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# Immediate Plasticity of Parietal-Frontocentral Functional Connections in Music-Reality based Post-Stroke Rehabilitation

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***Abstract*— Post-stroke neuronal plasticity was always viewed as a localized gain-of-functionality. The reorganization of neurons neighboring the lesioned brain tissues is able to compensate for the function of damaged neurons. However, it was also proposed that distant interconnected brain regions could be affected by stroke. Changes in functional connections across the brain were found associated with motor deficiency and recovery. Parietal-frontocentral functional connectivity was found related to the performance of motor imagery. This study aims to evaluate the EEG-based parietal-frontocentral functional connectivity in post-stroke patients, and to investigate the immediate effect of rehabilitation training toward these connections. Pairwise functional connectivity was extracted from healthy subjects and post-stroke patients during standing and walking. Significant reductions in P3-FC4 and P3-C4 connectivity strengths were found in post-stroke patients during both standing and walking conditions. Immediate improvement in the reduced connections was observed with the intervention of a previously proposed, motivation-based rehabilitation system, which was known as the mixed-reality music rehabilitation (MR$^2$) system. This indicates the relationship between left parietal functional connectivity and stroke-related motor performance. These findings suggest the feasibility to evaluate the immediate plasticity of functional connectivity during post-stroke rehabilitation.**

## I. Introduction

Rehabilitation after stroke aims to promote neuronal plasticity in the affected motor cortex [1]. Conventionally, post-stroke plasticity was viewed as a localized functionality. It was long shown that neurons surrounding affected brain regions (perilesional areas) could reorganize to assist the function of damaged neurons [2]. Functional magnetic resonance imaging (fMRI) studies showed the reorganization of perilesional brain areas following motor [3] recovery in post-stroke patients. Hence, the activation of perilesional areas is monitored to assess the efficiency of post-stroke rehabilitation training [4]. Recent study based on electroencephalography (EEG) signals has shown the activation of perilesional motor cortex areas in companion with the improvement of flexion angle of the hemiplegic knee [4]. The study also found significant perilesional activation in patients who underwent rehabilitation training with the proposed mixed-reality music rehabilitation (MR$^2$) system. However, the brain is made from dense interconnected neuronal network. It was expected that stroke could indirectly affect brain tissues at distant sites, which these sites could be the upstream or downstream connected nodes of the damaged brain area [5].

Functional connectivity (FC) is an emerging technique to study the connections between various brain regions. FC is the statistical estimation of functional dependency from brain signals recorded using neuroimaging modalities such as fMRI or EEG [6], [7]. Functional connectivity has revealed the deterioration of interhemispheric FC in post-stroke patients [8], [9]. FC between left and right motor cortices was found associated with motor deficits in post-stroke patients [8]. Spatial neglect, one of the main symptoms of stroke, was found related to the reduction in interhemispheric parietal connections [8] and frontoparietal connections [9]. It was proposed that disruption of FC in post-stroke patients is manifested in both resting state and task execution state [10]. These studies inform that stroke could affect non-localized, distant and interconnected brain regions. These affected connections could be potentially monitored to evaluate the recovery process of motor functions. Recent research found changes in sensorimotor related FC which is associated with the recovery of motor function following rehabilitation training [11], [12]. These findings hint at the possibility of neurorehabilitation based on functional connectivity, which we could monitor the recovery of brain network throughout the rehabilitation process.

Previous study found that alpha band functional connections between left parietal cortex and frontocentral cortex are significantly correlated to the performance during imagination of motor activity [13]. Motor imagery shares similar neuromechanisms with motor execution [14], [15], we hypothesize that similar connections could potentially associate with post-stroke motor deficit. The existing literature mainly investi-

