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自主權對於促進巴金森氏症患者動作學習之效果

Effects of Autonomy on Motor Learning in People with Parkinson's Disease

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中文摘要

背景：巴金森氏症患者因動機、認知功能以及動作學習的障礙，導致其動作表現或學習新動作的成效不佳。因此，找尋促進巴金森氏症患者動作學習的方法，將可增進臨床復健的成效。自主權是指個人擁有自我決定的權利和能力，在環境中能夠自主做出選擇和決定。在動作學習中給與學習者選擇練習的參數能夠增加他們的自主權，進而增加學習的內在動機與認知資源的投入。自主權已被廣泛的證實可以促進健康年輕人的動作學習能力，且背後的神經生理機制已被初步討論。然而目前只有一篇研究探討自主權對巴金森氏症患者動作學習的影響，因此本研究欲探討給與自主控制回饋時機對於巴金森氏症患者動作學習的效益，以及其相關神經生理機制。

研究目的：探討提供巴金森氏症患者自主權對於動作學習之成效，及其相關神經生理機制。

研究方法：本研究招募原發性巴金森氏症患者，並依照受試者性別、年紀與疾病嚴重度輪流分配至自主組和共軛組以進行手指按壓任務的學習。其中自主組在練習時能夠選擇得到回饋的時機，共軛組則依照自主組的選擇接收相同時機的回饋。每位受試者在實驗第一天接受基本評估，包括情緒、認知功能與動作能力評估。在基本評估之後，將以經顱磁刺激術記錄受試者大腦皮質的興奮性，之後進行手指按壓任務的練習。此外，受試者在練習後需要填寫動機量表以及學習策略問卷。受試者在第二天將進一步練習手指按壓任務，並馬上以手指按壓任務測試觀察其立即留存效果，同時以受試者自評誤差分數觀察他們對任務表現的知覺。之後再進行經顱磁刺激術記錄受試者在學習之後大腦皮質的興奮性變化。受試者在練習之後的第七天將進行追蹤測試及經顱磁刺激術評估。

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結果：共有三十二位受試者完成試驗，其中十六位被分配至自主組，十六分配至共軛組。經過兩天的訓練之後，自主組與共軛組的手指按壓任務準確率皆顯著增加（$p < 0.001$）。兩組受試者在第二天的留存評估中表現相近，但自主組在第七天的評估中較共軛組有更好的動作任務留存（group-by-time interaction $p = 0.040$）。

學習策略問卷的結果顯示多數受試者在感知到良好和不好的表現後皆想要獲得回饋，而兩組的動機量表分數沒有顯著的差異。自評誤差分數則顯示，兩組在第二天與第七天的評估中都有相近的表現。

經顱磁刺激術的數據顯示，自主組的皮質脊髓興奮性在第七天的追蹤測試中有顯著的增加，而共軛組則沒有明顯的變化（group-by-time interaction $p = 0.041$）。

總結：提供巴金森氏症患者自主權有助於促進其動作學習的成效，且伴隨皮質興奮性的增加。然而實驗沒有發現顯著的訊息處理和動機效應，顯示巴金森患者能夠自主控制回饋時機，可能是透過其他機制促進其學習效應。

關鍵字：巴金森氏症、自主權、動作學習、皮質興奮性、經顱磁刺激術

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Abstract

Background: People with Parkinson's disease (PD) are known to have impaired motor learning and low motivation, which pronouncedly limit the effectiveness of training or acquiring new motor skills. Exploring methods to promote motor learning and motivation can thus enhance the effectiveness of clinical rehabilitation for people with PD. Autonomy refers to the sense of learner to actively participate in determining their own behavior. Providing learners with choices in the learning process (i.e., self-controlled practice) can increase their autonomy, thereby enhancing intrinsic motivation and cognitive resources for learning. Self-controlled practice has been shown to promote motor learning abilities, and the associated neurophysiological mechanisms have been discussed in healthy young adults. However, there is only one study to date intended to explore the effect of autonomy on motor learning in PD, and the neurophysiological mechanisms have not yet been studied.

Study purpose: The present study aimed to investigate whether an self-controlled practice would benefit motor learning for individuals with PD.

Method: This study recruited people with idiopathic PD. Participants were matched in pairs and consecutively allocated into the self-control group (SELF) and the yoked group (YOKED) to practice a finger-pressing trajectory-matching task. Participants in the SELF group had the choice to either receive performance feedback or not during practice, while those in the YOKED group received feedback according to the choices made by their counterparts. Each participant underwent baseline assessments on the first day (D1), including emotional status, cognitive function, and motor ability assessments. Following the assessments, neurophysiological outcomes were assessed with transcranial magnetic stimulation (TMS) before practicing the finger-pressing task. Additionally, participants needed to complete the motivation questionnaire and report their strategy for requesting

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feedback after the practice sessions. On the second day (D2), participants underwent additional practice of the finger-pressing tasks. Later, a retention and a transfer test were conducted to observe their immediate learning effects. At the same time, participants' self-reported error estimation scores were used to assess their perception of task performance. TMS was also used to record changes in cortical excitability after the learning session. On the seventh day (D7) of the experiment, participants returned to the lab and completed a follow-up retention test, along with the TMS assessments.

Result: 32 participants were recruited into the study, with 16 assigned to the SELF group and 16 to the YOKED group. After two days of training, the accuracy of finger-pressing tasks increased significantly in both the SELF and the YOKED groups ($p < 0.001$). While both groups showed similar performance at the D2 retention test, the SELF group had greater retention of the motor task than the YOKED group on D7 (group-by-time interaction $p = 0.040$).

When interviewing the participants' strategy for requesting feedback, it seemed that most participants preferred receiving feedback after good or bad trials equally. The results from the motivation questionnaire showed no significant difference between the two groups. Regarding the error estimation scores, both the SELF and YOKED groups showed similar ability in estimating their motor performance.

As for the TMS data, participants in the SELF group showed an increase in resting motor evoked potential (MEP) from D2 to D7, while the YOKED group showed similar resting MEP on D2 and D7 (group-by-time interaction $p = 0.041$).

Conclusion: Providing self-controlled feedback to patients with PD might benefit motor learning, accompanied by an increase in corticomotor excitability. However, this study did not find significant changes in the cognitive-processing ability or motivation in performing

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the task, suggesting that there might be other mechanisms that facilitated motor learning in people with PD.

Keywords: Parkinson's disease, autonomy, motor learning, corticomotor excitability, transcranial magnetic stimulation

doi:10.6342/NTU202401486

目次

doi:10.6342/NTU202401486

doi:10.6342/NTU202401486

圖次

doi:10.6342/NTU202401486

表次

doi:10.6342/NTU202401486

Chapter 1: Introduction

1.1 Background

Parkinson's disease (PD) is a neurodegenerative disorder associated with progressive loss of dopamine in the basal ganglia. [1] This disease is characterized by cardinal motor signs, including tremor, rigidity, bradykinesia, and postural instability. [1,2] In addition to the commonly recognized motor symptoms, non-motor symptoms such as cognitive dysfunction, motor learning deficits, and psychological problems are commonly observed in people with PD. [3] These non-motor impairments may influence the rehabilitation effects and eventually decrease the functional ability and quality of life. [4]

Multiple evidences have shown that patients with PD are impaired in motor learning. [5] Compared to non-disabled age-matched adults, patients with PD require a greater amount of practice to learn a motor skill. [4,5] Additionally, patients with PD appear to have difficulty generalizing a learned motor skill from the original practice context to a novel context. [6,7] Besides from the motor learning deficits, it is often observed that many patients with PD show little motivation to learn/relearn a new task, which may also negatively influence motor learning and rehabilitation effects. [8] Therefore, exploring potential strategies to enhance motor learning and increase motivation is important for facilitating better rehabilitation for people with PD.

One of the most commonly used methods to enhance motivation in the literature is to provide autonomy during practice or so called 'self-controlled practice', that is the learners are able to self-control practice variables (e.g., feedback). Numerous evidences conducted on healthy young adults have shown that providing self-control during practice may enhance the learners' perceived autonomy and facilitate motor learning. [9] Some researchers proposed that autonomy is a key component of intrinsic motivation; hence, providing autonomy by giving

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self-control over practice variables could induce greater engagement in motor learning. [9] Some other studies have also shown that providing learners control over practice variables promotes deeper cognitive processing and improves the effectiveness of motor learning. [10,11] These mechanisms are posited to underlie the motivation and the cognitive benefits of self-controlled practice. [12]

Some beginning studies have used neuroimaging tools to explore the neurophysiological mechanisms associated with the benefits of autonomy in motor learning. [13,14] Functional magnetic resonance imaging (fMRI) studies revealed that providing participants with choices in motor tasks would facilitate the activation of the prefrontal cortex, anterior cingulate cortex, and striatum, which are known to be related to cognitive and motivational control. [15] Electroencephalography (EEG) studies showed that learners with self-controlled practice had greater activation of the frontal cortex, which was suggested to be related to cognitive processing. [16-18] However, these studies were mostly conducted to examine the neuro-mechanisms related to self-control while performing a motor task (i.e., motor control), while there is still limited knowledge on the effect of self-controlled practice in inducing changes in corticomotor excitation associated with motor learning. [19,20] Hence, it would be interesting to use transcranial magnetic stimulation (TMS) to determine the changes in corticomotor excitability associated with self-controlled practice. [21]

While most of the evidences to date were conducted in non-disabled young adults, very limited evidence has explored the effects of autonomy on motor learning in people with PD, known to have low motivation and poor motor learning ability. To the best of our knowledge, only one study to date investigated the effect of autonomy in PD and found that providing self-control of the timing to use an assistive pole might benefit them in learning a stabilometer balance task. [22] Moreover, this study showed that the participants who had self-control were more motivated to perform the task than those in the yoked group, suggesting

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that self-controlled practice might enhance motor learning through motivational support. However, whether self-controlled practice can induce changes in cognitive processing remains to be determined, and the potential associated neural mechanisms have yet to be explored in people with PD. Therefore, this study aimed to investigate the effect of self-controlled practice on motor learning in individuals with PD and its associated corticomotor excitability changes.

