as well as stroke characteristics, indicating that cortical activation is an important marker associated not only with brain, but as well as movement recovery.

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Figures

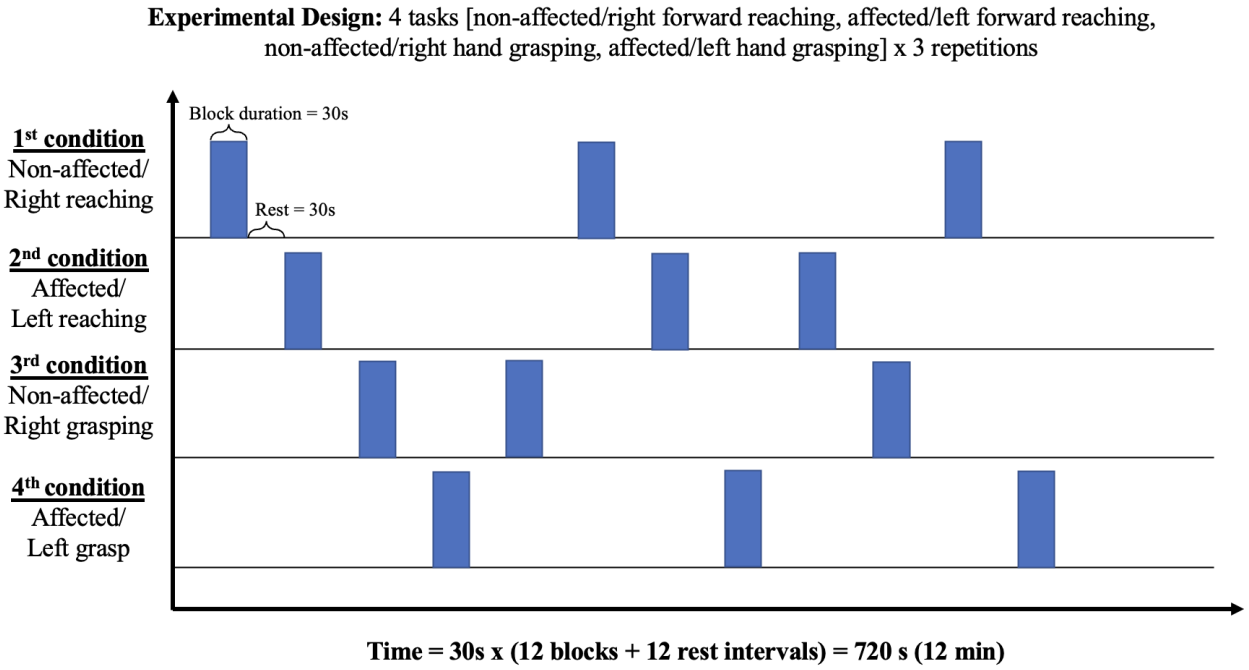

Figure 1. The experimental protocol. Each block consists of 30 seconds of the upper limb task and 30 seconds of rest.

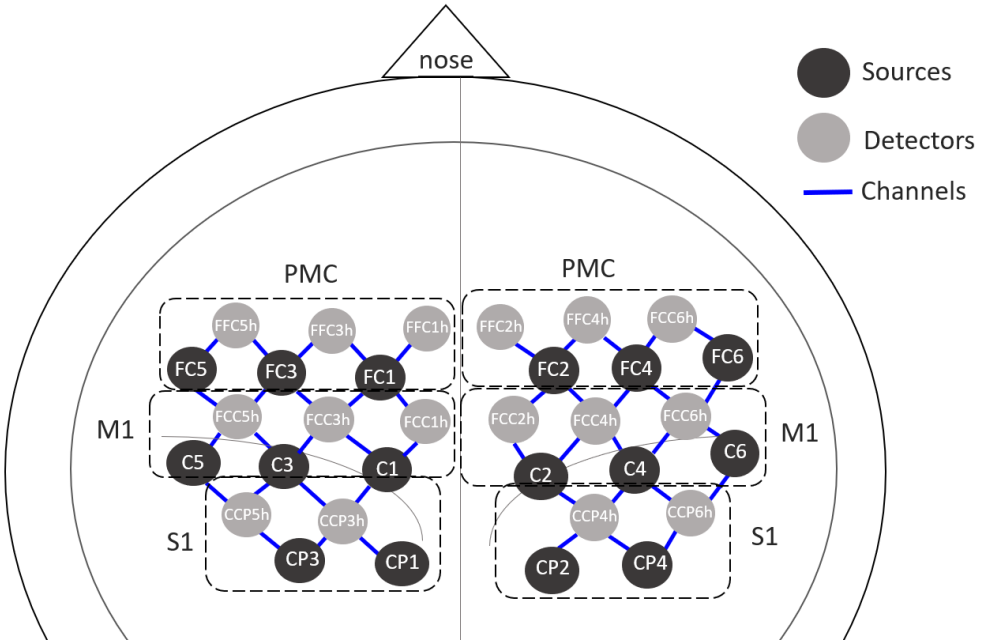

Figure 2. fNIRS optode placement over the brain areas of interest (bilateral PMC, M1, and S1), defining a total of 44 channels.

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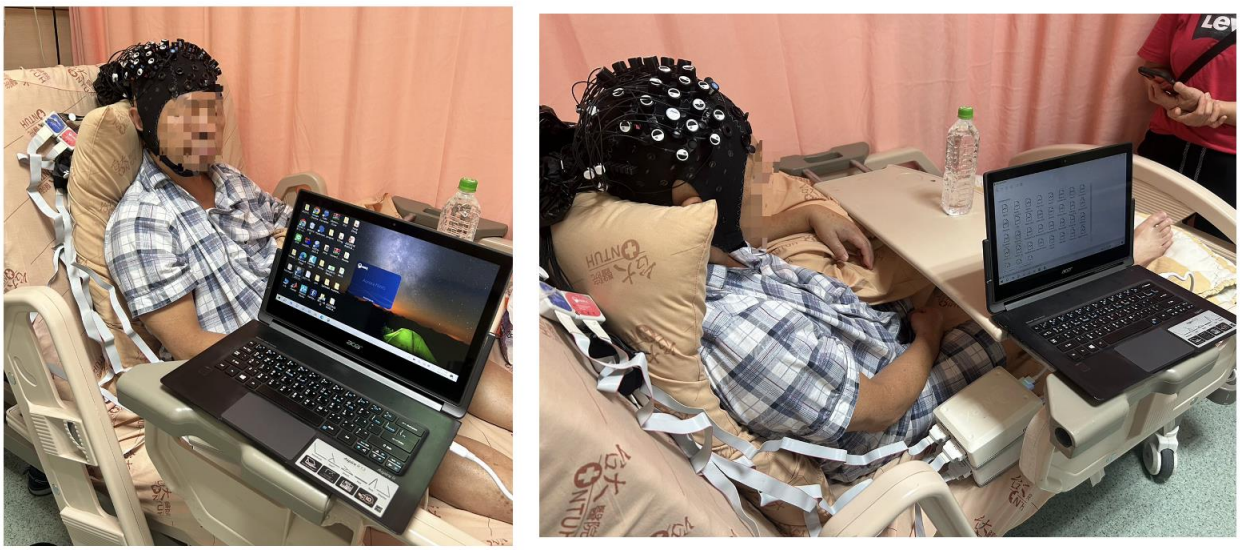

Figure 3. Experimental set-up

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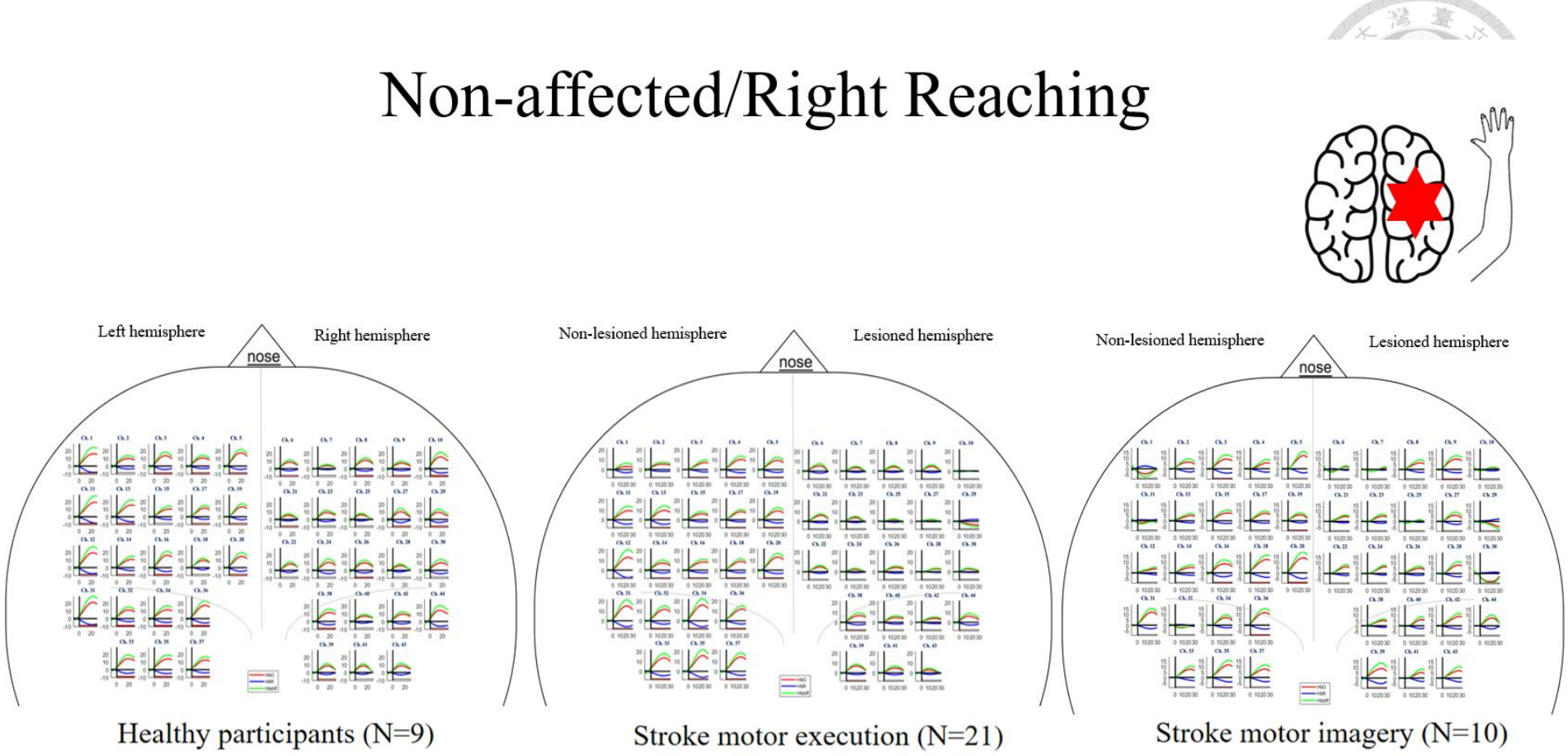

Figure 4. Cortical activation during forward reaching of the non-affected arm (right arm for healthy). Red bars beneath the channel(s) indicate statistically significant differences in cortical activation ($p < 0.05$).

