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A Virtual Reality (VR) based Comprehensive Freezing of Gait (FOG) Neuro-electrophysiologic Evaluation System for People with Parkinson's Disease (PD)

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Abstract— **Although Freezing of gait (FOG) is one of the most frustrating phenomena for people with Parkinson's Disease (PD), especially in their advanced stage, it is one of the least explained syndromes. The current studies only showed beta oscillations existed in frontal cortex-basal ganglia networks. Further studies need to be carried out. However, simultaneously recording neuro-electrophysiologic signals during walking is always a challenge, especially for Electroencephalogram (EEG) and Local Field Potential (LFP). This paper demonstrated a Virtual Reality (VR) based system which can trigger FOG and record biological signals at the same time. Moreover, the utilisation of VR will significantly decrease space requirements. It will provide a safer and more convenient evaluation environment for future participants. One participant with PD helped to validate the feasibility of the system. The result showed that both EEG and LFP could be recorded at the same time with trigger markers. This system design can be used to trigger freezing episodes in the controlled environment, differentiate subtypes of gait difficulties, and identify neural signatures associated with freezing episodes.**

Clinical relevance — **This paper proposed a VR-based comprehensive FOG neuro-electrophysiologic evaluation system for people with PD. It had the advantages of minimum space requirement and wireless LFP data collection without externalised leads. This paper was to indicate a larger study which would formally recruit larger populations with PD and FOG. Future studies would explore FOG-related brain network coherence.**

I. INTRODUCTION

Parkinson's Disease (PD) is a neurodegenerative disease associated with a motor impairment such as rigidity, bradykinesia, tremor and freezing of gait[1]. One of the most prevalent phenomena among people with PD is Freezing of Gait (FOG)[2]. A recent review investigated 35 studies and revealed that the prevalence of FOG in PD was 39.9%[2]. FOG was often observed in people with PD during turning, passing narrow spaces, passing doors, and stressful situations[3]. Whilst FOG is one of the most disturbing syndromes, its neuro-electrophysiologic mechanism of it is one of the least understood[4]. The beta rhythm was found to be related to rigidity and bradykinesia in PD[5]. Toledo et. al. further recognised the existence of high-beta band oscillations related coherence in the frontal cortex–basal ganglia networks[6]. Notwithstanding, this study also raised challenges in confirming the causal relationship between high-beta and FOG. It also additionally required episodic events recording for further FOG and beta band correlation analysis. Therefore, a comprehensive FOG Neuro-electrophysiologic evaluation system was required.

Rather than other phenomena, FOG is a heterogeneous symptom with fairly differentiated manifestations in different individuals[7]. The dopaminergic sensitivity of FOG can be divergent[3], [8]. Some may be dopaminergic sensitive whilst others could be dopaminergic resistant[4]. The L-dopa provoked FOG was also observed in previous studies[3]. The episodic and unpredictable nature of FOG has made it ambitious to investigate this special phenomenon.

Despite being a motor impairment, FOG was also correlated to the cognitive status[9], [10]. Peterson et. al. also provoked that the FOG might be ascribed to a higher level brain function such as coordinating posture rather than a lower level, such as sensorimotor impairments[11]. This may imply that the FOG could be triggered by visualising the tasks such as turning, passing narrow spaces, and passing doors. In 2013, Gilat et. al. established a study using Virtual Reality (VR) to trigger FOG[12]. They observed the participants' FOG whilst the participants were stepping in the VR environment. In 2015, Waechter et. al. proposed a VR method to induce FOG and measured Electroencephalogram (EEG) at the same time[13]. The purpose was to find correlations between EEG and FOG. Nevertheless, the Local Field Potential (LFP) which was essential for deep brain nuclei analysis[14] was not included as part of the measurement.