1.2 Study purpose

This study aimed to investigate the effects of autonomy/self-controlled practice on motor learning and the associated neurophysiologic changes in people with PD.

1.3 Specific aims and hypothesis

Specific aim 1: To investigate the effect of self-controlled practice on motor learning in people with PD.

Hypothesis 1: Participants in the self-control (SELF) group showed greater improvement and better retention of the practiced motor task than the yoked (YOKED) group.

Specific aim 2: To investigate the neurophysiological changes associated with self-controlled practice in people with PD.

Hypothesis 2: Compared to the YOKED group, participants in the SELF group would show greater neurophysiological changes as measured by transcranial magnetic stimulation.

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Chapter 2: Literature Review

2.1 Introduction of Parkinson's disease

Parkinson's disease (PD) is the second most common neurodegenerative disease. [23] The disease occurs worldwide with a rapid increase in new cases, especially in Asia and other high-income countries. [24,25] According to the review of the Global Burden of Disease (GBD) study in 2016, approximately 6.1 million people worldwide suffer from PD. [26] The progression of the disease would induce multiple motor and non-motor symptoms, and the increasing number of patients diagnosed of PD may cause a substantial socioeconomic burden.

The pathophysiology of PD is associated with progressive loss of nigrostriatal dopamine cells and abnormal deposition of α-synuclein in Lewy bodies. [1] This disease is characterized by cardinal motor signs, including bradykinesia, rigidity, tremor, and postural instability. [1,2] Besides, non-motor symptoms, such as cognitive decline, depression, anxiety, sleep disorder, and autonomic dysfunction, are commonly observed in people with PD. [1-3] Among these non-motor symptoms, cognitive decline has been suggested to affect the functional activity of PD severely. [27] Patients may show impairment in several cognitive domains, including executive function, memory, and motor learning. [28,29] Impairment in these cognitive functions, especially motor learning, would pronouncedly influence the effects of clinical rehabilitation. [4] Specifically, their challenges in motor learning manifested as requiring more practice than non-disabled adults to learn motor tasks and relying more on explicit learning strategies, such as external cues, visual feedback, and other augmented feedback. [4,5] The over-reliance on external cues can lead to cue dependency, limiting their learning effectiveness. [4] Moreover, they seemed to have difficulty transferring the learned skill to different contexts, suggesting a context-dependency in learning. [6,7] Since clinical

doi:10.6342/NTU202401486

rehabilitation is a process for people with PD to learn/relearn motor skills, impairment in motor learning would, therefore, reduce the effect of clinical rehabilitation.

Besides from motor learning impairment, patients with PD are found to have low motivation, which would also affect motor learning. [5,30] Previous studies found that patients with PD could demonstrate better motor performance [31-33] and cognitive control [34] when motivated. For instance, an experiment by Kojovic and colleagues (2014) found that participants with PD showed increased movement speed when they received monetary rewards in a simple reaction time paradigm. [32] This suggested that reward-induced motivation might enhance motor performance in patients with PD. Furthermore, this improvement in motor performance was related to the modulation of dopamine medication. [33] Chong and colleagues (2015) found that participants with PD engaged less effort in squeezing a hand-held dynamometer when they were provided with the lowest reward. [33] Nevertheless, when provided with higher rewards, participants in the dopamine ON state invested more effort in the motor task than those in the dopamine OFF state, suggesting that dopamine increased patients' motivation to engage in the motor tasks. [33] Therefore, it was suggested that the pathological dopamine depletion in patients with PD decreased their willingness to invest effort as compared to controls, [33] and affecting their motor performance. [31]

The above-mentioned studies suggested that enhancing the motivation of patient with PD might temporarily overcome their motor and cognitive deficits, [32,34] which could potentially enhance their motor learning ability. However, studies have yet to identify the effect of manipulating motivation to improve motor learning in patients with PD. To address this research gap, this study aimed to explore whether interventions targeting motivation can enhance motor learning in PD.

doi:10.6342/NTU202401486

2.2 Introduction of autonomy

In the past decades, research has focused on the importance of autonomy (or identified as 'perception of control' in some research) and its benefits on motor control and learning. [9,35] Deci and Ryan (2000) posited the Self-Determination Theory (SDT), suggesting that autonomy (i.e., self-control) is one of the human fundamental psychological needs (along with competence and relatedness), which may, therefore, boost one's intrinsic motivation. [35] According to the SDT, autonomy is defined as the feelings of willingness and choice in activities undertaken. [35,36] Evidence from neurophysiological studies supported the ideas proposed by these theories, showing that autonomy may enhance the activation of brain regions related to motivation. [14,37,38] An fMRI study conducted by Leotti and Delgado (2011) demonstrated that participants who were given choices exhibited increased activity in the ventral striatum and midbrain. [14] In this study, participants were asked to make choices by pressing one of two keys to earn experimental dollars. [14] The task included trials with both a free-choice condition and a no-choice condition. [14] The fMRI results revealed that participants showed higher activation in the ventral striatum and midbrain during the free-choice condition compared to the no-choice condition. [14] Additionally, participants' subjective ratings indicated a preference for the free-choice condition over the no-choice condition. [14] Given that the ventral striatum and midbrain are associated with affective and motivational processes, [39] the increased activation in these brain areas suggests that perceived autonomy can enhance individuals' motivation in related activities. [14]

2.3 Providing autonomy/self-controlled practice enhances motor learning

In the literature of motor learning, the advantages of self-controlled practice have been shown that learners demonstrated better performance when they were able to choose or

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manipulate their own practice condition. [12] Studies related to self-control practice were usually designed to compare the performance or learning effect between participants in a self-control (SELF) group and a yoked (YOKED) group. [40] The SELF group is allowed to self-select part of their practice condition or when to receive feedback, while the YOKED group passively receives the variable(s) according to the decision of their counterparts. [40] The first published study was conducted by Janelle and her colleagues (1995), who recruited 60 college students to learn a golf ball underhand tossing task. [41] Participants were randomly assigned to one of the five groups, including a self-controlled feedback group and a yoked group. [41] The results showed that participants with self-controlled feedback had greater accuracy than those in the yoked group at the retention test. [41] This suggested that self-control practice may enhance motor learning. [41] A meta-analysis reported by Jimenez-Diaz and colleagues (2021) further supported the benefits of self-controlled practice. [42] The study assessed the effectiveness of self-controlled feedback on motor learning in healthy adults from 8 studies. [42] The SELF group chose when to receive feedback, while the YOKED group received feedback schedule as the SELF counterpart. [42] The standardized mean difference effect size of the included studies showed that both the SELF and YOKED groups significantly improved their motor skill performance throughout the acquisition phase. [42] Nevertheless, the SELF group had better retention of learned motor skills, while the YOKED group showed decreased motor skill performance at the retention test. [42] This indicated that self-control feedback might benefit motor learning, which is shown in the learners' enhanced motor skill retention. [42]

Besides from the self-controlled feedback, it was found that providing choices of task-irrelevant conditions may also benefit learning. A study by Lewthwaite and colleagues (2015) recruited healthy young adults to learn a golf-putting task. [43] Participants in the SELF group were able to choose the color of the ball to use, an incidental choice not directly related to

doi:10.6342/NTU202401486

task performance, while those in the YOKED group had no choice but received the selected choice according to their counterparts.[43] The results showed that participants in the SELF group performed better during the retention test on the following day.[43] Since the choice provided in the study was incidental to task performance, it was thus suggested that having a sense of autonomy may be the key to facilitating motor learning.