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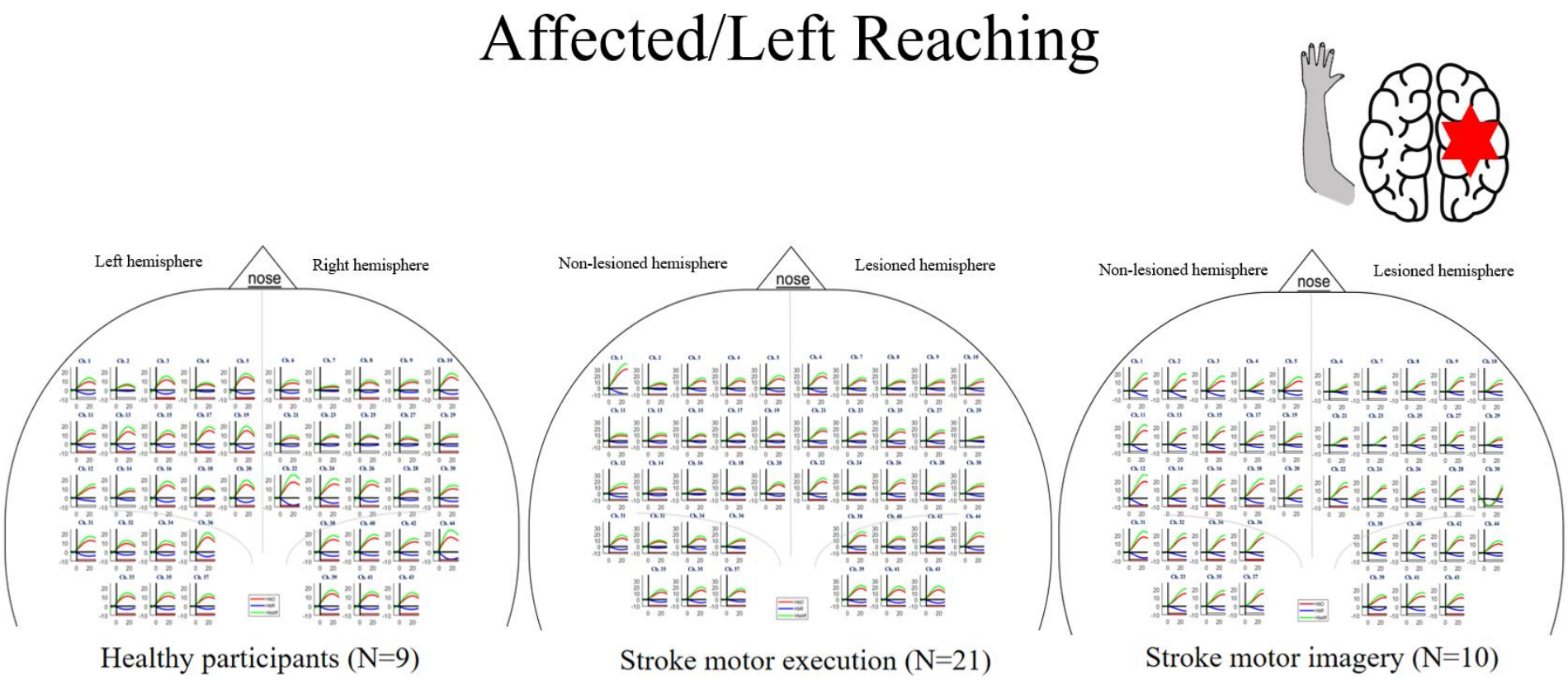

Figure 5. Cortical activation during forward reaching of the affected arm (left arm for healthy). Red bars beneath the channel(s) indicate statistically significant differences in cortical activation ($p < 0.05$).

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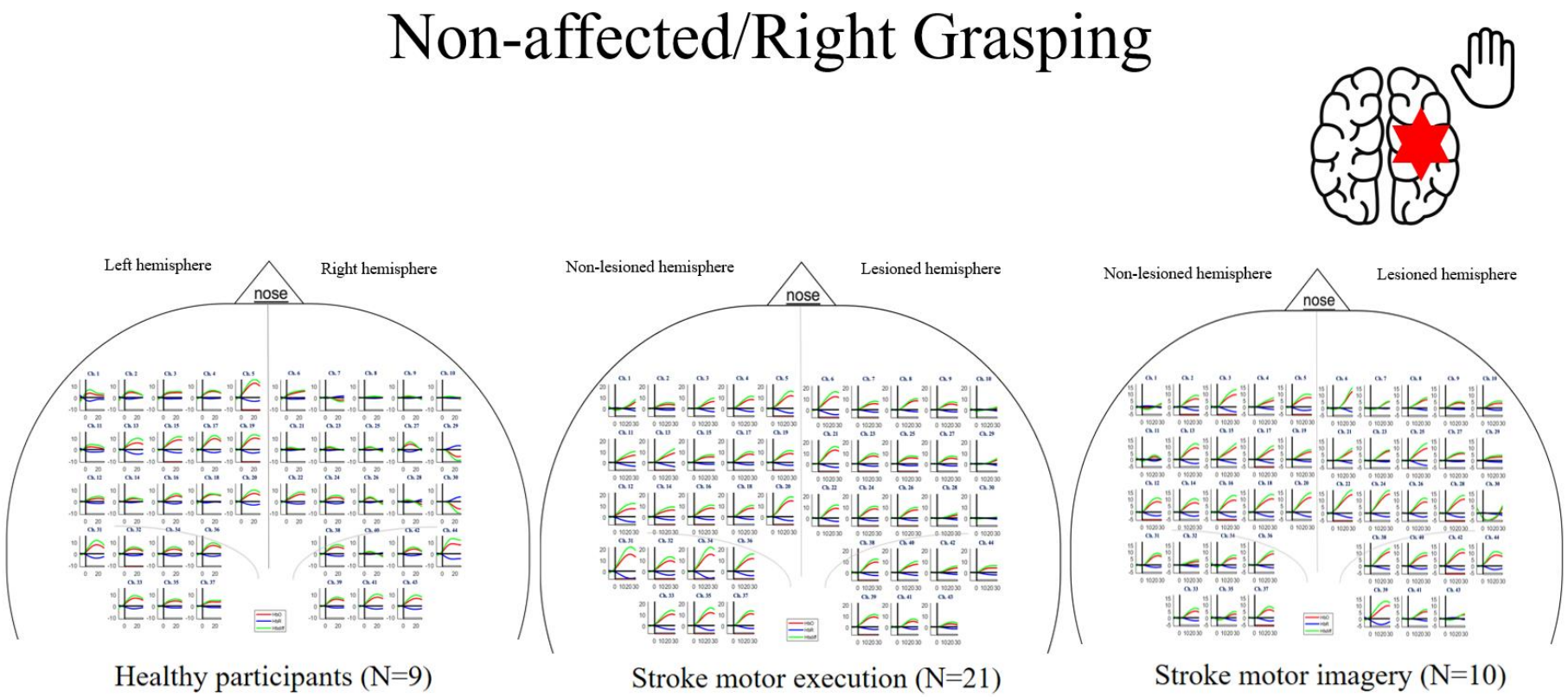

Figure 6. Cortical activation during grasping of the non-affected hand (right hand for healthy). Red bars beneath the channel(s) indicate statistically significant differences in cortical activation ($p < 0.05$).

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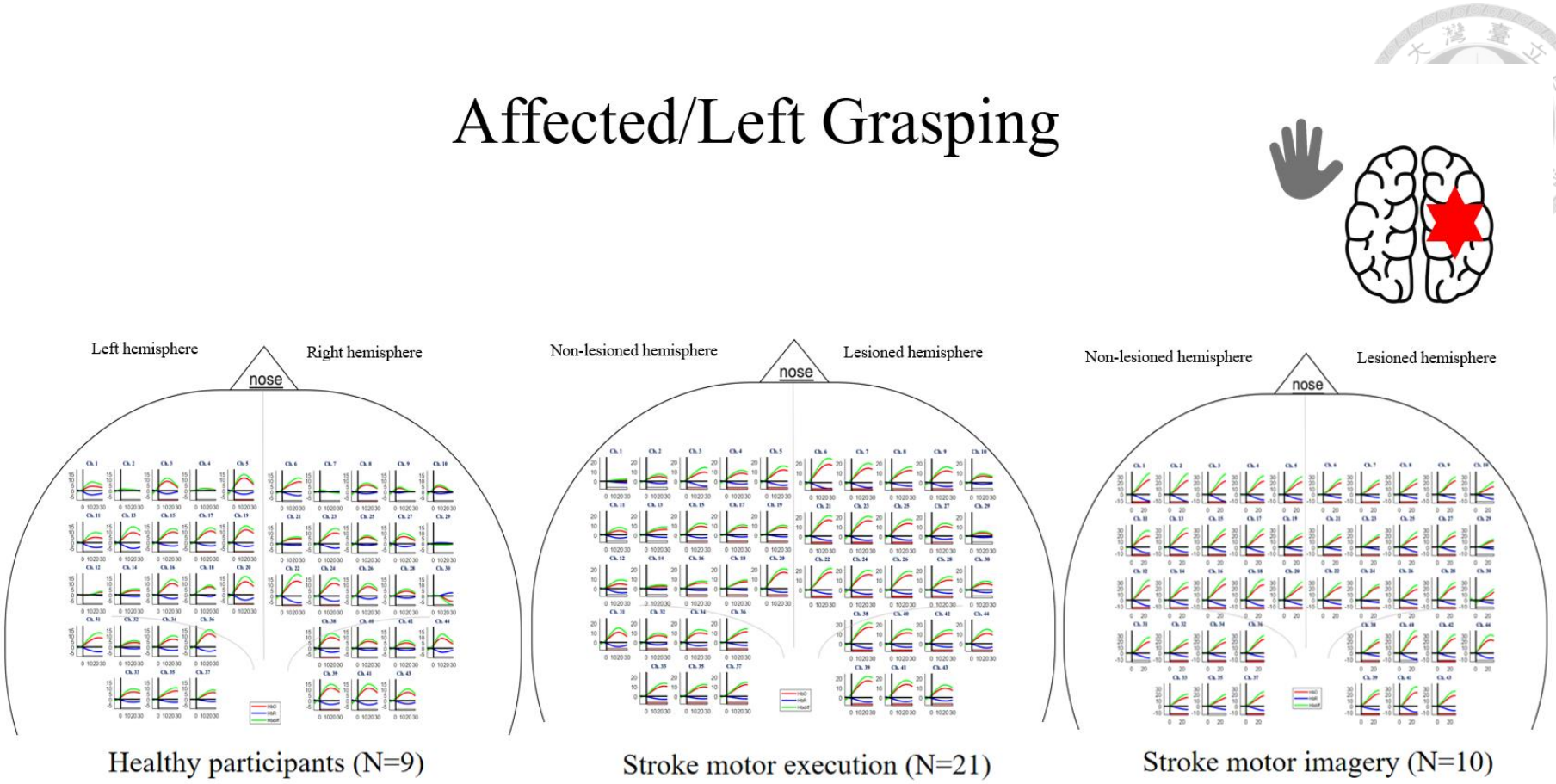