In regards to LFP, it was most commonly recorded through externalised leads in Deep Brain Stimulation (DBS) treatment[15]. However, the externalised leads were usually cut off at the end of surgery[16]. Although there was no evidence to support the increased infection risk of externalised leads, the concerns were still raised by the public[17]. Accordingly, the population was significantly limited in studies involving LFP recording[18]. Thanks to the development of wireless technology, wireless LFP recording was developed[19]. Albeit the elimination of externalised leads requirement, the distance of high-quality LFP recording

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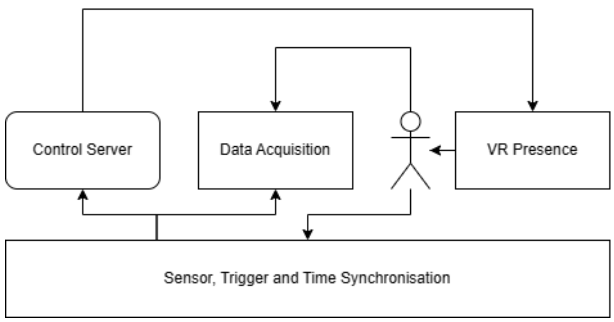

Fig. 1. The overall diagram demonstrates the data stream between each component. The control server was responsible for VR presence graphic calculation. The VR presence was a pair of VR glasses which provided an immersive environment for the participant. The biological signals such as EEG, EMG, ECG, LFP and video recordings were obtained by the data acquisition system. The trigger system was detecting the foot pressure from the participant and sent signals to all distributed sub-systems for trigger and time synchronisation purposes.

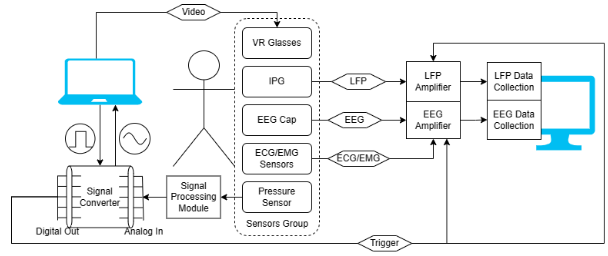

Fig. 2. This figure illustrated details of the system design. VR - Virtual Reality, IPG - Implantable Pulse Generator, EEG - Electroencephalograph, ECG - Electrocardiogram, EMG - Electromyography, LFP - Local Field Potential. The status of the participant was monitored by a group of sensors. The sensors' data was collected by two computers. One of the computers was also responsible for VR video generation.

is still restricted[20]. It was recommended that the electromagnetic shielding enclosure is better to be used whilst recording electrical signals, such as EEG and LFP[21]. Howbeit the probability of infrastructure that could include FOG stimulation, the practical limitations, such as budget and space limitations, would make most investigators and sponsors hesitate.

This paper proposed a VR-based comprehensive neuro-electrophysiologic evaluation system for people with PD. In the current stage, this system was narrowed down to a specific task which was used for FOG studying. However, the concept of this system was not limited to FOG. It consisted of a VR presence system, a neuro-electrophysiologic signal acquisition system, and a trigger system. It had the capability of presenting VR tasks and recording various biological signals at the same time. A simple walking task paradigm was designed for triggering FOG. This study included one single case of a person with PD who implanted DBS. The results indicated that the proposed system could trigger FOG. Furthermore, it provided extra benefits and convenience for offline analysis.

II. METHOD

A. DEVICE SETUP

The overall structure of this system contains three main components: a VR presence system, a neuro-electrophysiologic signal acquisition system, and a trigger system. There were two computational devices used in this system. One was called the control server which provided VR presence graphic calculation and signals to the trigger system (see Fig.1). The other one was a part of the data acquisition system. It was for various biological signals collection including EEG, Electromyography (EMG), Electrocardiogram (ECG), LFP, and video recording for the participant.

The centre server (the left computer in Fig.2) provided videos to the VR glasses. The participant was equipped with a group of sensors: LFP sensors (IPG), EEG sensors (EEG Cap), ECG/EMG sensors, and pressure sensors. These sensors would monitor the status of the participant. Once the pressure sensor detected pressure, it would send signals to the signal converter. This signal converter was responsible for conveying analogue signals to the central server and generating digital signals based on the instructions from the central server. The threshold of the pressure sensor was set to three kilograms. The hypothesis was when the participant stood on one single pressure sensor, at least three kilograms should be detected, and vice versa.

As soon as the step pressure signal was received, the central server would send three commands simultaneously. The first command was to move the VR view one step forward. The content of the second and the third command was the same. It was a trigger to indicate the EEG amplifier and LFP amplifier that the step was made. This message could be sent concurrently because of a cable splitter.