The benefits of self-controlled practice on motor learning can be explained via the 'motivational aspect'[43-49] and/or the 'cognitive aspect.'[10,11,17,27,50-52] According to the OPTIMAL theory proposed by Wulf and Lewthwaite (2016), the perception of autonomy may enhance the learner's motivation throughout the learning process.[9] An enhanced motivation may increase the goal-action coupling, facilitating motor performance and learning.[9] A study by Post and colleagues (2016) examined the motivational effects of self-controlled practice on learning a golf chip shot task.[44] In the study, 44 healthy young adults were allocated to the SELF group or the YOKED group.[44] Those in the SELF group could choose whether to receive split-screen replay after each practice trial, while those in the YOKED group were informed that they would see the replay randomly after some trials.[44] The participants' motivation to learn the task was also assessed with the Intrinsic Motivation Inventory (IMI), which contained items in different subscales (i.e., interest/enjoyment, perceived competence, perceived autonomy, effort/tension, and pressure/tension) with a 7-point rating scale.[53] The higher score measured in the IMI indicated that participants were more intrinsically motivated to engage in the task.[53] The results showed that participants in the SELF group had better accuracy in the one-day delayed retention test as compared with those in the YOKED group. Furthermore, the SELF group had a higher IMI score compared to the YOKED group after the practice trials, indicating that participants who had self-control split-screen replay were more motivated to learn the task. This supported the OPTIMAL theory that having the perception of autonomy may enhance individuals' motivation to learn a

doi:10.6342/NTU202401486

task, thereby benefiting their learning. Wulf and colleagues (2018) conducted a similar study that recruited 32 college students to learn a lassoing skill. [45] Participants were randomly assigned to either the SELF group or the YOKED group. [45] Those in the SELF group were able to choose the color of the mat under the target before each session of practicing trials, while the YOKED group was told that the mat might be changed before each session of the trials. [45] The results of throwing accuracy showed that the SELF group outperformed the YOKED group in both the practice trials and the retention test. [45] Besides, the authors also measured participants' affective state with the Self-Assessment Manikin, a 9-point rating scale consisting of nine faces with different degrees of expression. [45] After the practice phase, the SELF group showed more positive effects than the YOKED group. [45] This supported the notion that self-controlled practice in learning positively influences individuals' affective states and benefits the learning process. [40]

The effect of self-controlled practice may also be related to the learners' perception of competence when learning a novel skill. [46-48] Competence is the perception of learners' capabilities to master a task or challenge. [36] The experience of success would increase learners' motivation and, therefore, enhance learning. [46,47] This notion was supported by previous studies that found the learners tend to receive feedback on their performance after good trials. [46,49] A study by Chiviacowsky and Wulf (2002) examined the effect of self-control feedback in learning a sequential timing task with 30 young adults randomly assigned to the SELF group and the YOKED group. [46] The SELF group could decide when to receive feedback during practice, while the YOKED group received feedback as scheduled by their counterpart in the SELF group. [46] The results showed that the SELF group had better performance in the transfer test compared to the YOKED group. [46] When the participants were asked about their preferences for feedback, most of them indicated that they preferred to receive feedback after they felt a good trial. [46] It was thus suggested that learners may find

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repeating a good performance easier than correcting errors from a poor trial. [46] This difference in effort might motivate the learners to perform better, thereby benefiting motor learning. [46] Another study designed by Bund and Wiemeyer (2004) investigated the effect of self-controlled practice in healthy young adults. [48] Participants were required to learn a table tennis stroking task, with the SELF group allowed to manipulate the schedule of video instruction, while the YOKED group received the same schedule chosen by their counterpart. [48] As a result, participants in the SELF group showed better learning effect than the YOKED group at the retention test. [48] The study also assessed the participants' feelings of self-efficacy (i.e., the expectation about one's capabilities to learn or perform specific skills [54]) to learn the task with 10-item task-specific scale designed by the authors in both the practice session and retention test. [48] The SELF group revealed higher self-efficacy beliefs than the YOKED group, suggesting that self-controlled practice has positive effects on psychological states. [48]

Apart from the motivation perspective, some evidence suggested that cognitive processing may play an important role in self-controlled learning. It has been proposed that learners who can control when to receive feedback may increase their cognitive neuronal processing by retrieving related information and comparing the difference between performance and actual movement goals. [51] To investigate the potential cognitive processing induced by self-controlled practice, motor learning studies have used the 'error estimation method' to examine the participants' ability to estimate performance errors/accuracy. [10,11] The estimation of error, usually presented with root mean square error (RMSE), is mostly carried out after the participants complete a trial and compared with the actual RMSE of that trial. The greater accuracy of their estimation (i.e., less difference between the estimated and actual errors) may reflect greater cognitive involvement during the learning process. [55,56] Carter and Ste-Marie (2017) conducted a study by asking healthy young adults to learn a manipulandum task. [11] Participants were divided into task-relevant, task-irrelevant, and no-choice groups. [11]

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Those in the task-relevant group were able to decide when to receive feedback, while those in the task-irrelevant group had the choice about the color of the arm wrap and a video game to play on the next day. [11] Participants in the no-choice group were provided with feedback determined by the task-relevant group, along with the arm warp and video game determined by the task-irrelevant group. [11] The results showed that the task-relevant group performed with higher accuracy in the trials than both task-irrelevant and no-choice groups at both the retention and transfer tests. [11] In addition, the task-relevant group was more precise in error estimation compared to the other two groups. [11] This finding suggested that participants in the task-relevant group could process deeper information regarding the task and, therefore, outperform the others. [11] Some other studies supported the notion of cognitive processing by imposing an additional task between the motor tasks and the feedback. [57,58] It was thought that the time between the completion of a trial and the presence of feedback was when error estimation occurred in the brain. [57] As error estimation is important for motor learning according to the cognitive processing explanation, disruption of this period might weaken the self-control learning effect. Carter and Ste-Marie designed a study by adding an interpolated activity after completing each motor task trial. [57] The study recruited healthy young adults and allocated them into four groups: SELF group, YOKED group, SELF with interpolated activity group, and YOKED with interpolated activity group. [57] The participants practiced a manipulandum task and performed a cognitive task upon movement completion to identify a two-digit number through trial and error. [57] Participants returned to the laboratory on the next day to complete the retention and transfer tests. [57] The results showed that participants in the SELF group performed better than all other groups at the retention and transfer tests, while the SELF with interpolated activity group performed similarly to the two YOKED groups. [57] This suggested that the interpolated activity disrupted the learners' cognitive processing and eliminated the learning benefits of self-controlled feedback. [57]

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The above-mentioned studies have shown that providing self-controlled practice could benefit motor learning via motivational and/or cognitive mechanisms. However, all of the studies mentioned above were conducted with healthy young adults. Whether self-controlled practice can benefit motor learning for people with PD has been less investigated. A study by Chiviacowsky and colleagues (2012) was the first to determine the potential benefit of self-controlled practice in patients with PD using a stabilometer task. [22] During practice, the participants in the self-control group could choose when to use a balance pole, while the balance pole was provided to the yoked group according to their counterpart's choice. [22] The results showed that the self-control group learned better than the yoked group with an enhanced perceived autonomy, [22] providing a preliminary evidence of the benefit for the benefit of self-controlled practice on motor learning in people with PD. Nevertheless, this study did not explore how autonomy/self-controlled practice affected the cognitive processing of patients with PD, nor the underlying neural mechanism. Therefore, our study aimed to further investigate the possible effect of autonomy/self-control practice on cognitive processing and the associated corticomotor excitability in patients with PD.

2.4 Possible neurophysiological changes associated with autonomy/self-controlled practice on motor learning

Despite the above-mentioned behavioral studies, very limited evidence supports the neurophysiological changes associated with self-controlled practice and motor learning. A study by Murayama and his colleagues (2015) supported both the motivational and cognitive explanation of self-controlled practice with functional magnetic resonance imaging (fMRI) findings. [15] In the study, the participants played a stopwatch task, with trials involving either a self-selected stopwatch (self-determined-choice condition) or an assigned stopwatch (forced-

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choice condition). [15] The participants were required to stop the stopwatch at a target time of 5s, and the neural activity was obtained through fMRI scanning simultaneously. [15] The behavioral results showed that participants performed better in the self-determined choice trials than in the forced-choice condition. [15] The fMRI results showed that the participants had higher activation of the striatum and dorsal anterior cingulate cortex (dACC) when performing the task in the self-determined-choice condition than in the forced-choice condition. [15] Since the striatum was suggested to involve in affective and motivational processes, [59] the perception of choice may boost up the emotional contribution of participants to the task. [15] Meanwhile, the recruitment of the dACC may reflect an updating of information, which accounted for the cognitive commitment to the task. [15] More interestingly, the fMRI results showed that the activation of the ventromedial prefrontal cortex (vmPFC) after receiving feedback was modulated by the self-choice condition. [15] It was found that the activation of vmPFC was increased after success feedback under both the self-determined-choice and the forced-choice conditions. [15] However, after receiving failure feedback, the activation of vmPFC increased/maintained under the self-determined-choice condition but decreased in the forced-choice condition. [15] Furthermore, the activation of vmPFC was positively related to participants' task performance (higher activity of vmPFC was related to better performance). [15] As this study showed that self-controlled practice may prevent the drop of vmPFC activation in response to negative feedback, it was proposed that self-controlled practice enhances task performance associated with resilience to failure feedback. [15]

Apart from the fMRI findings, electroencephalography (EEG) studies showed that self-controlled practice may boost cognitive control in practicing motor tasks. [16,17] An EEG study by Grand and colleagues (2015) supported the effect of self-control learning on cognitive factors. [17] In the study, feedback-related negativity (FRN) was measured to reflect

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the extent of an individual's feedback processing. [17] FRN signal was measured at the frontocentral scalp with approximately 250–300ms after feedback presentation, with more negative amplitudes indicating a greater extent of feedback processing. [60] The study recruited 32 young adults to learn a bean bag throwing task with EEG measurement. [17] Participants in the SELF group were able to choose whether to receive feedback after each trial, while those in the YOKED group were informed whether they would receive feedback upon completion of each trial. [17] The behavioral data showed that the SELF group was more accurate than the YOKED group at the retention and transfer tests. [17] EEG results showed that participants in the SELF group had larger FRN mean amplitude than the YOKED group. [17] Accompanied by the behavioral data, this suggested the SELF group processed greater feedback-related information during the acquisition phase, therefore benefiting their motor learning. [17] Another study by Pathania and her colleagues (2019) examined the learners' motivation and information processing when learning a video game with self-controlled task difficulties. [18] In the study, two EEG signals were evaluated: the frontal alpha asymmetry (ΔFAS) and the midline frontal theta (ΔMFT). [18] The ΔFAS was associated with motivation and emotional state, while the ΔMFT was correlated with cognitive control and may be sensitive to changes in cognitive processing. [18] Throughout the practice sessions, participants in both the SELF and YOKED groups showed similar ΔFAS signals, suggesting that the participants' motivation might not be affected by the self-control practice condition. [18] Nevertheless, the SELF group had a greater increase of ΔMFT across practice sessions than the YOKED group, suggesting that the SELF group might have greater cognitive processing than the YOKED group. [18] These EEG findings highlighted that cognitive processing might be critical for the learning advantages associated with self-controlled practice.