Figure 7. Cortical activation during grasping of the affected hand (left hand for healthy). Red bars beneath the channel(s) indicate statistically significant differences in cortical activation ($p < 0.05$)

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Tables

Table I. Demographic data of all participants

	Stroke individuals			Healthy (n=9)
	All stroke individuals (n=31)	**Motor Execution (n=21)**	**Motor Imagery (n=10)**	
Gender (M/F)	24/7	18/3	6/4	2/7
Ischemic/hemorrhagic	22/9	17/4	5/5	---
Lesioned hemisphere (right/left)	14/17	8/13	6/4	---
Days poststroke onset	32.76 ± 20.67	32.09 ± 19.71	34.30 ± 23.78	---
Age	63.58 ± 11.85	58.50 ± 21.45	64.80 ± 14.64	51.10 ± 12.24
Brunnstrom Stage				---
Proximal	3.61 ± 1.52	4.65 ± 0.83	2.70 ± 0.67	---
Distal	4.06 ± 1.19	4.17 ± 1.44	2.30 ± 0.67	---
FMA-UE	37.88 ± 25.37	51.09 ± 18.69	8.80 ± 5.88	---

All data are presented in means and standard deviations

M = male; F = female

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Table II. Brain Activation during non-affected/right arm reaching and grasping

Channel	Healthy		Stroke				Group p-value	Task p-value	Group* task p-value
			Motor Execution		Motor Imagery				
	Right reaching	Right grasping	Non-affected reaching	Non-affected grasping	Non-affected reaching	Non-affected grasping			
Ch. 1 (contra-PMC)	0.12 ± 0.11	0.02 ± 0.04	0.05 ± 0.17	0.04 ± 0.13	-0.03 ± 0.22	0.060 ± 0.03	0.125	0.180	**0.002****
Ch. 2 (contra-PMC)	0.08 ± 0.11	0.06 ± 0.06	0.08 ± 0.16	0.08 ± 0.09	0.03 ± 0.20	0.07 ± 0.22	0.292	0.437	0.110
Ch. 3 (contra-PMC)	0.10 ± 0.08	0.04 ± 0.08	0.11 ± 0.17	0.09 ± 0.15	0.04 ± 0.14	0.06 ± 0.04	0.955	0.297	0.346
Ch. 4 (contra-PMC)	0.08 ± 0.07	0.04 ± 0.07	0.08 ± 0.13	0.10 ± 0.09	0.09 ± 0.21	0.03 ± 0.08	0.170	0.855	0.637
Ch. 5 (contra-PMC)	0.13 ± 0.12	0.09 ± 0.07	0.08 ± 0.20	0.10 ± 0.12	0.11 ± 0.13	0.03 ± 0.09	0.319	0.375	0.650
Ch. 6 (ipsi-PMC)	0.06 ± 0.08	0.03 ± 0.07	0.06 ± 0.10	0.12 ± 0.12	0.06 ± 0.16	0.09 ± 0.11	**0.009**+**	0.459	0.231
Ch. 7 (ipsi-PMC)	0.03 ± 0.05	-0.01 ± 0.04	0.06 ± 0.11	0.08 ± 0.12	0.08 ± 0.13	0.07 ± 0.09	**0.002**+&**	**0.047*cf**	0.322
Ch. 8 (ipsi-PMC)	0.07 ± 0.07	-0.01 ± 0.07	0.01 ± 0.18	0.09 ± 0.14	0.10 ± 0.15	0.05 ± 0.09	0.098	0.103	0.232
Ch. 9 (ipsi-PMC)	0.06 ± 0.05	0.004 ± 0.05	0.05 ± 0.15	0.05 ± 0.13	0.02 ± 0.13	0.06 ± 0.18	0.130	**0.037*cf**	0.548
Ch. 10 (ipsi-PMC)	0.09 ± 0.10	-0.01 ± 0.08	-0.03 ± 0.18	-0.01 ± 0.13	-0.12 ± 0.13	-0.02 ± 0.22	0.552	0.146	0.208
Ch. 11 (contra-M1)	0.13 ± 0.09	0.01 ± 0.05	0.08 ± 0.151	0.09 ± 0.13	0.15 ± 0.30	0.012 ± 0.20	**0.015*+^**	0.092	**0.032***
Ch. 12 (contra-M1)	0.14 ± 0.10	0.02 ± 0.07	0.13 ± 0.30	0.13 ± 0.16	0.04 ± 0.16	0.12 ± 0.21	**0.020*&**	0.387	**0.007****
Ch. 13 (contra-M1)	0.11 ± 0.09	0.05 ± 0.13	0.14 ± 0.12	0.09 ± 0.13	0.07 ± 0.16	0.16 ± 0.13	0.114	0.425	0.140
Ch. 14 (contra-M1)	0.07 ± 0.03	0.02 ± 0.07	0.11 ± 0.12	0.07 ± 0.07	0.04 ± 0.10	0.10 ± 0.04	**0.026*&**	0.226	0.308
Ch. 15 (contra-M1)	0.07 ± 0.09	0.06 ± 0.08	0.14 ± 0.11	0.05 ± 0.08	0.11 ± 0.16	0.09 ± 0.15	0.117	0.211	0.584
Ch. 16 (contra-M1)	0.11 ± 0.09	0.04 ± 0.09	0.10 ± 0.10	0.12 ± 0.13	0.13 ± 0.16	0.09 ± 0.15	0.432	0.707	0.902
Ch. 17 (contra-M1)	0.06 ± 0.06	0.07 ± 0.10	0.13 ± 0.10	0.08 ± 0.09	0.07 ± 0.21	0.11 ± 0.16	0.473	0.203	0.213
Ch. 18 (contra-M1)	0.03 ± 0.05	0.05 ± 0.09	0.11 ± 0.12	0.08 ± 0.06	0.09 ± 0.16	0.03 ± 0.05	0.106	0.297	0.230
Ch. 19 (contra-M1)	0.06 ± 0.05	0.08 ± 0.04	0.10 ± 0.14	0.11 ± 0.06	0.11 ± 0.12	0.03 ± 0.09	0.638	0.394	0.209
Ch. 20 (contra-M1)	0.09 ± 0.06	0.05 ± 0.13	0.17 ± 0.18	0.16 ± 0.18	0.17 ± 0.21	0.08 ± 0.08	0.062	0.215	0.534
Ch. 21 (ipsi-M1)	0.04 ± 0.05	0.04 ± 0.06	0.09 ± 0.10	0.12 ± 0.09	0.07 ± 0.18	0.15 ± 0.15	**0.001**+**	0.264	0.055
Ch. 22 (ipsi-M1)	0.06 ± 0.12	0.05 ± 0.11	0.09 ± 0.13	0.15 ± 0.13	0.06 ± 0.19	0.10 ± 0.17	**0.003**+^**	0.081	0.170
Ch. 23 (ipsi-M1)	0.07 ± 0.03	0.01 ± 0.11	0.04 ± 0.17	0.10 ± 0.11	0.08 ± 0.20	0.12 ± 0.19	0.161	0.124	0.333
Ch. 24 (ipsi-M1)	0.05 ± 0.05	0.03 ± 0.08	0.05 ± 0.12	0.08 ± 0.12	0.03 ± 0.07	0.01 ± 0.12	**0.026*^**	**0.015*acf**	0.638
Ch. 25 (ipsi-M1)	0.03 ± 0.04	0.01 ± 0.05	0.03 ± 0.13	0.08 ± 0.12	-0.05 ± 0.17	0.12 ± 0.09	**0.018*+**	**0.004**ac**	0.144
Ch. 26 (ipsi-M1)	0.07 ± 0.07	0.01 ± 0.10	0.06 ± 0.15	0.09 ± 0.16	0.03 ± 0.10	0.01 ± 0.17	**0.042*^**	0.064	0.419
Ch. 27 (ipsi-M1)	0.07 ± 0.08	0.03 ± 0.06	0.01 ± 0.20	0.02 ± 0.14	-0.04 ± 0.08	0.03 ± 0.17	0.399	0.065	0.421
Ch. 28 (ipsi-M1)	0.04 ± 0.06	-0.002 ± 0.05	0.04 ± 0.15	0.04 ± 0.16	0.01 ± 0.11	0.08 ± 0.17	0.262	0.051	0.439
Ch. 29 (ipsi-M1)	0.04 ± 0.02	-0.03 ± 0.08	-0.03 ± 0.21	0.03 ± 0.14	-0.13 ± 0.19	0.04 ± 0.17	0.806	**0.019*c**	0.099
Ch. 30 (ipsi-M1)	0.08 ± 0.04	-0.03 ± 0.07	-0.002 ± 0.19	0.05 ± 0.17	-0.03 ± 0.17	-0.01 ± 0.08	0.132	0.338	0.410
Ch. 31 (contra-S1)	0.14 ± 0.01	0.06 ± 0.08	0.15 ± 0.18	0.154 ± .13	0.12 ± 0.17	0.13 ± 0.09	0.052	0.680	0.265
Ch. 32 (contra-S1)	0.09 ± 0.05	0.03 ± 0.04	0.12 ± 0.14	0.13 ± 0.11	0.10 ± 0.16	0.03 ± 0.10	0.279	0.647	0.191
Ch. 33 (contra-S1)	0.11 ± 0.07	0.04 ± 0.05	0.17 ± 0.13	0.12 ± 0.08	0.05 ± 0.20	0.04 ± 0.09	**0.026*+**	0.367	0.510
Ch. 34 (contra-S1)	0.08 ± 0.03	0.03 ± 0.08	0.12 ± 0.08	0.13 ± 0.11	0.13 ± 0.14	0.06 ± 0.16	**0.036*+**	0.606	0.570
Ch. 35 (contra-S1)	0.11 ± 0.07	0.04 ± 0.07	0.12 ± 0.15	0.12 ± 0.12	0.10 ± 0.21	0.07 ± 0.09	0.145	0.818	0.896
Ch. 36 (contra-S1)	0.13 ± 0.07	0.04 ± 0.09	0.17 ± 0.12	0.12 ± 0.09	0.14 ± 0.12	0.09 ± 0.12	0.114	0.122	0.546
Ch. 37 (contra-S1)	0.09 ± 0.07	0.03 ± 0.06	0.14 ± 0.07	0.14 ± 0.09	0.09 ± 0.08	0.07 ± 0.05	**0.001**+^**	0.249	0.454