Fig.3 demonstrated the physical connections of the system. Fig.3 (A) was the signal converter connected to pressure sensors, trigger cables, and the central server. On the analogue input side (Fig.2), the signal converter was connected by sensors through signal processing modules (Fig.2). On the digital output side (Fig.2), the converter was connected to D-subminiature 25 (DB25) cable. Port 0 was connected to strobe 0 in DB25. Port 1-7 were connected to D1-D7 in DB25. Finally, the signal converter was connected to the central server. The pressure sensors were made in a foot shape (see Fig.3 (B)). Fig.3 (C) exhibited the overall connections. The mobile workstation was equipped with various amplifiers for biological signal collection. A laptop equipped with Graphic Processing Unit (GPU) was used as a central server.

B. TASK PARADIGM DESIGN

The purpose of this VR task was to induce FOG. Therefore, three situations were designed in the VR. An enclosed space with three separate rooms was initially established in VR. These three rooms were connected by three structures: an open door, a corner, and a narrow corridor (see Fig.4). The participant was instructed to step on one spot. As described above, once the step was detected, the VR would move forward to make the illusion that the participant was walking on their own. To simulate a more realistic walking, the VR

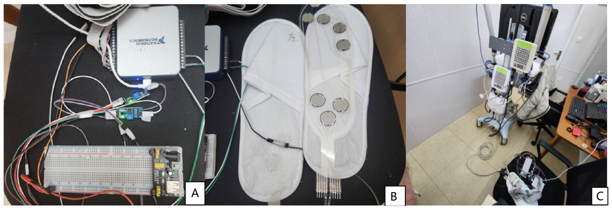

Fig. 3. A. On the analogue input side, the signal converter was connected by two signal processing modules. on the digital output side, eight ports were connected to a D-subminiature 25 (DB25) cable. B. The other side of the signal processing module was a foot shape sensor group. C. A laptop (right) was used as a central server. A mobile workstation was equipped with several amplifiers for biological signal collection.

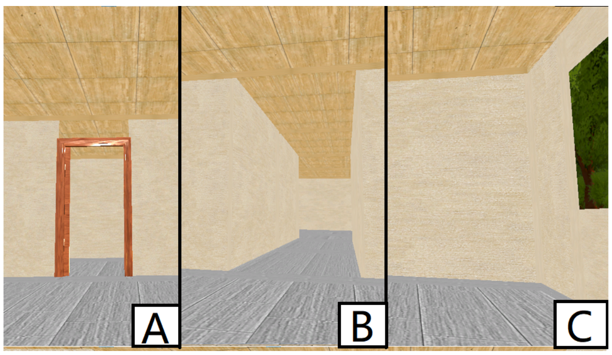

Fig. 4. Three situations were simulated in Virtual Reality (VR) tasks: (A) passing doors; (B) passing narrow space; (C) turning around. The VR room was also decorated by windows with a view of trees and grasses.

view was set to move up five centimetres and then down five centimetres. For a more comfortable experience, windows were added to each room. A forest with trees and grasses under sunshine was made as the background in this VR task.

The VR view started from the first room where the participant should be facing a door. The participant was instructed to step then. The VR view would take the participant to pass the first door (see Fig.4 (A)). And then a corner would be presented in front of the participant. The participant was instructed to step without turning in reality. The VR view would take the participant to turn instead. Between the second room and the third room, there was a narrow corridor (see Fig.4 (B)). The participant was then directed to continue stepping. At the end of the third room, stepping would make the VR view turn back. And then the VR tour would loop back. The participant was asked to step for three to four minutes depending on their preference, followed by three to four minutes resting. During the resting, the EEG, EMG, ECG, LFP, and videos kept recording. The participant was asked to run the same procedure twice.