While the fMRI and EEG studies provided preliminary exploration of the neural correlates associated with self-controlled practice, little is known whether self-controlled

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practice may induce changes in corticomotor excitation. Moreover, the above-mentioned studies used fMRI and EEG to examine brain activation during motor performance, which might not necessarily reflect the neuroplastic changes as a result of motor learning. Transcranial magnetic stimulation (TMS) is an often-used noninvasive stimulation neuroimaging technique that evaluates corticomotor excitability associated with motor learning. [19,20] A study by Smyth and colleagues (2010) examined the relationship between the plasticity of the primary motor cortex (M1) and motor learning by manipulating the feedback frequency. [61] The study recruited healthy young adults to learn a waveform tracking task while receiving different feedback frequencies (100% vs. 50%), and the result showed that the participants who received 50% feedback frequency performed better than those who received 100% of feedback at the retention test. [61] TMS data showed that only the 50% feedback group participants, who had better motor task retention, had elevated M1 excitability at the retention phase, showing M1 may be involved in the offline consolidation of motor learning. [61] Meanwhile, reduced short-latency intracortical inhibition (SICI) was found in both groups after the training phase, suggesting that SICI might be related to use-dependent plasticity. [61] This study suggested that more successful motor learning was associated with increased M1 excitability at retention, indicating that M1 may play a role in the representation of acquired motor skills. Additionally, TMS has been widely used to examine cognitive processing. [62] A series of experiments by Lin and colleagues (2008, 2009, 2010, 2011) used TMS to demonstrate that M1 was related to error-based information-processing during non-movement periods. [63-66] Since deeper information processing has been proposed as one potential mechanism of self-controlled practice, it would be intriguing to explore whether any changes in corticomotor excitability occured after self-controlled practice. Hence, this proposed research planned to use TMS as an imaging tool to probe the influence of self-controlled practice on motor learning.

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2.5 Summary of review

In summary, individuals with PD are known to have deficits in motor learning as well as poor motivation to learn and perform motor tasks. [30] From the review above, providing autonomy/self-control during practice could facilitate motor learning by enhancing the learners' motivation and/or cognitive processing. Since most evidence to date was conducted with healthy young adults, whether providing autonomy/self-control can also benefit motor learning in people with PD has not been fully investigated. Moreover, the neural plastic changes associated with autonomy/self-controlled practice in PD have not been investigated. Therefore, the purpose of the present study was to explore whether providing autonomy/self-controlled practice could facilitate motor learning in PD. Furthermore, neurophysiological changes associated with self-controlled practice would be investigated with TMS.

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Chapter 3: Methods

3.1 Participants

Participants diagnosed with idiopathic PD were recruited from the neurology clinic of the National Taiwan University Hospital. The inclusion criteria were: (i) age above 20 years old, (ii) able to follow instructions to perform the tasks (Montreal Cognitive Assessment ≥ 24), and (iii) no surgery or injury of the upper extremities in the past 6 months. Participants were excluded if they had (i) other neurological disorders in addition to PD, (ii) severe hand tremor in upper extremities (score ≥ 3 in Questions 15 to 18 of Part III of the Unified Parkinson's Disease Rating Scale), (iii) symptoms of anxiety or depression (score > 6 in either the anxiety subscale or depression subscale of the Hospital Anxiety and Depression Scale), (iv) deep brain stimulation or pacemaker implanted, (v) medical history of seizure, (vi) a blood-relative with history of epilepsy, (vii) unstable medical conditions, or (viii) pregnancy.

3.2 Study procedure

This was a cross-sectional experimental study. Eligible participants were required to sign the informed consent approved by the Research Ethics Committee of National Taiwan University Hospital before participating the study (**Appendix 1**). The participants were matched in pairs based on age, sex, and disease severity as measured by Hoehn and Yahr Scale. The first participant who came into the study of each pair was assigned to the SELF group, while the second was assigned to the YOKED group.

The participants were asked to visit the lab for three days during 'ON' medication state. On Day 1 (D1), the participants took part in cognitive, motor, emotional, and

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neurophysiology assessments. After the baseline assessments, the participants practiced a finger-pressing trajectory-matching task. The task required the participants to press a force gauge with their 2nd or 3rd fingers of the more affected hand to produce a target waveform trajectory as accurately as possible. The participants in the SELF group could choose when to receive feedback during the practice trials, while those in the YOKED group were informed that the feedback would be presented randomly by the program. The acquisition phase of the task was divided into two consecutive days, which contained 2 blocks of 36 practice trials on Day 1 and Day 2 separately. After completion of the practice trials on each day, the participants were required to complete the motivation questionnaire to assess their interest in the task, along with perceived competence and autonomy. [53] Besides, a questionnaire was used to inquire about the participants' strategies in both groups for requesting feedback (**Appendix 2**). [46,49] The participants in the SELF group were asked when and why they requested feedback. Meanwhile, the participants in the YOKED group were asked whether they received feedback after the right trials. If the answers from the participants in the YOKED group were negative, they would be asked about their preferred timing to receive feedback. On Day 2 (D2), after completing all the practice trials, there were an immediate retention test (R1) and a transfer test (T1), along with the error estimation test to examine the participants' own performance. After the behavioral motor task, the TMS neurophysiological assessment was performed. The participants were then required to return to the lab 5 days later, on Day 7 (D7), to complete a delayed retention test (R2) and a delayed transfer test (T2) followed by error estimation and the neurophysiological assessment. The study procedure is presented in **Figure 1**.

3.3 Finger-pressing trajectory-matching task

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A finger-pressing trajectory-matching task was designed for the participants to practice in this study. The participants were instructed to perform two rapid finger-pressings on a force gauge to produce a target waveform trajectory as accurately as possible. Participants were asked to sit comfortably on a chair with their forearms resting on a table and facing a computer monitor. A force gauge (FORCE TENTM FDX; Wagner Instruments, Greenwich, USA) was used to measure the vertical forces produced by the fingers. Prior to each trial, all sensor signals were set to zero when subjects placed their fingertips on the sensor and relaxed their hands, and the threshold of force detection to start recording data was set at 1N. As a result, the sensors measured only active downward forces. A custom Python program (Python Software Foundation, Python Language Reference, version 3.11, Delaware, United States) was designed with the force gauge for data acquisition at a sampling rate of 10Hz for both analysis and participants' feedback. As indicated in **Figure 2**, a target waveform and a goal movement time were displayed on the computer screen for 3000ms at the beginning of each trial. Later, a 'Ready' and a 'Go' signal were shown to the participants with 1000ms apart. Participants were instructed to begin the trial whenever they were ready, as this was not a reaction time task. Movement time was defined as the onset of pressure detected by the force gauge. The computer monitor remained blank during the trials, and the feedback was displayed for 5000ms after the trial completion. On those trials without feedback, a blank screen was displayed for 5000ms.

Before practicing the finger-pressing task, all participants were informed about the instructions for performing the motor task, and an example of the feedback was provided. The feedback included a graphic presentation of the participant's movement trajectory superimposed on the goal waveform. Additionally, the root mean square error (RMSE) was also provided as numerical feedback for performance accuracy. Participants were told that a smaller RMSE value indicated better performance. During the practice trials on D1 and D2,

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the participants in the SELF group could choose whether they wanted to receive feedback at the end of each practice trial. The participants in the YOKED group received feedback according to their counterpart's choices. The yoking procedure aimed to ensure that any learning differences were due to the provision of choice instead of the feedback schedule.

Three designated waveform trajectories were scheduled in a pseudorandom order during the practice trials and the retention tests (**Figure 3**). The acquisition phase consisted of two sessions of 36 trials on each day (a total of 72 trials per day), resulting in 144 practice trials for the two-day practice. Participants had a 5-minute rest between the two practice sessions on each day. Besides, feedback was provided in a faded order throughout practice. The participants received 100% feedback during the 1st session of practice, 75% in the 2nd practice session (27 trials out of 36 trials), 50% in the third session (18 trials), and 25% in the last session (9 trials). Hence, the participants in the SELF group were limited in the number of choices throughout practice. During each session, all the requests had to be used. The restriction of the number of feedback requests was to equalize the frequency of feedback received by all participants between the two groups.