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Ch. 38 (ipsi-S1)	0.08 ± 0.04	0.06 ± 0.06	0.05 ± 0.09	0.11 ± 0.15	0.03 ± 0.14	0.09 ± 0.15	**0.047*+**	**0.015*acf**	0.375
Ch. 39 (ipsi-S1)	0.05 ± 0.06	0.03 ± 0.06	0.04 ± 0.12	0.11 ± 0.15	0.07 ± 0.14	0.06 ± 0.14	0.149	**0.050*c**	0.578
Ch. 40 (ipsi-S1)	0.06 ± 0.07	0.01 ± 0.07	0.02 ± 0.10	0.06 ± 0.11	0.02 ± 0.12	0.07 ± 0.17	**0.035*+**	**0.026* acf**	0.174
Ch. 41 (ipsi-S1)	0.10 ± 0.04	0.07 ± 0.11	0.07 ± 0.12	0.12 ± 0.14	0.10 ± 0.16	0.06 ± 0.15	0.081	0.170	0.555
Ch. 42 (ipsi-S1)	0.07 ± 0.04	0.03 ± 0.06	0.03 ± 0.08	0.08 ± 0.15	0.12 ± 0.17	0.10 ± 0.15	0.288	0.691	0.288
Ch. 43 (ipsi-S1)	0.07 ± 0.10	0.05 ± 0.08	0.06 ± 0.11	0.08 ± 0.19	0.08 ± 0.19	0.11 ± 0.11	0.115	0.139	0.669
Ch. 44 (ipsi-S1)	0.11 ± 0.11	0.06 ± 0.07	0.06 ± 0.14	0.12 ± 0.19	0.03 ± 0.30	0.04 ± 0.23	0.373	0.071	0.440

All data are presented in means and standard deviations

Abbreviations: contra- = contralateral; ipsi- = ipsilateral; PMC = premotor cortex; M1 = motor cortex; S1 = somatosensory cortex

* = $p < 0.05$

** = $p < 0.01$

+ = significant difference between motor execution and healthy groups

^ = significant difference between motor execution and motor imagery groups

& = significant difference between motor imagery and healthy groups

a = significant difference between non-affected/right reach and affected/left reach

b = significant difference between non-affected/right reach and non-affected/right grasp

c = significant difference between non-affected/right reach and affected/left grasp

d = significant difference between affected/left reach and non-affected/right grasp

e = significant difference between affected/left reach and affected/left grasp

f = significant difference between non-affected/right grasp and affected/left grasp

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Table III. Brain Activation during affected/left arm reaching and grasping

Channel	Healthy		Stroke				Group p-value	Task p-value	Group* task p-value
			Motor Execution		Motor Imagery				
	Left reaching	Left grasping	Affected reaching	Affected grasping	Affected reaching	Affected grasping			
Ch. 1 (ipsi-PMC)	0.07 ± 0.11	-0.01 ± 0.06	0.08 ± 0.22	0.05 ± 0.13	0.13 ± 0.16	0.28 ± 0.21	0.125	0.180	**0.002****
Ch. 2 (ipsi-PMC)	0.04 ± 0.07	-0.002 ± 0.06	0.08 ± 0.17	.10 ± 0.11	0.04 ± 0.12	0.24 ± 0.34	0.292	0.437	0.110
Ch. 3 (ipsi-PMC)	0.09 ± 0.06	0.06 ± 0.06	-0.01 ± 0.23	0.1 ± 0.13	0.06 ± 0.18	0.18 ± 0.33	0.955	0.297	0.346
Ch. 4 (ipsi-PMC)	0.07 ± 0.04	0.02 ± 0.05	0.10 ± 0.16	0.11 ± 0.13	0.04 ± 0.23	0.10 ± 0.16	0.170	0.855	0.637
Ch. 5 (ipsi-PMC)	0.10 ± 0.05	0.07 ± 0.03	0.03 ± 0.18	0.13 ± 0.15	0.01 ± 0.23	0.06 ± 0.13	0.319	0.375	0.650
Ch. 6 (contra-PMC)	0.06 ± 0.06	0.05 ± 0.04	0.17 ± 0.18	0.15 ± 0.10	0.02 ± 0.10	0.14 ± 0.27	**0.009**+**	0.459	0.231
Ch. 7 (contra-PMC)	0.03 ± 0.05	0.002 ± 0.04	0.11 ± 0.17	0.15 ± 0.17	0.07 ± 0.18	0.23 ± 0.20	**0.002**+&**	**0.047*cf**	0.322
Ch. 8 (contra-PMC)	0.05 ± 0.05	0.04 ± 0.06	0.13 ± 0.17	0.17 ± 0.20	0.07 ± 0.21	0.19 ± 0.21	0.098	0.103	0.232
Ch. 9 (contra-PMC)	0.07 ± 0.08	0.02 ± 0.04	0.14 ± 0.20	0.15 ± 0.17	0.13 ± 0.20	0.21 ± 0.33	0.130	**0.037*cf**	0.548
Ch. 10 (contra-PMC)	0.05 ± 0.08	0.02 ± 0.07	0.05 ± 0.20	0.05 ± 0.23	0.003 ± 0.12	0.12 ± 0.22	0.552	0.146	0.208
Ch. 11 (ipsi-M1)	0.08 ± 0.09	0.01 ± 0.06	0.08 ± 0.25	0.09 ± 0.19	0.20 ± 0.22	0.33 ± 0.25	**0.015*+^**	0.092	**0.032***
Ch. 12 (ipsi-M1)	0.05 ± 0.08	0.08 ± 0.07	0.16 ± 0.29	0.06 ± 0.14	0.12 ± 0.08	0.32 ± 0.26	**0.020*&**	0.387	**0.007****
Ch. 13 (ipsi-M1)	0.10 ± 0.11	0.08 ± 0.08	0.03 ± 0.16	0.132 ± 0.12	0.14 ± 0.24	0.22 ± 0.24	0.114	0.425	0.140
Ch. 14 (ipsi-M1)	0.06 ± 0.10	0.03 ± 0.07	0.15 ± 0.25	0.08 ± 0.16	0.18 ± 0.25	0.21 ± 0.19	**0.026*&**	0.226	0.308
Ch. 15 (ipsi-M1)	0.07 ± 0.05	0.07 ± 0.09	0.05 ± 0.11	0.15 ± 0.19	0.14 ± 0.12	0.18 ± 0.23	0.117	0.211	0.584
Ch. 16 (ipsi-M1)	0.11 ± 0.11	0.08 ± 0.03	0.14 ± 0.20	0.12 ± 0.16	0.11 ± 0.23	0.14 ± 0.14	0.432	0.707	0.902
Ch. 17 (ipsi-M1)	0.11 ± 0.09	0.08 ± 0.09	0.11 ± 0.22	0.13 ± 0.12	0.05 ± 0.12	0.26 ± 0.36	0.473	0.203	0.213
Ch. 18 (ipsi-M1)	0.08 ± 0.08	0.03 ± 0.07	0.08 ± 0.14	0.10 ± 0.15	0.11 ± 0.12	0.21 ± 0.28	0.106	0.297	0.230
Ch. 19 (ipsi-M1)	0.11 ± 0.11	0.07 ± 0.07	0.09 ± 0.14	0.11 ± 0.14	0.07 ± 0.07	0.20 ± 0.26	0.638	0.394	0.209
Ch. 20 (ipsi-M1)	0.11 ± 0.10	0.09 ± 0.11	0.11 ± 0.16	0.17 ± 0.14	0.01 ± 0.15	0.17 ± 0.26	0.062	0.215	0.534
Ch. 21 (contra-M1)	0.04 ± 0.06	0.04 ± 0.06	0.17 ± 0.17	0.14 ± 0.07	0.003 ± 0.10	0.16 ± 0.21	**0.001**+**	0.264	0.055
Ch. 22 (contra-M1)	0.13 ± 0.10	0.08 ± 0.09	0.23 ± 0.20	0.21 ± 0.12	0.02 ± 0.10	0.19 ± 0.25	**0.003**+^**	0.081	0.170
Ch. 23 (contra-M1)	0.06 ± 0.12	0.07 ± 0.11	0.15 ± 0.24	0.20 ± 0.23	0.02 ± 0.10	0.20 ± 0.25	0.161	0.124	0.333
Ch. 24 (contra-M1)	0.11 ± 0.10	0.06 ± 0.04	0.18 ± 0.23	0.19 ± 0.21	0.06 ± 0.13	0.14 ± 0.12	**0.026*^**	**0.015*acf**	0.638
Ch. 25 (contra-M1)	0.07 ± 0.09	0.05 ± 0.09	0.19 ± 0.23	0.17 ± 0.17	0.04 ± 0.09	0.16 ± 0.19	**0.018*+**	**0.004**ac**	0.144
Ch. 26 (contra-M1)	0.12 ± 0.13	0.06 ± 0.10	0.16 ± 0.21	0.24 ± 0.25	0.03 ± 0.15	0.13 ± 0.20	**0.042*+^**	0.064	0.419
Ch. 27 (contra-M1)	0.05 ± 0.08	0.05 ± 0.09	0.13 ± 0.25	0.15 ± 0.17	0.03 ± 0.18	0.14 ± 0.25	0.399	0.065	0.421
Ch. 28 (contra-M1)	0.06 ± 0.09	0.03 ± 0.06	0.06 ± 0.14	0.18 ± 0.22	0.07 ± 0.14	0.15 ± 0.13	0.262	0.051	0.439
Ch. 29 (contra-M1)	0.06 ± 0.07	-0.01 ± 0.05	0.07 ± 0.18	0.09 ± 0.24	0.05 ± 0.12	0.18 ± 0.27	0.806	**0.019*c**	0.099
Ch. 30 (contra-M1)	0.05 ± 0.07	-0.02 ± 0.09	0.10 ± 0.17	0.17 ± 0.28	0.03 ± 0.13	0.16 ± 0.24	0.132	0.338	0.410
Ch. 31 (ipsi-S1)	0.10 ± 0.12	0.06 ± 0.10	0.15 ± 0.24	0.13 ± 0.19	0.21 ± 0.24	0.30 ± 0.32	0.052	0.680	0.265
Ch. 32 (ipsi-S1)	0.08 ± 0.08	0.02 ± 0.05	0.08 ± 0.26	0.08 ± 0.19	0.05 ± 0.15	0.19 ± 0.12	0.279	0.647	0.191
Ch. 33 (ipsi-S1)	0.09 ± 0.09	0.05 ± 0.08	0.13 ± 0.16	0.14 ± 0.19	0.11 ± 0.16	0.16 ± 0.14	**0.026*+**	0.367	0.510
Ch. 34 (ipsi-S1)	0.07 ± 0.08	0.05 ± 0.07	0.13 ± 0.18	0.12 ± 0.15	0.06 ± 0.14	0.17 ± 0.19	**0.036*+**	0.606	0.570
Ch. 35 (ipsi-S1)	0.07 ± 0.05	0.05 ± 0.07	0.14 ± 0.25	0.13 ± 0.18	0.05 ± 0.19	0.13 ± 0.22	0.145	0.818	0.896
Ch. 36 (ipsi-S1)	0.12 ± 0.12	0.06 ± 0.08	0.10 ± 0.13	0.15 ± 0.13	0.0 ± 0.103	0.17 ± 0.20	0.114	0.122	0.546
Ch. 37 (ipsi-S1)	0.08 ± 0.03	0.04 ± 0.06	0.12 ± 0.17	0.18 ± 0.15	0.04 ± 0.09	0.16 ± 0.19	**0.001**+^**	0.249	0.454

