Perspective

Potential role of biofeedback therapy for Parkinson's disease

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Parkinson's disease (PD) is a neurological disorder characterized by rigidity, tremor, bradykinesia, and postural instability. Gait disturbance is one of cardinal symptoms of PD and affects the activities of daily living and quality of life. This symptom in advanced PD patients is usually refractory to medication and surgical intervention such as deep brain stimulation (Morishita et al., 2016). Therefore, physical therapy with an efficient exercise program is important to maintain or improve gait ability. Among the various rehabilitation programs, biofeedback therapy is drawing attention as a rehabilitation method. Biofeedback is a technique that aims to make unconscious or involuntary bodily processes perceptible so that patients can control them consciously. We recently reported the effect of biofeedback therapy using a robot suit hybrid assistive limb (HAL) on PD patients (Kotani et al., 2020). HAL is a robotic exoskeleton designed to facilitate movements and was developed based on the "interactive biofeedback" theory (Morishita and Inoue, 2016). Specifically, the movement of the robot is triggered by bioelectric signals detected by surface electrodes. It supports the spontaneous movement of impaired muscles and generates sensory feedback. In our study, we used the HAL lumbar type. Eight patients with advanced PD participated in this study. The participants performed HAL-assisted core exercises and squats, one session per day, for a total of five sessions. In our study, exercise with HAL improved walking ability after the short period of the five sessions, and the effect was maintained for 3 months. We considered that the HAL exercises were successful because the biofeedback of HAL is predominantly via the proprioceptive receptors. The robot enables patients to achieve repetitive movements.

Various methods such as visual feedback, auditory stimulation, and vibration stimulation are employed for biofeedback therapy in PD patients. The effects of visual feedback have been examined in several studies. Bonassi et al. (2016) reported improved hand bradykinesia in PD patients who performed a finger sequence with a 10-minute mirror visual feedback. In another study, the head and trunk orientation of 17 PD patients was measured using an inertial sensor, and this was projected as visual biofeedback on the informative eyewear to control the posture. Compared with eyes opened and eyes closed, there were significantly fewer falls when visual biofeedback was used (Caudron et al., 2014). In a randomized control trial of 42 PD patients, the participants played 20 sessions of balancing games using visual feedback and audible feedback from an avatar displayed on a PC screen. Compared to the group without feedback, the group with feedback improved their balance performance and this effect was maintained for a month (Carpinella et al., 2017). The effects of auditory feedback were also reported by Mirelman et al. (2011). In their study, PD patients underwent 18 sessions of postural control training by receiving inclination and trunk acceleration feedback through auditory stimulation. This significantly improved balance (Mirelman et al., 2011). Visual and auditory feedback is an effective trigger for PD patients to recognize and adjust their muscle coordination that is usually difficult to notice. Ronsse et al. (2011) also reported that visual feedback increases occipital lobe activity while auditory feedback increases temporal lobe, supplementary motor area, and cerebellum activity. Additionally, 20 PD patients underwent six gait tasks and six stance tasks using an artificial vibrotactile feedback system in which the headband vibrates when the trunk shakes. Compared to the group without feedback, the group with feedback was stable with less body sway (Nanhoe-Mahabier et al., 2012). However, a biofeedback program for PD has not been established.

Notably, exercise with the HAL lumbar type produces proprioceptive feedback from the erector spinae muscles, reinforcing the defective route from the spinal cord. An advantage of HAL is that sensory feedback and movement output are performed simultaneously, and robot-assisted exercise enables repetitive movements without fatigue. The enhanced sensory input activates the central nervous system, and its output to the low activity motor neurons that specifically innervate the paraspinal muscles. The robot assists the insufficient muscle output so that the input and the output are correctly coupled, and a positive feedback cycle can be performed. These may normalize the impaired motor output in PD patients and contribute to the improvement of motor function and gait disorders. In addition, it is possible that low-load rhythmical exercise using HAL activates the central pattern generator (CPG) of the spinal cord and improves the disturbance of coordinated rhythmic locomotion, which is one of the symptoms of PD.

The CPG is a part of the neuronal network that automatically generates neural activities that are the basis of rhythmical motor behaviors such as walking, hopping, and breathing. It is considered that PD patients have impaired motor rhythm due to inhibitory output from the basal ganglia, which leads to abnormal functioning of CPG. Asai et al. (2003) reported that PD patients' lower limb rhythmic movements had abnormal changes in their relative phase compared to those of healthy participants when examined by a CPG model. Abnormalities in CPG appear as behavioral delays and gait freezing, which adversely affect the activities of daily living. Controlling CPGs from external sources is difficult and there have been only a few reports of gait training on hanging treadmills, but the evidence seems to be insufficient (MacKay-Lyons, 2002). Our data suggest that robot-assisted uniform and low-load exercise improves the effortful movements of PD patients and promotes rhythm formation. We propose that the advantage of biofeedback therapy using HAL is that the feedback can adjust the formed rhythm through proprioceptive input, thus enabling movement optimization (**Figure 1**).