At the retention tests on D2 and D7, participants were required to perform one block of 9 trials without feedback. The target waveforms were the same as those performed in the practice phase. After each testing trial, the participants were asked to estimate their error (in RMSE) with respect to the overall movement accuracy. Error estimation (EE) was verbalized by the participants and recorded in an Excel spreadsheet for data analysis. The EE represented participants' cognitive processing while performing the trials. [67] The lower EE score indicated that the participants had a more precise perception regarding their performance and, thus, were more accurate in estimating their performance during the trials. [67] After the retention test, the participants were asked to perform a transfer test consisting of 3

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trials of a new target waveform trajectory. Similar to the retention test, participants were required to estimate their errors after the completion of each trial.

3.4 Outcome measures

3.4.1 Baseline assessment

Baseline evaluation included the characteristics (i.e., basic demographic data, more disease-affected side, disease severity, disease duration, levodopa-equivalent dose conversion of drugs) of the participants, cognitive function (Montreal Cognitive Assessment, MoCA), motor performances (Unified Parkinson's Disease Rating Scale, UPDRS), and emotions (Hospital Anxiety and Depression Scale, HADS).

3.4.1.1 Montreal Cognitive Assessment

General cognitive function was assessed with the Montreal Cognitive Assessment (MoCA). It is a widely used screening tool for detecting cognitive impairment and has been shown to be highly reliable and valid in the PD population. [27,68] MoCA examines several cognitive domains: attention, language, memory, executive function, and visuospatial function. The total score of MoCA is 30 points, and a higher score indicates better cognitive function. A cut-off point of 24 has been suggested to differentiate mild cognitive impairment in PD. [69]

3.4.1.2 Unified Parkinson's Disease Rating Scale

The Unified Parkinson's Disease Rating Scale (UPDRS) is a well-established and most frequently used rating tool for the evaluation of the disease severity of PD. The internal

doi:10.6342/NTU202401486

consistency and validity have been established to be excellent for UPDRS. [70] In this study, we only assessed Part III, the motor subscale of the UPDRS (UPDRS-III), to investigate the motor impairment of participants. The total score of UPDRS-III is 72. The higher the score, the more severe the patient's motor symptoms.

3.4.1.3 Hospital Anxiety and Depression Scale

Symptoms of anxiety and depression of the participants were assessed with the Hospital Anxiety and Depression Scale (HADS). The HADS consists of 14 questions, which can be categorized into the anxiety (HADS-A) and depression (HADS-D) subscales. Each question scores from 0 to 3, with a total score of 21 in both the anxiety and depression subscales. [71] A higher score indicates that the participants have more severe anxiety and depression symptoms. [71] The cut-off point of the HADS for patients with PD was reported as 6 in each subscale to identify the depression and anxiety symptoms in PD. [72] To avoid the impact of anxiety or depression in this study, participants scoring 6 or above on either the anxiety or depression subscale were not included.

3.4.2 Root mean square error (RMSE) of the finger-pressing trajectory-matching task

Overall performance accuracy of the finger-pressing trajectory-matching task was assessed with the RMSE, which was the mean difference between the target waveform and the participant's movement trajectory calculated over their actual movement time. The RMSE was calculated with the formula of $RMSE = \sqrt{\frac{\sum_{i=1}^{n}(y_i - \hat{y}_i)^2}{n}}$. While 'n' indicated the sample size recorded in the goal movement time, the $(y_i - \widehat{y_i})$ was the difference between the predicted force value (the designated waveform) and the observed force value (the waveform

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trajectories performed by the participants). RMSE is sensitive to errors in both spatial and temporal domains and captures both variability and bias of the performed motor response. [73] All participants completed the 2-day practice phase, with two sessions of 36 trials each day. The RMSE of each trial was calculated, and an average of 9 trials was determined for each block (B1 to B16) in the acquisition phase and retention tests. Since there was only one new waveform in the transfer test, an average of 3 trials was calculated.

3.4.3 Strategy for requesting feedback

Participants were interviewed about their strategy for requesting feedback after completing the practice trials each day. The participants in the SELF group were asked when and why they requested feedback. Meanwhile, the participants in the YOKED group were asked whether they received feedback after the trials that they wanted feedback. If the answer were negative, they would be further asked about their preferred timing to receive feedback. The questionnaire is presented in **Appendix 2**.

3.4.4 Motivation questionnaire

We used a motivation questionnaire to measure participants' subjective experiences related to the task. In previous motor learning studies, most researchers used the standard IMI with 22-item versions, including four subscales in the assessment protocol. [74] The four subscales were interest/enjoyment, perceived competence, perceived choice, and pressure/tension. The questions in the inventory were designed with a 7-point Likert scale. A score of 1 indicated that the participants 'strongly disagree' with the description of each question, while a score of 7 indicated that participants 'strongly agree' with the questions.

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The mean score of the questions in each subscale was used for interpretation, with a higher score indicating greater intrinsic motivation of participants to engage in the learning task.

In this study, participants were required to complete a questionnaire with subscales of interest, perceived competence, and perceived autonomy after the practice trials. Questions in interest and perceived competence were taken directly from the IMI to determine the participants' subjective motivation after completing their practice trials. [53] The perceived autonomy subscale was not taken directly from the IMI because most of the original questions were not phrased around the choice during practice trials. Instead, we chose the modified questions used by Carter and Ste-Marie. [11] Taken together, 14 questions were included in the motivation questionnaire of this study, and the questionnaire was presented in **Appendix 3**.

3.4.5 Error estimation score

During the retention and transfer tests, participants were instructed to estimate their RMSE value after completion of each trial. Error estimation (EE) score was used to assess the cognitive processing of participants during the trials. [10,11] The accuracy of participants' total EE was calculated using the formula EE score = $\sqrt{(CE^2 + VE^2)}$, as constant error (CE) captured the participants' estimation bias (estimated RMSE – actual RMSE), and variable error (VE) was the standard deviation of these estimation bias. [67] A lower EE score indicated that the participants had a more precise perception regarding their performance and, thus, were more accurate in estimating their errors during the trials. [67]

3.4.6 Neurophysiological evaluations

doi:10.6342/NTU202401486

Transcranial magnetic stimulation (TMS) is a non-invasive neuroimaging tool commonly used to evaluate corticomotor excitability. [21] A TMS device (The Magstim Company Ltd, Whitland, UK) was used to determine the neurophysiological changes of corticomotor excitability before and after the acquisition phase. Surface electromyography (EMG) was used to measure the output of TMS. The electrodes of surface EMG were placed over the muscle belly of the first dorsal interosseous (FDI) of the more affected hand. A ground electrode was placed over the styloid process of the ulna. The sampling rate of the EMG signals was set at a frequency of 12500Hz and a band-pass filter at 0 to 1000Hz.

Before TMS measurement, participants were required to complete a TMS safety questionnaire to ensure they could receive TMS. [75] During the TMS measurement, the hotspot and motor threshold of FDI were first determined. Participants were seated with elbow flexion at 90 degrees with forearm and wrist pronated. A lycra cap marked with dots was placed on the heads of the participants to help with the hot-spotting procedure and to ensure consistency in applying TMS stimuli. To identify the cortical excitability changes after learning, TMS pulses were delivered through the figure-of-eight coil to the opposite hemisphere of the practice hand. The hotspot was defined as the stimulation site where the largest and most consistent motor-evoked potential (MEP) could be elicited at a given stimulation intensity. [76] The resting motor threshold (RMT) was determined as the minimum stimulus intensity required to elicit an MEP in the relaxed FDI with at least an amplitude of 50 μV in five out of ten consecutive trials. [77] After determining the hotspot and RMT, single pulse and paired pulse stimuli were delivered to obtain TMS outcomes.

The outcomes from the single pulse paradigm included the RMT, resting MEP, active MEP, and cortical silent period (CSP). Resting and active MEPs were acquired when the stimuli were delivered while the target muscle was at rest or contracted, respectively. [76] CSP, obtained under the muscle contraction condition, was when EMG activity was suppressed for

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a few hundred milliseconds after the MEP. [76] This CSP has often been used to indicate the inhibitory mechanism within the corticospinal tract. [21] Paired-pulse paradigm measured the intracortical excitation and inhibition. [21] Two consecutive stimuli were applied to the scalp under the paired-pulse paradigm. The first pulse was the conditioning stimulus and the second pulse was the testing stimulus. [21] By adjusting the interval between the two stimuli and the intensity of the stimuli, we could obtain intracortical facilitation and inhibition. [21] Short-latency intracortical inhibition (SICI) and intracortical facilitation (ICF) were obtained in this study. [21] SICI reflected the intracortical inhibition mediated by GABAa and was acquired when the inter-stimulus interval was set at 2 milliseconds (ms) and 3ms. [21] ICF mediated by glutamatergic receptors represents intracortical facilitation, and the inter-stimuli interval was set at 10ms and 12ms. [21] The mean value of the SICI ratio obtained with inter-stimulus intervals of 2ms and 3ms was used to analyze the changes in participants' intracortical inhibition, while the mean value of the ICF ratio obtained with inter-stimulus intervals of 10ms and 12ms was recorded to analyze the changes in their intracortical facilitation.