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Ch. 38 (contra-S1)	0.11 ± 0.08	0.08 ± 0.07	0.20 ± 0.20	0.24 ± 0.19	0.080 ± 0.10	0.17 ± 0.23	**0.047*+**	**0.015*acf**	0.375
Ch. 39 (contra-S1)	0.08 ± 0.06	0.06 ± 0.05	0.09 ± 0.12	0.15 ± 0.15	0.08 ± 0.10	0.18 ± 0.16	0.149	**0.050*c**	0.578
Ch. 40 (contra-S1)	0.08 ± 0.07	0.05 ± 0.06	0.18 ± 0.23	0.21 ± 0.19	0.07 ± 0.14	0.10 ± 0.16	**0.035*+**	**0.026* acf**	0.174
Ch. 41 (contra-S1)	0.10 ± 0.11	0.09 ± 0.11	0.20 ± 0.22	0.21 ± 0.16	0.13 ± 0.22	0.11 ± 0.13	0.081	0.170	0.555
Ch. 42 (contra-S1)	0.09 ± 0.11	0.04 ± 0.07	0.14 ± 0.20	0.16 ± 0.22	0.09 ± 0.12	0.09 ± 0.11	0.288	0.691	0.288
Ch. 43 (contra-S1)	0.09 ± 0.09	0.05 ± 0.10	0.17 ± 0.19	0.21 ± 0.19	0.14 ± 0.14	0.17 ± 0.20	0.115	0.139	0.669
Ch. 44 (contra-S1)	0.13 ± 0.13	0.07 ± 0.11	0.19 ± 0.22	0.20 ± 0.19	0.11 ± 0.13	0.25 ± 0.36	0.373	0.071	0.440

All data are presented in means and standard deviations

Abbreviations: contra- = contralateral; ipsi- = ipsilateral; PMC = premotor cortex; M1 = motor cortex; S1 = somatosensory cortex

* = $p < 0.05$

** = $p < 0.01$

+ = significant difference between motor execution and healthy groups

^ = significant difference between motor execution and motor imagery groups

& = significant difference between motor imagery and healthy groups

a = significant difference between non-affected/right reach and affected/left reach

b = significant difference between non-affected/right reach and non-affected/right grasp

c = significant difference between non-affected/right reach and affected/left grasp

d = significant difference between affected/left reach and non-affected/right grasp

e = significant difference between affected/left reach and affected/left grasp

f = significant difference between non-affected/right grasp and affected/left grasp

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Table IV. Laterality Index for Stroke and Healthy Participants

	Healthy (n=9)	Motor Execution (n=21)		Motor Imagery (n=10)		Group p-value	Task p-value	Group*task p-value
		Non-affected	Affected	Non-affected	Affected			
Reaching	0.24 ± 0.40	0.55 ± 0.44	0.09 ± 0.50	0.36 ± 0.81	-0.31 ± 0.56	**0.030*^**	**0.000**acdf**	0.718
Grasping	0.39 ± 0.29	0.29 ± 0.51	0.07 ± 0.52	0.23 ± 0.53	-0.15 ± 0.30			

* = $p < 0.05$

** = $p < 0.01$

+ = significant difference between motor execution and healthy

^ = significant difference between motor execution and motor imagery

& = significant difference between motor imagery and healthy

a = significant difference between non-affected reach and affected reach

b = significant difference between non-affected reach and non-affected grasp

c = significant difference between non-affected reach and affected grasp

d = significant difference between affected/left reach and non-affected/right grasp

e = significant difference and non-affected grasp between affected reach and affected grasp

f = significant difference between non-affected grasp and affected grasp

Table V. Correlations between Brain Activation and Stroke Characteristics

Stroke	Fugl-Meyer Assessment	Days post-stroke
Non-affected reaching		
Ch 2 (non-lesioned PMC)	-	r = 0.364; p = 0.044
Ch 21 (lesioned M1)	-	r = -0.399; p = 0.026
Affected reaching		
Ch 15 (non-lesioned M1)	r = -0.381; p = 0.038	-
Ch 21 (lesioned M1)	r = 0.499; p = 0.005	-
Ch 22 (lesioned M1)	r = 0.418; p = 0.021	-
Non-affected grasping		-
Ch 5 (non-lesioned PMC)	r = 0.427; p = 0.019	-
Ch 9 (non-lesioned M1)	r = 0.468; p = 0.009	-
Ch 32 (non-lesioned M1)	r = 0.452; p = 0.012	-
Ch 18 (non-lesioned M1)	r = 0.430; p = 0.018	-
Ch 33 (non-lesioned S1)	r = 0.405; p = 0.027	-
Ch 37 (non-lesioned S1)	r = 0.462; p = 0.010	-
Affected grasping		
Ch 1 (non-lesioned PMC)	r = -0.446; p = 0.014	-
Ch 11 (non-lesioned M1)	r = -0.440; p = 0.015	-
Ch 12 (non-lesioned M1)	r = -0.468; p = 0.009	-

Abbreviations: PMC = premotor cortex; M1 = motor cortex; S1 = somatosensory cortex

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Appendices

Appendix 1. Area(s) of brain lesion for each participant

Participant	Gender	Age (years)	Execution of tasks	Lesioned brain area(s)
1	Female	55	Motor imagery	Right frontoparietal intracerebral hemorrhage with expansion as convexity subarachnoid hemorrhage and subdural hematoma, ICH score = 2
2	Male	69	Motor execution	Acute ischemic stroke, left anterior choroidal artery territory
3	Male	39	Motor imagery	Intracerebral hemorrhage, right basal ganglion, about 35ml, ICH score = 0
4	Male	47	Motor execution	Intracerebral hemorrhage, left thalamus
5	Male	69	Motor execution	Acute ischemic stroke, right periventricular white matter to posterior putamen
6	Female	78	Motor execution	Acute ischemic stroke at right posterior cerebral artery territory, cardioembolic type
7	Male	68	Motor execution	Left thalamic intracerebral hemorrhage, 9 mL, with intraventricular hemorrhage, ICH score = 1
8	Female	54	Motor execution	Acute ischemic stroke, right thalamus
9	Male	75	Motor execution	Acute ischemic stroke, right MCA, M2, & ACA A3
10	Male	71	Motor execution	Acute ischemic stroke, left paramedian pons
11	Male	69	Motor execution	Infarct, left posterior limb of internal capsule
12	Male	57	Motor execution	Acute right pontine infarction
13	Male	61	Motor imagery	Intracerebral hemorrhage at right thalamus with intraventricular hemorrhage, ICH score = 1
14	Male	64	Motor imagery	Acute infarction in the right middle cerebral artery with distal right MCA M1 occlusion
15	Male	48	Motor execution	Infarction in left distal MCA territory
16	Male	75	Motor execution	Left middle cerebral artery infarction
17	Female	54	Motor imagery	Left basal ganglion intracerebral hemorrhage with intraventricular hemorrhage
18	Male	63	Motor execution	Acute ischemic stroke, left internal capsule posterior limb and left temporo-parietal white matter
19	Male	39	Motor execution	Spontaneous intracerebral hemorrhage at left thalamus, about 10 mL, with intraventricular hemorrhage
20	Male	64	Motor execution	Acute ischemic stroke over right cerebellum
21	Male	79	Motor imagery	Acute ischemic stroke over left pontine
22	Female	81	Motor imagery	Acute ischemic stroke, right posterior putamen with extension to periventricular white matter
23	Female	71	Motor execution	Acute ischemic stroke, left MCA proximal M2 territory, due to left proximal M2 occlusion
24	Male	64	Motor execution	Acute ischemic stroke, at right lentiform nucleus, external capsule, right fronto-parietal lobe, and corona radiata
25	Male	56	Motor imagery	Acute ischemic stroke, left middle cerebral artery territory, middle one (M1) occlusion
26	Male	59	Motor execution	Acute ischemic stroke, right middle cerebral artery, posterior M2 branch
27	Male	73	Motor execution	Acute ischemic stroke at left periventricular white matter
28	Female	74	Motor imagery	Acute ischemic stroke, right anterior choroidal artery territory infarction and left putaminal infarction
29	Male	74	Motor execution	Acute ischemic stroke, mainly at left middle cerebral artery (MCA) inferior M2 territory, and small infarcts at left frontal and right parietal lobes
30	Male	80	Motor execution	Right thalamic intracerebral hemorrhage 3 cc., ICH score=1
31	Male	85	Motor imagery	Left putaminal hemorrhage, 7ml, ICH score=1

ICH = intracerebral hemorrhage

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Appendix 2. Institutional Review Board Approval Letters from National Taiwan University Hospital

電子公布欄公文

國立臺灣大學醫學院附設醫院　函

機關地址：100225 台北市中山南路7號
聯絡人：謝芳芳
聯絡電話：02-3366-7191

受文者：如行文單位

發文日期：中華民國112年1月19日
發文字號：校附醫倫字第1123700265號
速別：普通件
密等及解密條件或保密期限：
附件：

主旨：有關台端所主持之「中風後執行上肢近端與遠端功能性動作任務之大腦激活情形：近紅外光分析儀研究/Brain Activation Patterns during Proximal and Distal Upper Limb Functional Tasks in Stroke: A Functional Near-Infrared Spectroscopy Study」（本院案號：202212018RIND）學術臨床試驗/研究案，符合簡易審查條件及研究倫理規範，通過本院D研究倫理委員會審查，同意核備，並提第136次會議報備追認，惟應依說明辦理，請查照。

說明：

一、本臨床試驗/研究核准之有效期限自發文日起1年，計畫主持人應於許可到期日前10週至前6週向研究倫理委員會提出持續審查申請，並經審查同意後，方可繼續執行。

二、本臨床試驗/研究計畫若需變更、暫停執行、中途終止或結束時，主持人應向本會提出審查申請。計畫主持人並須依國內相關法令及本院規定通報嚴重不良反應事件及非預期問題。

三、本院研究倫理委員會同意之文件版本日期如下：

(一)臨床試驗/研究計畫書：Version 3; 2022/12/30。

(二)中文摘要：Version 1; 2022/12/01。

(三)受試者說明及同意書：Version 4, 2023/01/12。

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(四)簡易心智/認知狀態量表 (MMSE)：Version 1; 2022/11/29。