C. DATA COLLECTION AND ANALYSIS

The EEG, EMG, and ECG data were captured by using one EEG amplifier. The EMG was used for gait analysis. The ECG was used to offset artefacts in EEG channels. The EEG data collection software provided real-time video recording with embedded time synchronisation. The LFP was captured through a wireless connection to the Implantable

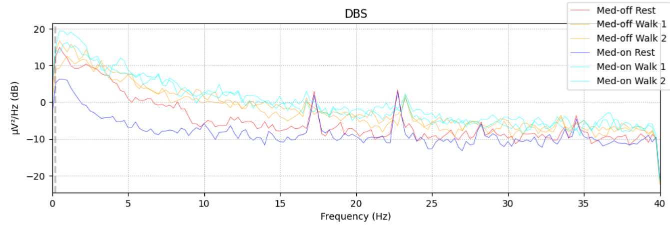

Fig. 5. This figure illuminated Local Field Potential (LFP) in different conditions. The comparison states were among med-off-rest, med-off-walk, med-on-rest, and med-on-walk.

Pulse Generator (IPG) implanted in the participant. The DBS was implanted in the Subthalamic Nucleus (STN) of the participant. Only left STN LFP was recorded, as the participant stated worse dyskinesia on the right side of the body. The DBS was turned off whilst the LFP was recording. The participant was informed before the DBS was turned off. The stepping information was recorded by the central server. The sides of the feet were recorded alongside time with a precision of milliseconds.

The original EEG and LFP data were filtered by notch filters. Attributed to the power frequency differences in amplifiers, the EEG data were filtered by a 50 Hz notch filter whilst the LFP had a notch filter at 40 Hz. The analysis included Power Spectrum Density (PSD). The PSD of different conditions, medication off resting, medication off stepping, medication on resting, and medication off stepping, were calculated. The PSD was calculated based on 30 seconds to 120 seconds of each state, where the FOG-related tasks were presented. The different conditions were annotated by different colours in the result section. To unify the diagram, only frequencies below 40 Hz were presented in the result figures.

III. RESULTS

A. OBSERVATION

The participant reported difficulties passing doors and walking on ramps in daily life. The major symptom of the participant was bradykinesia. And slow movements were observed when the participant walked through real doors. During the participant's using the system, no uncomfortable feelings were reported. In medication off-state, the participant disclaimed FOG in VR simulated passing doors, passing narrow corridors, and turning. However, a low frequency of stepping was observed during these tasks in the participant's medication off-state. Besides, the slow responses to the clinicians were observed during passing doors in medication off-state.

B. NEURO-ELECTROPHYSIOLOGIC SIGNALS ANALYSIS

The LFP result showed significant spikes over 16-18 Hz and 22-24 Hz (beta band) in resting conditions (see Fig.5). The overall beta bands' power increased in walking conditions. In light of the medication state, the medication on the state had a more significant beta bands shift than the medication off state. Fig. 6 and 7 demonstrated EEG,

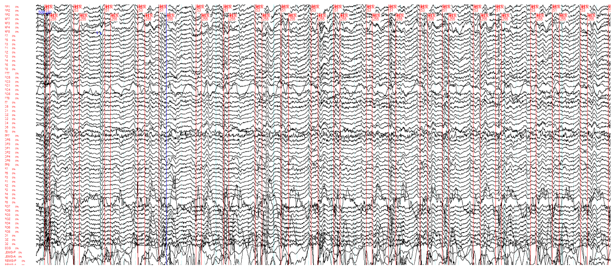

Fig. 6. This figure demonstrated the Electroencephalograph (EEG), Electrocardiograph (ECG), and Electromyography (EMG) recordings with triggers marked in real-time.

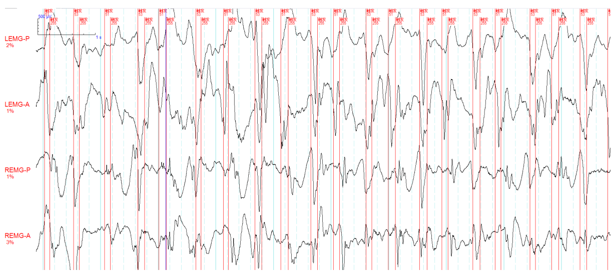

Fig. 7. This figure is a zoomed-in demonstration for Electromyography (EMG) recording with triggers marked in real-time. The occurrence of triggers and EMG indicated that the trigger was marked simultaneously with biological signals recording.