3.5 Data analysis

All acquired data was analyzed with SPSS 25.0 (Chicago, IL, USA). Normality of the data was determined using the Shapiro-Wilk test. Outliers were identified as the data greater than 1.5 interquartile ranges (IQRs) above the third quartile (Q3) or below the first quartile (Q1). [78] Intention to treat analysis was used for the outliers, which was replaced with the group mean. [79] Descriptive statistics were used to describe the baseline characteristics of the sample. Demographic data was compared between the two groups using independent t-test and Chi-squared test for continuous and categorical data, respectively. Group differences

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observed in the baseline data would be controlled as covariates in further analysis. Task performance was analyzed with two-way mixed repeated measure analysis of variance (ANOVA) to determine the differences within group and between group. Individual RMSE data was grouped into 9-trial blocks for the practice phase and retention test, and 3-trial blocks for the transfer test. A 2 Groups (SELF, YOKED) x 16 Blocks (B1 to B16) repeated measures ANOVA was conducted for the practice trials data. The retention and transfer test results, along with the error estimation data, were analyzed with 2 Groups (SELF, YOKED) x 2 Time (R1, R2; T1, T2) repeated measure ANOVA. Tukey's post hoc test would be performed if main effects or group-by-time interactions were found. For the motivation questionnaire score, 2 Group (SELF, YOKED) x 2 Time (D1, D2) repeated measure ANOVA was used to analyze the subscale of interest, perceived competence, and perceived autonomy separately to identify the motivational changes of participants after the practice phase, with α value set at 0.05. Since the two groups had significant differences in the baseline TMS outcome, the TMS data was analyzed with 2 Groups (SELF, YOKED) x 2 Times (D2, D7) repeated measure analysis of covariance (ANCOVA) whilst using the baseline TMS data as covariate to control for the baseline TMS difference. The significant level was set at $p < 0.05$ for all comparisons. In addition to p values, the effect sizes were calculated using the partial eta squared (η_p^2).

3.6 Sample size estimation

To our best knowledge, there was only one study investigated the effects of self-controlled practice for motor learning in people with PD. Therefore, we estimated the sample size using two related studies with similar study design and our preliminary data. Chiviacowsky and colleagues (2012) investigated the effect of autonomy in learning a

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balancing task in people with PD, and they found that the participants in the self-controlled condition showed better performance during the retention trials. [22] The effect size (partial eta square, η_p^2) of between group difference was 0.14. [22] With the power set at 0.8 and the two-tailed type I error set at 0.05, the calculated total sample size needed for our study is 36. The study by Carter and Ste-Marie (2017) investigated the effect of self-controlled practice on learning manipulandum tasks in healthy young adults, and participants who had task-relevant choices showed significant learning effects. [11] Based on the effect size ($\eta_p^2 = 0.14$) reported for performance accuracy, [11] the estimated sample size was 36 for our study. According to our preliminary data, when learning a finger-pressing trajectory-matching task, participants with a self-controlled feedback schedule had a trend of better motor learning effect than those receiving a yoked feedback schedule. The effect size f was 0.31, and the estimated sample size was 24.

Since the calculated sample sizes differed from the above-mentioned studies, we decided to use the average of calculated sample size, which would be 32 for this study. Considering the possible drop-out rate of 10% and the inadaptable data of TMS assessment, we planned to include 36 participants for this proposed study.

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Chapter 4: Results

4.1 Demographic characteristics

To date, thirty-five patients have been recruited into the study. One patient withdrew from the experiment due to health issues. Two participants in the SELF group were excluded from the analysis as suitable matches were unavailable in the YOKED group based on their demographic criteria. Therefore, a total of thirty-two participants diagnosed with PD completed the study and were included in the analysis (**Figure 4**). Sixteen were allocated to the self-controlled (SELF) group, and sixteen were allocated to the yoked (YOKED) group. The demographic characteristics of participants are presented in **Table 1**. All participants completed the practice sessions, immediate retention, and follow-up retention tests of the finger-pressing trajectory-matching task. Due to personal concerns, such as unwillingness to receive TMS or having physical conditions that was not suitable for TMS, only twenty-four participants (twelve participants in each group) completed the TMS assessments.

4.2 Finger-pressing trajectory-matching task performance

Acquisition phase. Repeated measure ANOVA revealed that there was a significant main time effect ($F_{15, 450} = 8.318$, $p < 0.001$, $\eta_p^2 = 0.217$), with no group-by-time interaction ($F_{15, 450} = 0.638$, $p = 0.844$, $\eta_p^2 = 0.021$) nor main group effect ($F_{1, 30} = 1.228$, $p = 0.277$, $\eta_p^2 = 0.039$). As shown in **Figure 5**, both groups improved significantly throughout practice sessions.

Retention phase. Analysis of the retention tests showed a significant time main effect ($F_{1, 30} = 7.142$, $p = 0.012$, $\eta_p^2 = 0.192$) and a significant group-by-time interaction ($F_{1, 30} = 4.604$, $p = 0.040$, $\eta_p^2 = 0.133$), but no group main effect ($F_{1, 30} = 0.004$, $p = 0.953$, $\eta_p^2 < 0.001$).

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Tukey's post hoc tests of the group-by-time interaction showed that the RMSE of the SELF group remained similar between D2 (3.25 ± 0.13) and D7 (3.31 ± 0.13) (p = 0.712), while the RMSE of the YOKED group increased significantly from 3.02 ± 0.13 on D2 to 3.56 ± 0.13 on D7 (p = 0.002). The retention performance of both groups is shown in **Figure 6**.

Transfer test. Analysis of the transfer tests showed no significant group-by-time interaction ($F_{1, 30}$ = 0.038, p = 0.846, η_p^2 = 0.001), group main effect ($F_{1, 30}$ = 0.221, p = 0.642, η_p^2 = 0.007), nor time main effect ($F_{1, 30}$ = 2.875, p = 0.100, η_p^2 = 0.087). The performance of both groups in the transfer tests is shown in **Figure 7**.

4.3 Strategy for requesting feedback

The questionnaire regarding participants' strategies for requesting feedback was added in the middle of the study, hence only 20 participants completed the questionnaire regarding their strategies for requesting feedback (**Table 2**). On D1, seven out of ten (70%) participants in the SELF group reported requesting feedback after perceived good and bad trials equally. One participant requested feedback after a perceived good trial, while the remaining participants (2/10) asked for feedback mostly after a perceived bad trial. In response to when/why they did not ask for feedback during the practice, three out of ten participants in the SELF group answered 'mostly after a perceived bad trial.' Seven participants reported a strategy not listed in the questionnaire (e.g., 'I knew my performance', 'I was uncertain about my performance', and 'The choice was used up'). In the YOKED group, nine out of ten (90%) participants indicated receiving feedback after the right trials. Only one participant reported not receiving feedback after the right trials and preferred to receive feedback after a perceived good trial.

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On D2, eight out of ten (80%) participants in the SELF group reported requesting feedback after perceived good and bad trials equally, while the remaining participant (2/10) asked for feedback mostly after a perceived good trial. Five participants in the SELF group did not request feedback after perceiving a bad trial, while the remaining participants reported either not requiring feedback after perceiving a good trial (1/10) or a strategy not listed in the questionnaire (4/10) (e.g., 'I knew my performance', 'I was uncertain about my performance', and 'The choice was used up'). In the YOKED group, six participants (60%) thought they received feedback after the right trials, while four participants did not receive feedback after the right trial. These participants reported a preference for receiving feedback either after perceived good trials (2/4) or after perceived good and bad trials equally (2/4).

The results showed that most participants preferred to receive feedback after good or bad trials equally. Besides, the participants preferred not to receive feedback after they perceived bad trials, when they confirmed their performances, or when they were uncertain about their performance.

4.4 Motivation questionnaire

The motivation questionnaire was assessed after practice trials on D1 and D2. **Figure 8** shows the results of interest, perceived competence, and perceived autonomy subscales, which were analyzed separately.

Interest. Analysis of the mean score in the interest subscale showed no significant group-by-time interaction ($F_{1, 18} = 0.071$, $p = 0.793$, $\eta_p^2 = 0.004$), group main effect ($F_{1, 18} = 0.474$, $p = 0.500$, $\eta_p^2 = 0.026$), and time main effect ($F_{1, 18} = 0.387$, $p = 0.542$, $\eta_p^2 = 0.021$).

Perceived competence. For the perceived competence subscales, repeated measure ANOVA showed no significant group-by-time interaction ($F_{1, 30} = 0.282$, $p = 0.599$, $\eta_p^2 =$

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0.009), group main effect ($F_{1, 30} = 0.340$, $p = 0.564$, $\eta_p^2 = 0.011$), nor time main effect ($F_{1, 30} = 0.980$, $p = 0.330$, $\eta_p^2 = 0.032$).

Perceived autonomy. As the perceived autonomy subscales, repeated measure ANOVA showed a significant time main effect ($F_{1, 30} = 8.161$, $p = 0.008$, $\eta_p^2 = 0.214$), suggesting that both groups perceived less autonomy on D2 as compared to D1. However, there was no significant group-by-time interaction ($F_{1, 30} = 0.792$, $p = 0.381$, $\eta_p^2 = 0.026$) nor group main effect ($F_{1, 30} = 0.088$, $p = 0.769$, $\eta_p^2 = 0.003$).

The results from the motivation questionnaire showed that participants in both the SELF and YOKED groups had similar degrees of interest and perceived competence in the task. Besides, both groups showed a similar trend of decreased perceived autonomy from D1 practice sessions to D2 practice sessions.