(五)FM-UE eng 190303 PROTOCOL：Updated 2019-03-03。

(六)受試者招募：Version 3.0; 2023/01/06。

四、本院研究倫理委員會的運作符合優良臨床試驗準則及政府相關法律規章。

五、依據赫爾辛基宣言、世界衛生組織及International Committee of Medical Journal Editors(ICMJE)的規定，所有”臨床試驗案”應於公開網站登錄。且ICMJE規定，完成登錄者才能發表研究結果。

(一)計畫主持人請於招募第一位受試者前，登入美國National Institutes of Health網站https://register.clinicaltrials.gov，使用本院專用帳號，進行上傳登錄。(登錄步驟指引請見本院醫學研究部臨床試驗計畫案登錄指引網址：https://www.ntuh.gov.tw/NCTRC/Fpage.action?muid=2935&fid=2761)

(二)本院已向美國National Institutes of Health(NIH) ClinicalTrials.gov網站申請本院專用帳號，供本院計畫主持人(PI)登錄所主持之臨床試驗研究計畫，登入網頁之帳號及密碼如下列：

1、Organization：NTaiwanUH

2、User Name：NTUH

3、Password：99NTUH99

六、若屬介入性臨床試驗計畫，請於納入第一個個案(已簽署受試者同意書)時，於本會e-REC系統登錄第一位個案收案時間(操作步驟請詳臨床研究重要訊息通知單)，填入後e-REC系統將自動通知本院研究倫理委員會、藥劑部及臨床試驗中

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心。若非介入性臨床試驗計畫，於填報持續審查/結案報告前亦須先至研究倫理委員會e-REC系統登錄第一位個案收案時間，列印前述報告時方會呈現該時間資料。

七、計畫主持人及研究團隊應遵循之相關研究倫理規範，請參閱研究倫理委員會網頁https://www.ntuh.gov.tw/RECO，並遵照執行；臨床試驗/研究執行期間，請確實依據「人體研究法」之相關規定辦理；並請計畫主持人保存所有文件備查。

八、凡執行本院研究倫理委員會(REC)通過之臨床試驗或研究案，請研究人員在邀請可能參加試驗/研究之病友、家屬或民眾時，先分發給予「臺大醫院臨床試驗/研究參與者須知」單張，並依單張內容詳細說明參加本院之試驗或研究將受到之保護，若屬涉及病人照護、診斷或治療之介入性計畫，上述給予單張及知情同意之過程請記錄於病歷。

九、前述提及之「嚴重不良事件及非預期問題通報須知」、「臨床研究重要訊息通知單」、「台大醫院臨床試驗/研究參與者須知」表單請至本院研究倫理委員會網頁下載，並請依計畫需要辦理應辦事宜。

十、請持擬張貼之招募文宣至本院研究倫理委員會用印。

正本：國立臺灣大學醫學院物理治療學系暨研究所劉宴齊助理教授
副本：國立臺灣大學、本院研究倫理委員會行政中心

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Appendix 3. Participant Informed Consent Form

病歷號： 姓　名：

國 立 臺 灣 大 學 醫 學 院 附 設 醫 院

National Taiwan University Hospital

臨床試驗/研究受試者說明暨同意書

研究倫理委員會案號：202212018RIND

請詳細閱讀內容，待主持人或其授權人員向您說明後，再簽署同意書　　第 63 頁

計畫名稱 中文：中風後執行上肢近端與遠端功能性動作任務之大腦激活情形：近紅外光頻譜儀研究 英文：Brain Activation Patterns during Proximal and Distal Upper Limb Functional Tasks in Stroke: A Functional Near-Infrared Spectroscopy Study	
試驗機構：臺大醫院　復健部、 臺大醫學院 物理治療學系暨研究所	委託單位/藥廠：無 研究經費來源：自籌
試驗主持人：劉宴齊 協同主持人：林孟廷	職稱：　助理教授 職稱：主治醫師
24 小時緊急聯絡人：劉宴齊　　電話：0988525068 (若撥打時暫時未接通，請以簡訊或語音留言，研究人員將儘速與您聯繫)	
受試者姓名：　　病歷號碼：	

您被邀請參與此臨床試驗/研究，這份表格提供您本試驗/研究之相關資訊，試驗主持人或其授權人員將會為您說明試驗/研究內容並回答您的任何疑問，在您的問題尚未獲得滿意的答覆之前，請不要簽署此同意書。您不須立即決定是否參加本試驗/研究，請您經過慎重考慮後方予簽名。您須簽署同意書後才能參與本試驗/研究。如果您願意參與本試驗/研究，此文件將視為您的同意紀錄。即使在您同意後，您仍然可以隨時退出本試驗/研究而不需理由。

本試驗摘要(concise and focused presentation of the key information)

本試驗的研究目的為探討中風受試者在執行上肢近端與遠端的功能性活動之大腦皮質活化情形，並且進一步探討與健康受試者在執行上肢活動之腦部情形的差異。本實驗預計招收 30 位介於 20-85 歲的中風受試者以及 30 位健康成年受試者。您進入本研究後，將會被指導穿戴近紅外光頻譜儀執行上肢的近端與遠端功能性動作任務，在過程中會記錄您大腦皮質區的活化情形。我們想要邀請您參加上述研究試驗，您可以自由決定自己是否要參加這項試驗，並於試驗的任何一個階段，您都有權利隨時暫停或終止且不會造成任何不愉快或影響其日後醫事人員對您的醫療照顧。

以下內容為試驗之詳細程序及您應知事項，仍請您務必詳細閱讀。

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(一)試驗/研究目的：

探討在中風受試者與健康人執行上肢近端與遠端之功能性動作對於大腦的前運動皮質區(premotor cortex)、聯合運動皮質區(supplementary motor area)、主要動作皮質(primary motor cortex)及主要感覺皮質區(primary sensory cortex)之腦部活化情形。

(二)研究背景或藥品/醫療技術/醫療器材現況：

研究背景:

先前大部分研究探討腦部活化情形使用功能性核磁共振造影，然而因為功能性磁振造影之限制較多，例如因須維持姿勢固定不太適合執行多關節動作、不可有金屬植入物等因素，本實驗將使用限制較少且非侵入性之大腦功能性活化使用功能性進紅外光頻譜儀 (functional near-infrared spectroscopy, fNIRS)評估您執行功能性上肢動作時大腦皮質區之活化情形。近紅外光頻譜儀為使用光纖探頭發出可見光源 (波長為760及 850nm，頻率為7.81赫茲)，偵測並記錄大腦活化情形。分析儀的光纖線路會整齊收好，與儀器主機一起放置於小型網狀後背包(重量約0.5公斤)中，您須配戴帽套及後背包執行前述功能性上肢動作。近紅外光頻譜儀不會對您的身體有危害，也無不良反應，收取資料時，您也不會有任何感覺(Ernst et al, 2012)。**近紅外光頻譜儀並非醫療常規使用之儀器，目前僅供研究使用。**

近期多數研究著重於使用近紅外光頻譜儀監測健康人在執行不同活動時的腦部血流改變情形，探討大腦皮質與動作控制之間關係。在健康成年人中，肩部的屈曲和伸展運動會引起前額葉 (prefrontal cortex, PFC) 和前運動皮質 (premotor cortex, PMC) 的活化，而與手部抓握動作相比，肩部的運動會引起更多額外的大腦皮質區域的活化，包括感覺運動皮質 (sensorimotor cortex, SM1), 對側的輔助運動皮質 (supplementary motor area, SMA), 對側體感覺皮質 (primary somatosensory cortex, S1), 以及對側主要動作皮質 (primary motor cortex, M1) (Yeo et al., 2013; Jalalvandi et al., 2019; Yang et al., 2020)。本研究將提供臨床治療師對於中風受試者之大腦皮質活化及大腦可塑性之情形有更深入了解，並且可將此考量納入復健訓練設計。本研究不涉及藥品或醫療技術/器材。

(三)試驗/研究之納入與排除條件：

執行本研究計畫的醫師或相關研究人員將會與您討論有關參加本研究的必要條件。請您配合必須誠實告知我們您過去的健康情形，若您有不符合參加本研究的情況，將不能參加本研究計畫。

1. 納入條件(參加本試驗/研究的條件):

中風受試者的收案條件為：(1) 中風受試者的年齡介於20至85歲之間；(2) 第一次中風；(3) 生命徵象穩定;(4)因中風造成半側上肢動作損傷(布氏動作階段I至V, Brunnstrom Stage between stages Ⅰ to Ⅴ)。

健康成年人的收案條件為：1) 年齡20歲至85歲之間; 2)慣用手為右手。

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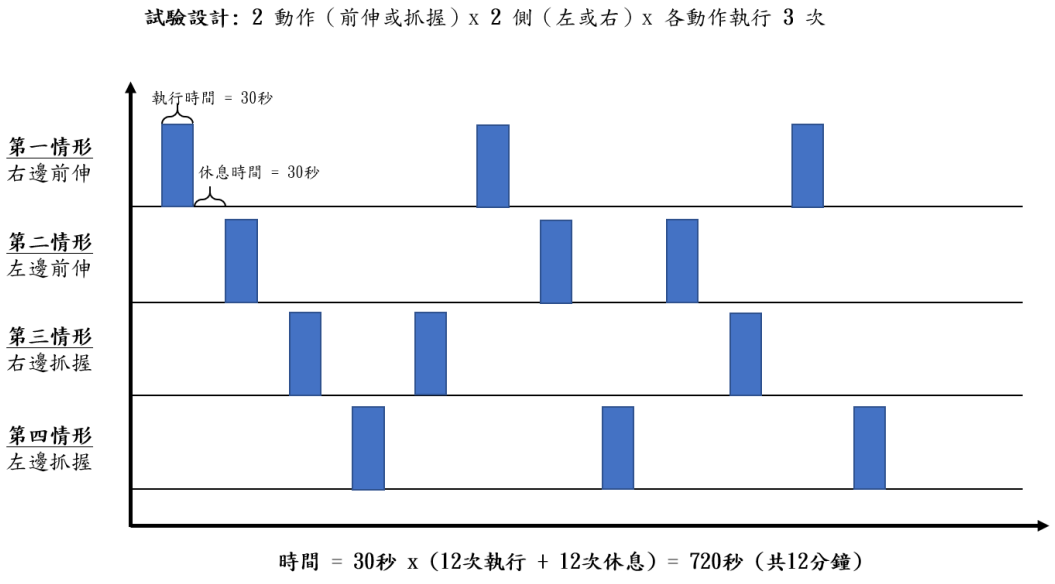
2.排除條件(若您有下列任一情況，您將無法參加本試驗/研究):

中風受試者與健康成年人之排案條件為：(1) 生命徵象不穩定；(2) 有癲癇病史；(3) 無法順從簡單指令且無法完成實驗任務 (follow orders)；(4)最近有使用抗憂鬱、抗焦慮、或其他精神類藥物可能影響腦部血流 (5) 腦中風影響雙側上肢肌力動作; (6) 有任何可能干擾參與研究的神經、心血管或肌肉骨骼系統疾病，將被排除此實驗。