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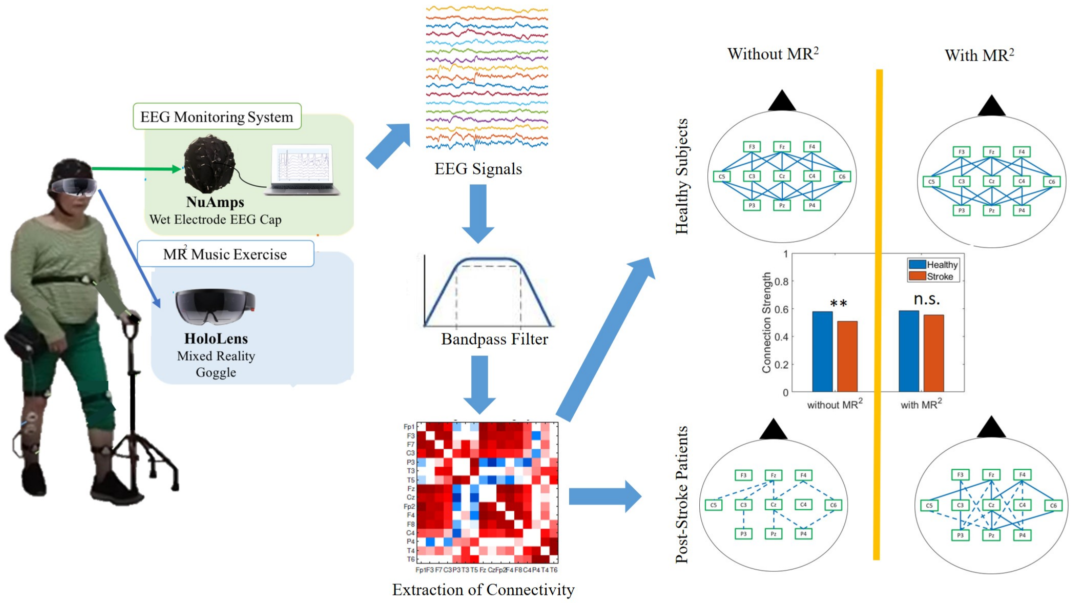


Fig. 1: The MR$^2$ system includes an EEG monitoring system and a mixed reality goggle to promote motivation in rehabilitation therapy. The differences in connectivity strength between healthy subjects and post-stroke patients was compared.

gated plasticity in fMRI-based functional connection from longitudinal studies spanning from days to years. Our previous study showed that mixed-reality music rehabilitation (MR$^2$) system could enhance post-stroke lower limb rehabilitation training, by increasing patients' range of motion and localized brain activity [4]. The objective of this study is to evaluate the EEG-based parietal-frontocentral functional connectivity in the post-stroke patients, and to investigate the immediate effect of MR$^2$ rehabilitation training toward these connections.

## II. Methodology

The EEG-based parietal-frontocentral functional connectivity in the post-stroke patients was compared with healthy individual, while undergoing rehabilitation training with or without MR$^2$ system. The immediate effect of MR$^2$ rehabilitation training toward these connections was evaluated. The experimental paradigm is as shown in figure 1.

### A. Subjects

The EEG dataset used in this study was as published in [4]. The EEG data were recorded from eight healthy subjects and nine post-stroke patients (five male and four female). All patients were suffering from walking difficulty due to lower limb stiffness, ranging from Brunnstrom Stage III to Brunnstrom Stage V. The mean age of the patients was 55. The healthy subjects include four female and four male volunteers with no history of neurological and psychological disorders. This study was approved by the Institutional Review Board of Kaohsiung Medical University Chung-Ho Memorial Hospital with case number KMUHIRB-E(I)-20170020.

### B. Experimental Design

The subjects conducted 30 seconds of standing phase (Stand 1), followed by 60 seconds of walking phase (Walk) and another 30 seconds of standing rest phase (Stand 2). Each subject underwent two paradigms with counterbalance to prevent adaptation – with or without mixed-reality music rehabilitation system during the walking phase. The MR$^2$ system aimed to improve motivation by providing a virtual feedback based on the gait of patients during rehabilitation training (the system architecture was detailed in [4]). The EEG data were acquired through NuAmps EEG system (Compumedics Neuroscan, Inc.) with 30 wet electrodes, at 1 kHz sampling rate and impedance under 20 k$\Omega$. The averaged A1 and A2 electrodes acted as the reference electrode, while Fpz acted as the ground electrode. The recording electrodes include FP1, FP2, F7, F3, Fz, F4, F8, FT7, FC3, FCz, FC4, FT8, T3, C3, Cz, C4, T4, TF7, CP3, CPz, CP4, TF8, T5, P3, Pz, P4, T6, O1, Oz and O2. A linear phase, minimum-order, finite impulse response (FIR) bandpass filter was applied to filter EEG signal within the frequency range of 8-13 Hz, which is the alpha band EEG.

### C. Data Analysis

Functional connectivity features were extracted from EEG epochs when subjects were standing and walking. The bivariate functional connectivity was extracted using Pearson's correlation from signals in all pairs of EEG electrodes. The computed correlation coefficients $r_{xy} \in [-1, 1]$ represent the weighted but undirected connectivity between brain regions. Based on this estimation, the connection strength is proportionate to the synchronization of voltage fluctuation between two recorded EEG signals, $x$ and $y$. Pearson's correlation is the division of the covariance of signals $x$ and $y$ by the product of their individuals standard deviations, as shown in Eq. 1.

$$r_{xy} = \frac{\sum_{i=1}^{T}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{T}(x_i - \bar{x})^2}\sqrt{\sum_{i=1}^{T}(y_i - \bar{y})^2}} \qquad (1)$$

where $\bar{x}$ and $\bar{y}$ are the mean amplitude of signal $x$ and $y$, while $T$ is the length of time series. Positive correlation $r_{xy} > 0$ indicates that the amplitude of both signals are synchronized; while the amplitude of $x$ and $y$ are inverted in negative