ECG, and EMG recordings with real-time triggers. The red vertical lines were triggers marked by the system automatically. Fig. 7 was a zoomed-in EMG signal with triggers. There were clearly concurrences between triggers and EMG, which indicated low latency in the system. Fig. 8 was LFP recordings with triggers. The red vertical lines on the top of the signals were trigger marks. The triggers were sent by the same device as EEG by a DB25 splitter. Therefore, the latency should be theoretically the same as EEG capture system.

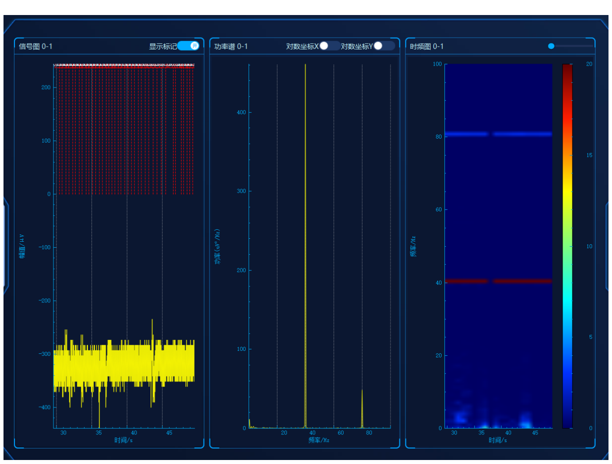

Fig. 8. This figure is Local Field Potential (LFP) recording with triggers marked in real-time.

IV. DISCUSSIONS

This paper proposed a system for comprehensive neuro-electrophysiologic evaluations for people with PD. The proposed VR system had the ability to trigger FOG. This indicated that in the future, this system could be used for FOG studies. As the FOG is one of the most frustrating but also one of the least understood phenomena in people with PD, the significance of exploring FOG, and neuro-electrophysiologic signals is obvious. Current studies only concluded that beta oscillations appeared in both frontal-cortex and deep brain structures such as STN[6]. Further investigations are necessary.

Notwithstanding, the spikes over 16-18 Hz and 22-24 Hz were abnormal. They were highly suspected of noises. This was confirmed by a further inquiry into the manufactory of DBS. As a result, the validated frequency band was limited to delta, theta, alpha and low-beta. Nevertheless, these bands still provided essential information about FOG[22]. From a practical perspective, the advantage of larger recruitment overwhelmed the disadvantage of the restricted frequency band. Moreover, the externalised DBS could always be connected to the system. Therefore, a further comparative study of using externalised DBS and wireless DBS in the same system was required in the future. Conclusively, as this is just a single case study, more studies are urged to validate the system.

In addition to physical environment simulation, the VR is also compatible with other cognitive stimulation, such as mathematics tasks and Question and Answer (Q&A) tasks. It was suggested by Shine et. al.[23] that the cognitive loads might also lead to FOG. The current VR design is consistent with cognitive tasks. For example, the mathematics task could be presented in front of the participants at all times whilst walking. This could reduce human factors in the experiment design, such as the accent of the investigator, and oddball attention-triggered Event-Related Potentials (ERP)[24]. Hence, in addition to FOG itself, this VR environment is adaptable to include other tasks which can help to investigate the cognition change associated with PD. This will reveal the role of deep brain structures, such as STN and GPi, in the cognition functions of the brain.

The purpose of this paper was not to conclude any correlations between EEG/LFP and FOG. The emphasis of this paper is to manifest the feasibility of using such VR based system to trigger FOG and record neuro-electrophysiologic signals at the same time. The proposed system design is the first step towards inspections of brain network coherence related to FOG. The attempts to study connections between the cortex and deep brain structures related to FOG would help us to better understand the mechanism of motor functions of people.

V. CONCLUSIONS

This paper presented a feasible VR-based comprehensive FOG neuro-electrophysiologic evaluation system for people with PD. The system exhibited the capability of presenting VR and recording neuro-electrophysiologic signals, such as

EEG, EMG, ECG, and LFP at the same time. The triggers marked in EEG and LFP could assist in extracting brain waves from both cortex and deep brain structures when FOG happens. This system design can be used to trigger freezing episodes in the controlled environment, differentiate subtypes of gait difficulties, and identify neural signatures associated with freezing episodes.

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ETHICS STATEMENT

The Ruijin Hospital Ethics Committee, Shanghai Jiao Tong University School of Medicine approved all experimental procedures involving human subjects

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