(四)本試驗/研究方法及相關程序：

本試驗為橫斷性實驗。我們會將近紅外光頻譜儀之帽套穿戴至您的頭上並請您執行左右側上肢動作任務，包含往前伸手動作 (前伸任務) 以及手部抓握動作 (抓握任務)。前伸動作為手臂往前伸並用手指輕碰前方的水瓶，而抓握動作為手肘至於桌面，由手指抓住前方的瓶子再放開。本試驗動作分為右邊前伸前、左邊前伸、右邊抓握、以及左邊抓握四種任務。任務順序將會是隨機的。每個動作任務將進行 30 秒，各執行 3 次，執行動作過程中將有 0.5 Hz 的節拍器提供速度的參考，請您盡量跟著速度完成此動作。對於上肢有嚴重癱瘓或無力情形之受試者，能以動作心向模式進行此試驗。為確認受試者能執行動作心像，本研究將使用動覺與視覺想像能力量表 (Kinesthetic and Visual Imagery Questionnaire, KVIQ) 作為量測中風受試者動作想像能力的指標。 Malouin 等人 (2007, 2008) 所設計的 KVIQ-20 分為兩部分，動覺與視覺，前者要求受試者想像「自己正在動作時，身體運動的感覺」並評估其感受強烈程度，而後者則要求受試者想像「有一個人正在動作的畫面」並評估該畫面的清晰程度 (Malouin et al., 2007; 2008)。KVIQ-20 曾經使用在罹患中風而有肢體癱瘓或障礙的病人即可使用，而本研究將使用 KVIQ-20 內的上肢相關動作作為評量標準。在試驗過程中我們將使用近紅外光頻譜儀探討您大腦活化的情形。總試驗時間包含穿戴器材約為 60 分鐘。



圖一、 研究流程圖

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使用的近紅外光頻譜儀為使用內含光纖探頭之帽套，此帽套連接到近紅外光頻譜儀上，利用光纖探頭所發出的可見光源(波長為 760 及 850nm，頻率為 10.2 赫茲)，偵側並記錄大腦活化情形於筆記型電腦。近紅外光頻譜儀為一非侵入性的腦部活化情形探測儀器，先前研究指出，近紅外光頻譜儀不會對您的身體有危害，也無不良反應(Ernst et al, 2012)，且收取資料時，您也不會有任何感覺。

圖二、於實驗執行期間，您將穿戴內含光纖探頭之帽套，並維持坐姿姿勢完成上肢的前伸與抓握動作任務。

(五)可能發生之風險及其發生率與處理方法：

1. 與試驗藥物/醫療器材/醫療技術相關的風險（本試驗使用藥物/器材/醫療技術的副作用)：

   本研究皆使用非侵入性研究儀器收取腦部活化相關資料，您在接受評估時，應沒有任何感覺且並不會感受到任何不適，然而，如果您有任何不舒服或不愉快的感覺，您隨時可以終止所有的研究程序，並退出研究。

2. 與試驗/研究過程相關的風險：

   本試驗之相關風險極低，您穿戴近紅外光頻譜儀進行任務時將會有研究人員隨時在您的身旁，您如果有任何不適，歡迎隨時提出，我們將會即時通報試驗主持人且安排後續處理，並視情況停止試驗。

(六)其他替代療法及說明：

您將對大腦活化及運作與動作行為之表現有更深入的了解，如果發現您有動作行為相關問題，您可接受常規治療。

(七)試驗/研究預期效益：

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您參加本試驗並不保證對您一定有效果。透過本試驗我們預期中風受試者在執行上肢動作任務大腦活化及腦血流改變情形與健康成人受試者的大腦情形會有不同表現。

(八)試驗/研究進行中受試者之禁忌、限制與應配合之事項：

試驗進行過程中，不會影響您的日常生活活動，在您生活上並沒有特別的禁忌或限制活動。

(九)受試者個人資料之保密：

台大醫院將依法把任何可辨識您的身分之記錄與您的個人隱私資料視為機密來處理，不會公開。研究人員將以一個研究代碼代表您的身分，此代碼不會顯示您的姓名、國民身分證統一編號、住址等可識別資料。如果發表試驗/研究結果，您的身分仍將保密。您亦瞭解若簽署同意書即同意您的原始醫療紀錄可直接受監測者、稽核者、研究倫理委員會及主管機關(若試驗受美國食品藥物管理局管轄，則主管機關包含美國食品藥物管理局)檢閱，以確保臨床試驗/研究過程與數據符合相關法律及法規要求，上述人員並承諾絕不違反您的身分之機密性。除了上述機構依法有權檢視外，我們會小心維護您的隱私。

(十)試驗/研究之退出與中止：

您可自由決定是否參加本試驗/研究；試驗/研究過程中也可隨時撤銷或中止同意，退出試驗/研究，不需任何理由，且不會引起任何不愉快或影響其日後醫師對您的醫療照顧。為了您的安全，當發生以下情形時，您必須退出試驗/研究：

(1) 癲癇發生
(2) 嚴重身體不適
(3) 有新獲得的神經或肌肉骨骼系統損傷嚴重影響參與本研究

當試驗/研究執行中有重要的新資訊(指和您的權益相關或是影響您繼續參與意願)，會通知您並進一步說明，請您重新思考是否繼續參加，您可自由決定，不會引起任何不愉快或影響其日後醫師對您的醫療照顧。

計畫主持人亦可能於必要時中止整個試驗/研究之進行。

當您退出本試驗/研究或主持人判斷您不適合繼續參與本試驗/研究時，在退出前已得到的資料將被保留，不會移除。在退出後您可決定是否同意試驗主持人繼續收集您的資料。

1. 退出後讓試驗主持人繼續收集我的資料，例如經由我的病歷記載取得後續醫療過程、實驗室檢查結果。繼續收集資料期間，仍會維護您的隱私和個人資料的機密性。

□同意收集。

□不同意本試驗/研究繼續收集或檢視我的資料，但可經由公共資料庫查詢之紀錄不在此限。

(十一) 損害補償與保險：

試驗/研究一定有風險，為確保因為參與試驗/研究發生不良反應致造成您的損害時所可能獲得之保障，請您務必詳閱本項說明內容：

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1. 如依本研究所訂臨床試驗/研究計畫，因發生不良反應造成損害，由國立台灣大學負補償責任。但本受試者同意書上所記載之可預期不良反應，不予補償。
2. 如依本研究所訂臨床試驗/研究計畫，因而發生不良反應或損害，本醫院願意提供專業醫療照顧及醫療諮詢。您不必負擔治療不良反應或損害之必要醫療費用。
3. 除前二項補償及醫療照顧外，本研究不提供其他形式之補償。若您不願意接受這樣的風險，請勿參加試驗/研究。
4. 您不會因為簽署本同意書，而喪失在法律上的任何權利。
5. 本研究未投保人體試驗責任保險。

若您確因參與本試驗/研究因而發生不良反應造成之損害，前述補償包括合理的醫療費用，惟應符合以下條件：您的損害並非故意造成；您遵守試驗醫師之醫療建議。

(十二)受試者之個人資料之保存、使用與再利用

1. 資料之保存、使用與再利用

在試驗/研究期間，依據計畫類型與您所授權的內容，我們將會蒐集與您有關的基本資料、量表、步態表現、腦部活化情形等資料與資訊，並以一個編號來代替您的名字及相關個人資料。前述資料若為紙本型式，將會與本同意書分開存放於研究機構之上鎖櫃中；若為電子方式儲存或建檔以供統計與分析之用，將會存放於設有密碼與適當防毒軟體之專屬電腦內。這些研究資料與資訊將會保存10年。

上述資料與資訊若傳輸至國外分析與統計，您仍會獲得與本國法規相符之保障，計畫主持人與相關團隊將盡力確保您的個人資料獲得妥善保護。

試驗結束後，我們可能將試驗資料用於神經性相關疾病，例如: 帕金森氏症或中風等相關研究。

(十三)受試者權益：

1. 如果您在試驗/研究過程中對試驗/研究工作性質產生疑問，對身為患者之權利有意見或懷疑因參與研究而受害時，可與研究倫理委員會聯絡請求諮詢，電話號碼為：(02)2312-3456轉263155。
2. 試驗/研究過程中，與您的健康或是疾病有關，可能影響您繼續接受臨床試驗/研究意願的任何重大發現，都將即時提供給您。如果您決定退出，醫師會安排您繼續接受醫療照護。如果您決定繼續參加試驗/研究，可能需要簽署一份更新版的同意書。
3. 如果您現在或於試驗/研究期間有任何問題或狀況，請不必客氣，可與在台大醫學院物理治療學系的劉宴齊助理教授聯絡（24小時聯繫電話：0988525068）。
4. 本同意書一式2份，試驗主持人或其授權人員已將1份已簽名的同意書交給您，並已完整說明本研究之性質與目的。劉宴齊助理教授已回答您有關研究的問題。
5. 參加試驗研究計畫之補助：本研究未提供補助。
6. 若試驗結束後 2 年內，發現有非預期且直接影響您的安全疑慮，亦將通知您。

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(十四)本研究預期可能衍生之商業利益及其應用之約定：

本研究預期不會衍生專利權或其他商業利益。

(十五)簽名：

1. 試驗主持人、或協同主持人或其授權人員已詳細解釋有關本研究計畫中上述研究方法的性質與目的，及可能產生的危險與利益。

試驗主持人/協同主持人簽名：_____

日期：_____年____月____日

在取得同意過程中其他參與解說及討論之研究人員簽名：_____

日期：_____年____月____日

2. 經由說明後本人已詳細瞭解上述研究方法及可能產生的危險與利益，有關本試驗/研究計畫的疑問，亦獲得詳細解釋。本人同意接受並自願參與本研究，且將持有已簽名的同意書。

受試者簽名：　　日期：_____年____月____日

出生年月日：_____年____月____日　電話：

國民身分證統一編號：　　性別：

通訊地址：

<擬由法定代理人/有同意權之人簽署，原計畫必須業經研究倫理委會審查同意可納入此類須代理同意的受試者族群(未成年人或無法自主行使同意成人等)>

法定代理人/有同意權之人簽名：　　日期：_____年____月____日

與受試者關係（請圈選）：配偶、父、母、兒、女、其他：_____

出生年月日：_____年____月____日　電話：

國民身分證統一編號：

通訊地址：

*適用醫療法第 79 條第 1 項但書或人體研究法第 12 條第 1 項但書情形者，其同意權之行使分別依醫療法第 79 條第 2 項、人體試驗管理辦法第 5 條或人體研究法第 12 條第 3、4 項規定辦理：

*受試者為**無行為能力者**(未滿七歲之未成年人者或受監護宣告之人)，由法定代理人簽名；受監護宣告之人，由監護人擔任其法定代理人。

* 受試者為**限制行為能力者**(滿七歲以上之未成年人或因精神障礙、其他心智缺陷，致其為意思表示、受意思表示、辨識其意思表示效果之能力，顯有不足，而受法院之輔助宣告者)，應得其本人及法定代理人或輔助人之同意。