Among the several types of biofeedback therapies, robot-assisted biofeedback exercise has the advantage of enabling

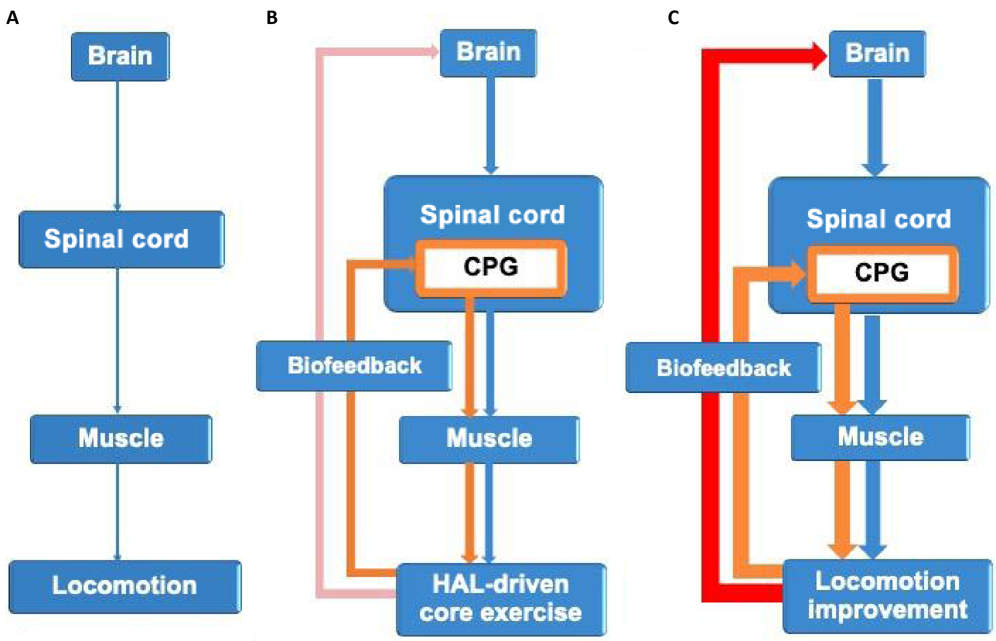

Figure 1 | Advantage of biofeedback therapy using HAL.
(A) Motor command without HAL. (B) HAL-assisted exercise activates brain and spinal cord CPG with feedback from proprioceptive input. (C) Optimized exercise repetition enhances biofeedback and improves locomotion. Adapted from Kotani et al. (2020). CPG: Central pattern generator; HAL: hybrid assistive limb.

patients to perform standardized and repetitive movements; however, further studies are required for the new therapy to be an established method. Multiple factors (i.e., physical frailty) can complicate PD patients' gait problems; therefore, gait training should be planned with a long-term strategy. In future studies, a control group that does not use HAL should be included when conducting randomized controlled trials. Even though the functional improvement effects could be maintained for about 3 months in our previous study, the effective dosage of therapy remains unknown. Also, the therapeutic effect of on and off medication states should be investigated. In 2020, Cyberdyne Inc. started a home rental program of HAL lumbar type for patients in Japan. This will increase the accessibility of the robot, which may also change the research paradigm.

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References

Asai Y, Nomura T, Sato S, Tamaki A, Matsuo Y, Mizukura I, Abe K (2003) A coupled oscillator model of disordered interlimb coordination in patients with Parkinson's disease. Biol Cybern 88:152-162.

Bonassi G, Pelosin E, Ogliastro C, Cerulli C, Abbruzzese G, Avanzino L (2016) Mirror visual feedback to improve bradykinesia in Parkinson's disease. Neural Plast 2016:8764238.

Carpinella I, Cattaneo D, Bonora G, Bowman T, Martina L, Montesano A, Ferrarin M (2017) Wearable sensor-based biofeedback training for balance and gait in parkinson disease: a pilot randomized controlled trial. Arch Phys Med Rehabil 98:622-630.e3.

Caudron S, Guerraz M, Eusebio A, Gros JP, Azulay JP, Vaugoyeau M (2014) Evaluation of a visual biofeedback on the postural control in Parkinson's disease. Neurophysiol Clin 44:77-86.

Kotani N, Morishita T, Yatsugi A, Fujioka S, Kamada S, Shiota E, Tsuboi Y, Inoue T (2020) Biofeedback core exercise using hybrid assistive limb for physical frailty patients with or without parkinson's disease. Front Neurol 11:1-10.

MacKay-Lyons M (2002) Central pattern generation of locomotion: A review of the evidence. Phys Ther 82:69-83.

Mirelman A, Herman T, Nicolai S, Zijlstra A, Zijlstra W, Becker C, Chiari L, Hausdorff JM (2011) Audio-biofeedback training for posture and balance in patients with Parkinson's disease. J Neuroeng Rehabil 8:35.

Morishita T, Higuchi M, Saita K, Tsuboi Y, Abe H, Inoue T (2016) Changes in motor-related cortical activity following deep brain stimulation for Parkinson's disease detected by functional near infrared spectroscopy: a pilot study. Front Hum Neurosci 10:629.

Morishita T, Inoue T (2016) Interactive bio-feedback therapy using hybrid assistive limbs for motor recovery after stroke: current practice and future perspectives. Neurol Med Chir (Tokyo) 56:605-612.

Nanhoe-Mahabier W, Allum JH, Pasman EP, Overeem S, Bloem BR (2012) The effects of vibrotactile biofeedback training on trunk sway in Parkinson's disease patients. Park Relat Disord 18:1017-1021.

Ronsse R, Puttemans V, Coxon JP, Goble DJ, Wagemans J, Wenderoth N, Swinnen SP (2011) Motor learning with augmented feedback: modality-dependent behavioral and neural consequences. Cereb Cortex 21:1283-1294.

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