TABLE I: Difference in connectivity strength between healthy subjects and post-stroke patients (mean±standard deviation).

| | Healthy Subjects | | | Post-Stroke Patients | | |
|---|---|---|---|---|---|---|
| Connection | Stand 1 | Walk | Stand 2 | Stand 1 | Walk | Stand 2 |
| P3-FC3 | 0.72±0.12 | 0.75±0.09** | 0.72±0.09*** | 0.74±0.12 | 0.77±0.09** | 0.77±0.08*** |
| P3-Fz | 0.61±0.15 | 0.66±0.11 | 0.60±0.14 | 0.60±0.13 | 0.67±0.10 | 0.63±0.12 |
| **P3-FC4** | **0.60**±0.16*** | **0.65**±0.12*** | **0.58**±0.14* | **0.50**±0.14*** | **0.55**±0.16*** | **0.54**±0.14* |
| P3-FCz | 0.67±0.14 | 0.71±0.10** | 0.66±0.13* | 0.67±0.13 | 0.74±0.08** | 0.70±0.10* |
| P3-Cz | 0.73±0.12 | 0.77±0.08 | 0.72±0.10* | 0.72±0.11 | 0.78±0.07 | 0.76±0.08* |
| **P3-C4** | **0.63**±0.14*** | **0.67**±0.11** | **0.61**±0.13*** | **0.51**±0.16*** | **0.59**±0.14** | **0.54**±0.15*** |

Mann–Whitney U test: $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

correlation $r_{xy} < 0$. The extracted real numbers represent the connectivity strength between two spatially distinct brain regions.

The difference in parietal connectivity strength between healthy subjects and post-stroke patients during standing and walking phases was investigated. Since it was found that $MR^2$ could improve motor related brain activity in term of localized EEG band power [4], we also investigated the difference in parietal-frontocentral connections of subjects with or without the assist of $MR^2$ system in this study. The inter-subject comparisons were conducted using Mann–Whitney U test. Instead of testing a global hypothesis, we were comparing each hypothesis independently to explore the possible dynamicity of brain connections between two groups under different conditions. This comparison paradigm was suggested to be analyzed without multiplicity adjustment [16]. The comparisons were to be performed with parietal-frontocentral connection, which was shown correlated to the performance of motor imagery in [13]. However since the EEG montages used in both studies were different, nearby connections including P3-FC3, P3-Fz, P3-FC4, P3-FCz, P3-Cz and P3-C4 were selected in this study.

## III. Results and Discussion

### A. Parietal Connectivity Strength

The results in table I summarize the connectivity strength between healthy subjects and post-stroke patients. Significant variations of parietal-frontocentral connectivity strength were observed between healthy subjects and post-stroke patients. Studies had shown that high-level motor behaviors including motor planning, motor intention, gestures imitation, sensory-motor integration, spatial awareness of body parts, and tools usage were modulated by the parietal cortex [17], [18]. Our results further suggest the relationship between left parietal functional connectivity and stroke-related motor deterioration.

The patients showed significantly stronger P3-FC3 and P3-FCz connections compared to the healthy subjects, in both walk and stand 2 phases. For parietal-to-midline connections, P3-Cz exhibited higher connectivity strength in post-stroke patients during the stand 2 phase; however there was no significant difference in P3-Fz connection between the two subject groups. Interestingly, we found the interhemispheric connections between the left parietal cortex (P3) and right frontocentral cortex (FC4 & C4) of post-stroke patients were significantly weaker in both stand 1, walk and stand 2 phases. This inherent disruption of functional connectivity in both standing and walking phases was consistently suggested by [10]. Besides that, interhemispheric motor [8], parietal [19] and frontoparietal [9] connections were found reduced in patients suffering from stroke. Dysconnectivity of the parietal lobe was also found in post-stroke patients in diffusion tensor imaging [20] and fMRI-based study [8].