4.5 Error estimation score

Retention. The EE was performed after the completion of each trial of the retention tests on D2 and D7, and the results are shown in **Figure 9**. The repeated measure ANOVA showed no significant group-by-time interaction ($F_{1, 30} = 0.004$, $p = 0.948$, $\eta_p^2 < 0.001$), group main effect ($F_{1, 30} = 0.196$, $p = 0.661$, $\eta_p^2 = 0.006$), or time main effect ($F_{1, 30} = 1.176$, $p = 0.287$, $\eta_p^2 = 0.038$). Both groups seemed to have similar EE abilities at the immediate and delayed retention tests.

Transfer. As the mean EE scores of the transfer test, repeated measure ANOVA showed no significant group-by-time interaction ($F_{1, 30} = 0.349$, $p = 0.559$, $\eta_p^2 = 0.011$), group main effect ($F_{1, 30} = 0.377$, $p = 0.544$, $\eta_p^2 = 0.012$), or time main effect ($F_{1, 30} = 0.001$, $p = 0.974$, $\eta_p^2 < 0.001$) (**Figure 9**). Participants in the SELF and YOKED groups showed similar

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EE scores, suggesting that both groups seemed to have equal EE abilities at the immediate and delayed transfer tests.

4.6 Neurophysiological changes

The changes in corticomotor excitability in both groups are shown in **Figure 10**. Repeated measure ANCOVA of the resting MEP showed significant group-by-time interaction ($F_{1, 21} = 4.755$, $p = 0.041$, $\eta_p^2 = 0.185$). Tukey's post hoc tests showed that the resting MEP of the SELF group increased significantly from 561.04 ± 95.12 μV at D2 to 947.37 ± 147.61 μV at D7 ($p = 0.012$), while the YOKED group showed similar resting MEP between D2 with 780.82 ± 95.12 μV and D7 with 723.07 ± 147.61 μV ($p = 0.687$). There was no significant group main effect ($F_{1, 21} < 0.001$, $p = 0.988$, $\eta_p^2 < 0.001$) nor time main effect ($F_{1,21} = 1.158$, $p = 0.294$, $\eta_p^2 = 0.052$) (**Figure 10A**). As for the active MEP, the group-by-time interaction ($F_{1, 21} = 0.640$, $p = 0.433$, $\eta_p^2 = 0.030$), group main effect ($F_{1, 21} = 2.319$, $p = 0.143$, $\eta_p^2 = 0.099$) and time main effect ($F_{1, 21} = 0.810$, $p = 0.378$, $\eta_p^2 = 0.037$) did not show significance (**Figure 10B**). For the CSP results (**Figure 10C**), the analysis showed no significant group-by-time interaction ($F_{1, 21} = 0.251$, $p = 0.622$, $\eta_p^2 = 0.012$), group main effect ($F_{1, 21} = 0.048$, $p = 0.829$, $\eta_p^2 = 0.002$) nor time main effect ($F_{1, 21} = 3.310$, $p = 0.083$, $\eta_p^2 = 0.136$).

As for the intracortical excitability, repeated measure ANCOVA of the SICI ratio (**Figure 11A**) showed no significant group-by-time interaction ($F_{1, 21} = 1.840$, $p = 0.189$, $\eta_p^2 = 0.081$), group main effect ($F_{1, 21} = 0.035$, $p = 0.853$, $\eta_p^2 = 0.002$) nor time main effect ($F_{1, 21} = 2.041$, $p = 0.168$, $\eta_p^2 = 0.089$). For the ICF ratio (**Figure 11B**), the results showed no significant group-by-time interaction ($F_{1, 21} = 0.002$, $p = 0.961$, $\eta_p^2 = 0.000$), group main effect

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($F_{1, 21} = 1.354$, $p = 0.258$, $\eta_p^2 = 0.061$) and main time effect ($F_{1, 21} = 1.996$, $p = 0.172$, $\eta_p^2 = 0.087$).

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Chapter 5: Discussion

This study aimed to determine the effects of autonomy, by providing self-control over practice variables, on motor learning in patients with PD. The results showed that self-controlled practice facilitated motor learning, as demonstrated by better motor task retention from D2 to D7 in the SELF group than the YOKED group. Additionally, the TMS results showed that the corticospinal excitability was increased at D7 in the SELF group but not in the YOKED group, suggesting that self-controlled practice induced neuroplastic changes in individuals with PD.

Providing self-controlled feedback has been proven to enhance motor learning in healthy young adults. Our study further demonstrated that providing self-controlled feedback can also facilitate motor learning in patients with PD. During the acquisition phase, the SELF and the YOKED groups showed a significant reduction of RMSE, suggesting that the participants in both groups have acquired the finger-pressing trajectory-matching task through practice. When comparing the motor task performance between the two groups at the retention tests, the SELF group showed similar RMSE between D2 and D7, but the YOKED group had significantly increased RMSE on D7 as compared to D2 (**Figure 6**). This result suggested that the SELF group benefited from self-controlled feedback in learning a new motor task. Our results seemed to be consistent with previous studies conducted on non-disabled adults. A meta-analysis by Jimenez-Diaz and colleagues (2021), found that non-disabled young participants who exerted self-control over feedback during practice showed better ability to retain the performance after practice. [42] Only one study to date conducted by Chiviacowsky and colleagues (2012) assessed the effect of self-controlled practice on motor learning in PD, and found that providing self-controlled use of an assistant tool could enhance balance performance on a stabilometer for patients with PD. [22] This underscore the novelty and importance of our study, which was the second study examining the effect of

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self-controlled practice in patients with PD, and the findings supported the notion that self-controlled feedback during practice could indeed benefit motor learning for people with PD.

In addition to the retention performance, we also explored whether self-controlled practice could benefit patients with PD in the transfer ability by testing them a new waveform. The results of the transfer test on D2 and D7 did not show any significant group difference, suggesting that self-controlled practice did not benefit patients with PD in the transfer test. This observation differed from previous studies conducted on healthy young adults, which showed that participants learned a motor task with self-controlled practice demonstrated superior motor performance at transfer tests. [11,17,44,46] We hypothesized that the differences in findings between people with PD and non-disabled young adults was attributed to the inherent motor learning impairment in people with PD, who often struggle to extend learning effects to other conditions. [4] As demonstrated in a study by Onla-or and Winstein (2008), participants with PD retained their motor learning effects only when tested under the same conditions as their practice, highlighting the context-specific nature of motor learning in this population. [80] Additionally, Lee and colleagues (2016) found that patients with PD had greater performance decline compared to non-disabled adults when testing conditions differed from the practice conditions, suggesting a higher degree of contextual dependency in motor learning than non-disabled adults. [6] Therefore, the limited effect of self-controlled practice for the transfer tests might be related to the motor learning deficits in PD.

To explore whether the benefit of self-controlled practice was due to enhanced 'motivation' in people with PD, we inquired the participants on their strategies in choosing when to receive feedback. The interview results showed that most participants preferred receiving feedback after perceiving both good and bad trials equally (**Table 2**). This observation was different from previous studies conducted on healthy young adults. [46,81] A study by Chiviacowsky and colleagues (2002) found that healthy young participants preferred

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to receive feedback when they perceived fewer errors being made or higher accuracy being achieved when learning a sequential timing task. [46] This observation suggested that healthy young adults utilized feedback to enhance their perceived competence as well as their motivation in motor learning. [46,81] On the other hand, a study by Carter and Patterson (2012) reported that elderly participants utilized a different strategy for requesting feedback from healthy young adults when learning to push and release a slider motor task. [49] It was found that while healthy young adults requested feedback after they perceived good trials, the elderly participants decided to receive feedback after both good and bad trials equally. [49] The requesting strategy of the elderly was similar to what we have observed in patients with PD of this study, suggesting that the participants might not use the feedback to enhance their competence and motivation but for motor learning guidance instead. It has been proposed that the strategy for requesting feedback might be related to the participants' information processing abilities. [82] Patients with PD are known to have a decline in cognitive function and working memory capacity, [28] and have been suggested to rely on external feedback in their learning process. [4] This might clarify the preference of patients with PD for receiving feedback after both good and bad trials in learning a motor task.

To further investigate whether self-controlled practice would influence motivation, we additionally asked the participants to complete the motivation questionnaire (**Appendix 3**) after completion of practice on both days. The results again did not find any significant group differences in interests, perceived competence, and perceived autonomy of the questionnaire. This finding was different from that has been reported by Chiviacowsky and colleagues (2012), who found a significantly higher perceived motivation for the self-controlled practice group as compared to the yoked group in participants with PD. [22] We speculate that the difference in findings might be due to the motor task being practiced. Since people with PD frequently struggle with balance problems and are fear of falling, [83] it is possible that the

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balance task used by Chiviacowsky and colleagues (2012) was more challenging to the participants, and they might have lower competence in performing the task. [22] Hence, providing the opportunity to self-control the practice condition might significantly impact their competence and motivation. Distinct from the balance task, the finger-pressing trajectory-matching task used in the current study had less threat to their balance. Additionally, the participants could not directly discern their performance, thus would rely more on external feedback to confirm their performance. It was, hence, possible that the self-controlled feedback provided more informational support in this process but limited its contributions to motivational support.