* 受試者雖非無行為能力或限制行為能力者，但因**意識混亂或有精神與智能障礙，而無法進行有效溝通和判斷時**，由有同意權之人簽名。有同意權人順序如下：

1. 屬新藥、新醫療器材、新醫療技術之人體試驗(人體試驗管理辦法第 5 條)：

(1)配偶。(2) 父母。(3) 同居之成年子女。(4)與受試者同居之祖父母。(5)與受試者同居之兄弟姊妹。(6) 最近一年有同居事實之其他親屬。

2. 屬人體研究（人體研究法第 12 條)：

(1)配偶。(2)成年子女。(3)父母。(4)兄弟姊妹。(5)祖父母。

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依前項關係人所為之書面同意，其書面同意，得以一人行之；關係人意思表示不一致時，依前項各款先後定其順序。前項同一順序之人，以親等近者為先，親等同者，以同居親屬為先，無同居親屬者，以年長者為先。

見證人簽名：_____日期：_____年____月____日

＊ 受試者、法定代理人或有同意權之人皆無法閱讀時，應由見證人在場參與所有有關受試者同意之討論。並確定受試者、法定代理人或有同意權之人之同意完全出於其自由意願後，應於受試者同意書簽名並載明日期。試驗/研究相關人員不得為見證人。

* 若意識清楚，但無法親自簽具者，得以按指印代替簽名，惟應有見證人。

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Appendix 4: Fugl-Meyer Assessment for Upper Extremity Form

FMA-UE PROTOCOL — Rehabilitation Medicine, University of Gothenburg

FUGL-MEYER ASSESSMENT
UPPER EXTREMITY (FMA-UE)
Assessment of sensorimotor function

ID:
Date:
Examiner:

Fugl-Meyer AR, Jaasko L, Leyman I, Olsson S, Steglind S: The post-stroke hemiplegic patient. A method for evaluation of physical performance. Scand J Rehabil Med 1975, 7:13-31.

A. UPPER EXTREMITY, sitting position					
I. Reflex activity			**none**	**can be elicited**	
Flexors: biceps and finger flexors (at least one) **Extensors**: triceps			0 0	2 2	
Subtotal I (max 4)					
II. Volitional movement within synergies, without gravitational help			**none**	**partial**	**full**
Flexor synergy: Hand from contralateral knee to ipsilateral ear. From extensor synergy (shoulder adduction/ internal rotation, elbow extension, forearm pronation) to flexor synergy (shoulder abduction/ external rotation, elbow flexion, forearm supination). **Extensor synergy:** Hand from ipsilateral ear to the contralateral knee	Shoulder Elbow Forearm	retraction elevation abduction (90°) external rotation flexion supination	0 0 0 0 0 0	1 1 1 1 1 1	2 2 2 2 2 2
	Shoulder Elbow Forearm	adduction/internal rotation extension pronation	0 0 0	1 1 1	2 2 2
Subtotal II (max 18)					
III. Volitional movement mixing synergies, without compensation			**none**	**partial**	**full**
Hand to lumbar spine hand on lap	cannot perform or hand in front of ant-sup iliac spine hand behind ant-sup iliac spine (without compensation) hand to lumbar spine (without compensation)		0	1	2
Shoulder flexion 0°- 90° elbow at 0° pronation-supination 0°	immediate abduction or elbow flexion abduction or elbow flexion during movement flexion 90°, no shoulder abduction or elbow flexion		0	1	2
Pronation-supination elbow at 90° shoulder at 0°	no pronation/supination, starting position impossible limited pronation/supination, maintains starting position full pronation/supination, maintains starting position		0	1	2
Subtotal III (max 6)					
IV. Volitional movement with little or no synergy			**none**	**partial**	**full**
Shoulder abduction 0 - 90° elbow at 0° forearm neutral	immediate supination or elbow flexion supination or elbow flexion during movement abduction 90°, maintains extension and pronation		0	1	2
Shoulder flexion 90° - 180° elbow at 0° pronation-supination 0°	immediate abduction or elbow flexion abduction or elbow flexion during movement flexion 180°, no shoulder abduction or elbow flexion		0	1	2
Pronation/supination elbow at 0° shoulder at 30°- 90° flexion	no pronation/supination, starting position impossible limited pronation/supination, maintains start position full pronation/supination, maintains starting position		0	1	2
Subtotal IV (max 6)					
V. Normal reflex activity assessed only if full score of 6 points is achieved in part IV; compare with the unaffected side			**hyper**	**lively**	**normal**
Biceps, triceps, finger flexors	2 of 3 reflexes markedly hyperactive 1 reflex markedly hyperactive or at least 2 reflexes lively maximum of 1 reflex lively, none hyperactive		0	1	2
Subtotal V (max 2)					
Total A (max 36)					

Approved by Fugl-Meyer AR 2010 — 1 — Updated 2019-03-03

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B. WRIST support may be provided at the elbow to take or hold the starting position, no support at wrist, check the passive range of motion prior testing		none	partial	full
Stability at 15° dorsiflexion elbow at 90°, forearm pronated shoulder at 0°	less than 15° active dorsiflexion dorsiflexion 15°, no resistance tolerated maintains dorsiflexion against resistance	0	1	2
Repeated dorsifexion / volar flexion elbow at 90°, forearm pronated shoulder at 0°, slight finger flexion	cannot perform volitionally limited active range of motion full active range of motion, smoothly	0	1	2
Stability at 15° dorsiflexion elbow at 0°, forearm pronated slight shoulder flexion/abduction	less than 15° active dorsiflexion dorsiflexion 15°, no resistance tolerated maintains dorsiflexion against resistance	0	1	2
Repeated dorsifexion / volar flexion elbow at 0°, forearm pronated slight shoulder flexion/abduction	cannot perform volitionally limited active range of motion full active range of motion, smoothly	0	1	2
Circumduction elbow at 90°, forearm pronated shoulder at 0°	cannot perform volitionally jerky movement or incomplete complete and smooth circumduction	0	1	2
	Total B (max 10)			

C. HAND support may be provided at the elbow to keep 90° flexion, no support at the wrist, compare with unaffected hand, the objects are interposed, active grasp		none	partial	full
Mass flexion from full active or passive extension		0	1	2
Mass extension from full active or passive flexion		0	1	2
GRASP				
a. Hook grasp flexion in PIP and DIP (digits II-V), extension in MCP II-V	cannot be performed can hold position but weak maintains position against resistance	0	1	2
b. Thumb adduction 1-st CMC, MCP, IP at 0°, scrap of paper between thumb and 2-nd MCP joint	cannot be performed can hold paper but not against tug can hold paper against a tug	0	1	2
c. Pincer grasp, opposition pulpa of the thumb against the pulpa of 2-nd finger, pencil, tug upward	cannot be performed can hold pencil but not against tug can hold pencil against a tug	0	1	2
d. Cylinder grasp cylinder shaped object (small can) tug upward, opposition of thumb and fingers	cannot be performed can hold cylinder but not against tug can hold cylinder against a tug	0	1	2
e. Spherical grasp fingers in abduction/flexion, thumb opposed, tennis ball, tug away	cannot be performed can hold ball but not against tug can hold ball against a tug	0	1	2
	Total C (max 14)			

D. COORDINATION/SPEED, sitting, after one trial with both arms, eyes closed, tip of the index finger from knee to nose, 5 times as fast as possible		marked	slight	none
Tremor		0	1	2
Dysmetria	pronounced or unsystematic slight and systematic no dysmetria	0	1	2
		≥ 6s	**2 - 5s**	**< 2s**
Time start and end with the hand on the knee	6 or more seconds slower than unaffected side 2-5 seconds slower than unaffected side less than 2 seconds difference	0	1	2
	Total D (max 6)			

TOTAL A-D (max 66)	

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H. SENSATION, upper extremity eyes closed, compared with the unaffected side		**anesthesia**	**hypoesthesia or dysesthesia**	**normal**
Light touch	upper arm, forearm palmary surface of the hand	0 0	1 1	2 2
		less than 3/4 correct or absence	**3/4 correct or considerable difference**	**correct 100%, little or no difference**
Position small alterations in the position	shoulder elbow wrist thumb (IP-joint)	0 0 0 0	1 1 1 1	2 2 2 2
			Total H (max12)	

I. PASSIVE JOINT MOTION, upper extremity, sitting position, compare with the unaffected side				**J. JOINT PAIN** during passive motion, upper extremity		
	only few degrees (less than 10° in shoulder)	decreased	normal	pronounced pain during movement or very marked pain at the end of the movement	some pain	no pain
Shoulder						
Flexion (0° - 180°)	0	1	2	0	1	2
Abduction (0°-90°)	0	1	2	0	1	2
External rotation	0	1	2	0	1	2
Internal rotation	0	1	2	0	1	2
Elbow						
Flexion	0	1	2	0	1	2
Extension	0	1	2	0	1	2
Forearm						
Pronation	0	1	2	0	1	2
Supination	0	1	2	0	1	2
Wrist						
Flexion	0	1	2	0	1	2
Extension	0	1	2	0	1	2
Fingers						
Flexion	0	1	2	0	1	2
Extension	0	1	2	0	1	2
Total (max 24)				**Total** (max 24)		

A. UPPER EXTREMITY	/36
B. WRIST	/10
C. HAND	/14
D. COORDINATION / SPEED	/ 6
TOTAL A-D (motor function)	/66

H. SENSATION	/12
I. PASSIVE JOINT MOTION	/24
J. JOINT PAIN	/24

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Appendix 5: Recruitment Poster

「本招募廣告經臺大醫院研究倫理委員會審查核准，轉載(貼)不得修改內容」。

受試者招募

計劃名稱: 中風後執行上肢近端與遠端功能性動作任務之大腦激活情形：近紅外光分析儀研究

研究目的：

本研究目的為探討在中風受試者以及健康人在執行上肢近端與遠端之功能性活動對於大腦前運動皮質區（premotor cortex)、聯合運動皮質區（supplementary motor area)、主要動作皮質（primary motor cortex)及主要感覺皮質區（primary sensory cortex)之活化情形。

受試者應配合事項：

至國立臺灣大學物理治療學系進行一次性評估，評估內容包含使用穿戴式近紅外光頻譜儀探討執行遠段及近端上肢功能性動作任務時之大腦皮質活化情形。本試驗動作分為右側前伸、左側前伸、右側抓握、以及左側抓握四種任務。評估需時間約 1.5 小時。

招募對象：

- 中風受試者：
  1）中風受試者的年齡介於 20 至 85 歲之間
  2）第一次中風
  3）生命徵象穩定
  4）因中風造成半側上肢動作損傷（布氏動作階段Ⅰ至Ⅴ)

- 健康成年人:
  1）年齡 20 歲至 85 歲之間
  2）慣用手為右手

若您有興趣參與或想進一步了解研究相關事項，歡迎您以電話或 E-mail 與我們聯絡：

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研究機關：國立臺灣大學　物理治療學系暨研究所
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