### B. Intervention of $MR^2$ Rehabilitation System

The intervention of $MR^2$ system was further evaluated with P3-FC4 and P3-C4 connections, as these inherent connections could allow monitoring of the recovery process. Instead of comparing the connectivity between patients with or without the intervention of $MR^2$ system, the comparisons were performed between healthy subjects and post-stroke patients in both conditions. This was to eliminate the effect of $MR^2$-induced, motor-unrelated changes in the brain activity. As shown in figure 2, without the aid of $MR^2$ system, healthy subjects demonstrated significantly stronger P3-FC4 and P3-C4 connections than post-stroke patients in all three phases (stand 1, walk, stand 2). Percentage difference (PD) was computed to compare the connectivity strength between healthy subjects and post-stroke patients, where PD was calculated as $\frac{|FC_{stroke} - FC_{healthy}|}{FC_{healthy}} \times 100$. With the intervention of $MR^2$ system, the differences in connectivity strength between the two subject groups were reduced. In the walking phase, the PD in connectivity strength reduced from 13.74% to 11.11% and 18.47% to 10.72%, respectively for P3-C4 and P3-FC4 connections. The decrease in connectivity strength between two subject groups persisted after the walking phase, where improvements of 3.72% (P3-C4) and 6.92% (P3-FC4) were observed. Besides that, although significant differences persisted, the p-values of P3-FC4 and P3-C4 connections had increased while the patients trained with $MR^2$ system. The walking P3-C4 connection and post-walking P3-FC4 connection of post-stroke patients show no significant difference with healthy subjects. This suggests that the parietal-frontocentral functional connectivity of post-stroke patients were approaching the connectivity strength of healthy subjects. The results were consistent with previous study using the same dataset [4]. *Chang et. al.* showed the improvement of motion range and localized EEG power activity in patients walking with $MR^2$ system. This study show the possibility of evaluating the immediate plasticity of functional connectivity following post-stroke training.

## IV. Conclusion

This study shows the change in parietal-frontocentral connectivity in post-stroke patients. The results suggest the inherent reduction of connectivity strength between the left parietal area and right frontocentral areas in both standing and walking conditions. Our results proposed that

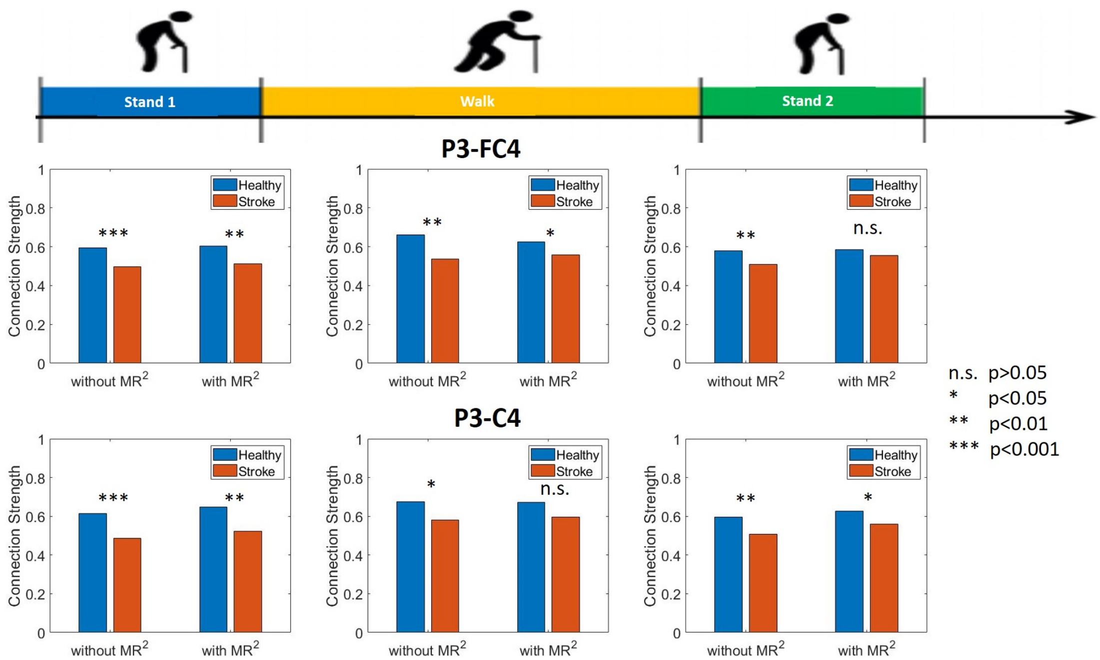


Fig. 2: Significant improvement of P3-FC4 and P3-C4 connections was observed when post-stroke patients were trained with $MR^2$ system. The difference in connectivity strength between patients and healthy subjects was less significant during and after $MR^2$ training paradigm.

patients who underwent rehabilitation with the intervention of motivation-based mixed-reality music rehabilitation ($MR^2$) system immediately exhibit functional connectivity closer to the healthy individuals. This could potentially allow the monitoring of EEG-based functional connectivity to realize the real-time evaluation of the recovery of central nervous system activity. Post-stroke recovery was affected by variables such as the initial severity, lesion volume, lesion location, age, gender and Fugl-Meyer Motor Score [21], [22]. Future research could study the plasticity of parietal-frontocentral connections with respect to these variables, in order to evaluate the functional connectivity in different patient groups.

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