Out of our expectations and different from what has been observed in previous studies, a decrease in perceived autonomy was noted in both groups from the practice sessions in D1 to D2. This might be related to the restricted number of feedback choices in this study. Our study provided participants with faded feedback frequency in the practice sessions and required the participants to use up all the choices. Since feedback frequencies on D2 (50% and 25%) were less than D1 (100% and 75%), the participants might feel having less amount of chance to control their choices and actions, which potentially would reduce their sense of autonomy. It has been found that even with healthy young adults, restricting the number of choices over the feedback schedule would influence the effect of self-controlled practice on autonomy and motivation. [10,11,84] On the other hand, the study conducted by Chiciacowsky and colleagues (2012) did not restrict the number of choices for participants with PD to use an assistive device during the stabilometer task, and they observed an increased motivation after self-controlled practice. [22] Hence, we speculated that the lack of group differences in perceived autonomy was probably a result of the restricted choices for feedback in this study.

doi:10.6342/NTU202401486

When using the error estimation ability to probe whether self-controlled practice could potentially enhance cognitive processing in people with PD, the results showed no significant differences between the two groups. This finding differed from the study by Carter and Ste-Marie (2017), who showed that learners with self-controlled feedback had better error estimation ability of their motor performance regarding the movement time goal at the retention test than those who received yoked feedback. [11] One possible reason could be attributed to the different difficulty level of error estimation between Carter and Ste-Marie's study (2017) and our study. Carter and Ste-Marie (2017) asked participants to estimate their movement time errors, whereas our study required participants to estimate their RMSE regarding task performance, encompassing both time and force variables. [11] The multidimensional nature of error estimation in our study might be too challenging for participants with PD. In fact, we found that participants showed a trend of better error estimation after D2 practice than after D1 practice, suggesting they might be able to improve in the error estimation. Nevertheless, participants with PD might require more practice to obtain a better error estimation ability, and it might not be directly related to self-controlled practice.

It should also be noted that the participants of Carter and Ste-Marie's study were healthy young adults, while those in our study were individuals with PD. Previous studies have found that people with PD have impaired motor prediction ability as compared with non-disabled adults. [85,86] Using a two-step test, Kawasaki and colleagues (2018) asked the participants to estimate the two-step distance they could reach with maximum effort. [86] Subsequently, they performed an actual two-step trial, and the estimation accuracy was calculated with the difference between the estimated distance and the actual distance. [86] It was found that patients with PD overestimated their stepping distance more frequently than the healthy elderly. [86] indicating an impairment in the error estimation ability in PD. [86]

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Neuroimaging studies have shown that error estimation ability is related to the activation of the frontal lobe. [87,88] Hence, the reduced effectiveness of self-controlled practice on error estimation in PD might be attributed to the impaired frontostriatal circuitry. [89] Of note, since this study was the first to investigate whether the benefit of self-controlled practice could be explained by increased cognitive processing (as demonstrated by enhanced error estimation ability), more studies in this field are needed to support our current finding.

According to the questionnaire and error estimation results, our study did not identify the motivation and cognitive effects of self-controlled practice in PD. Motivation deficit and cognitive impairment co-exist, as induced by dopamine depletion, in people with PD. [90] It might be difficult to separately identify their motivation and cognitive changes induced by self-controlled practice through behavioral measurements. Furthermore, our study examined the learning effect of participants with PD during their medication "ON" time, which might be a confounding factor related to their motivation and cognitive ability. [33] [34] These factors might, therefore, be related to our findings that support neither the motivation nor the cognitive hypothesis.

Apart from the behavioral outcomes, this study is the first to use TMS to identify the possible neuro-mechanisms associated with self-controlled practice in people with PD. Although testing the error estimation ability did not suggest increased cognitive processing after self-controlled practice, the TMS results revealed some interesting insights into the neuroplastic changes associated with self-controlled practice in patients with PD. It was found that the SELF group significantly increased in resting MEP from D2 to D7, which was not observed in the YOKED group. This increase in resting MEP indicated greater corticomotor excitability, which might be a net result of decreased inhibition and increased excitation of the intracortical neurons and the corticospinal tract. [21] The TMS findings and the behavioral results suggested that the benefit of self-controlled practice can be revealed at the

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delayed retention test. A study by Smyth and colleagues (2010) also found that the healthy young participants who learned better in a waveform-tracking task had an increased resting MEP of the primary motor cortex (M1) at retention. [61] Similarly, Lin and colleagues (2011) observed that non-disabled young adults who performed better at the retention test of a serial reaction time task also had a greater increase in M1 corticomotor excitability. These studies revealed that better retention of the learned motor task was accompanied by an increase in M1 excitability, which could represent a more efficient memory retrieval. [66] It had been suggested that increased corticospinal excitability could reflect the long-term potentiation-like mechanisms through motor task acquisition and play an important role in the consolidation of motor learning. [91,92] As the corticospinal excitability changes occurred without further practice, it was hypothesized that the motor memory developed during self-controlled practice continued to evolve with time, resulting in stronger memory consolidation and better corticospinal excitability.

To date, this is the first experiment conducted with TMS assessment to explore the possible neural mechanism of self-controlled practice in patients with PD. Previous studies using fMRI and EEG revealed that perceiving choice or autonomy induced the activation of the frontal region (i.e., anterior cingulate cortex and prefrontal cortex). [13] The anterior cingulate cortex (ACC) plays a particular role in detecting conflicts between representations, [93] while the prefrontal cortex corresponds to the action selection. [94] This suggested that self-controlled practice might facilitate a higher level of cognitive processing in motor learning. Our experimental results indicated that participants with PD improved in motor learning with self-controlled feedback and showed increased corticospinal excitability. However, this enhanced corticospinal excitability did not correspond with the measured error estimation ability, which was related to the activation of ACC. [87] Therefore, we posited that the brain regions associated with self-controlled practice in PD might differ from those involved in

doi:10.6342/NTU202401486

error estimation. As the measurement of TMS might reflect cognitive processing, [62] the TMS findings in our study might partly explained the cognitive hypothesis of self-controlled practice. A recent model suggested that decision-making and action selection might occur in parallel, as evidenced by changes in corticospinal excitability. [95] This finding could help elucidate the conflicting outcomes observed in self-controlled practice among patients with PD, where there was significant improvement in motor learning but no corresponding enhancement in error estimation abilities. Given that decision-making processing involves brain regions distinct from those implicated in error estimation, it is hypothesized that self-controlled practice might activate the decision-making process in PD patients, thereby influencing their motor control and potentially enhancing motor learning outcomes.

This study has several main limitations. First of all, we only used TMS to observe changes in corticomotor excitability associated with self-controlled practice. This approach limited our understanding of the specific brain regions involved in self-controlled practice in PD. Since this is the first study to date that used an imaging tool to assess neurophysiological changes induced by self-controlled practice in PD, more studies are needed in this field to support our current findings. Second, the psychometric properties of questionnaires (e.g., the motivation questionnaire and the questionnaire regarding participants' strategy for requesting feedback) in participants with PD were yet to be identified. As we did not find a questionnaire designed to assess the motivation of people with PD, we chose to translate several questions from the widely used motivation-related questionnaire for healthy young adults. [11,53] The difference in population might, therefore, influence the validity of the questionnaire. To effectively identify the motivation changes in participants with PD, further studies should select or design questionnaires with greater psychometric properties in this population. The third limitation of our study was that the participants with PD were assessed during their medication "ON" phase. It was suggested that dopamine might enhance

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motivation in people with PD to engage in motor tasks. [33] Participants involved in the motor task during the dopamine "ON" phase might somehow limit the motivation questionnaire sensitivity to explore the motivational effect of self-controlled practice. As we did not measure participants' learning effect under their medication "OFF" phase, we could not exclude the possible confounding effect of dopamine medication in self-controlled practice. Thus, more studies are needed to determine whether dopamine medication state is a factor influencing the motivation effect of self-controlled practice in people with PD.

Another potential limitation of the study was related to the design of the finger-pressing trajectory-matching task. Due to equipment limitations, our experiment only analyzed the RMSE with participants' motor performance within the target time. As participants' finger-pressing might exceed the target time, our analysis method cannot accurately calculate the overall error values. Therefore, more studies are needed to further examine the self-controlled practice effect in people with PD. Additionally, the faded feedback might be one of the limitations of the study. Previous experiments in self-controlled practice have found that limiting the number of choices available to participants can undermine their motivation to engage in the task. [11,84] We specifically limit the number of feedback for the participants to choose for 2 reasons. First, people with PD are known to rely heavily on external cues to perform motor tasks. [4] If the number of feedback was not limited to the patients, it was possible that the participants would choose to receive feedback after every practice trial, which could potentially confound our results. Second, since feedback is a key factor affecting motor learning, not controlling the number of feedback among subjects might lead to different learning effects, which in turn would also constrain the interpretation of the findings. Due to the above reasons, we chose to control the number of feedback that the participants can request to investigate the effect of self-controlled practice on motor

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learning. Nevertheless, more studies are needed to determine whether limiting the number of choices is a factor influencing the perceived autonomy and motivation in people with PD.

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Chapter 6: Conclusion

This is the first study to investigate the behavioral and neurophysiological effects of self-controlled practice on motor learning in people with PD. The results of this study showed that self-controlled practice was beneficial in facilitating motor learning in individuals with PD. Additionally, an increased resting MEP amplitude was observed at the delayed retention test, suggesting a greater corticospinal excitability. Clinical implications will be that clinicians may consider incorporating self-controlled practice into the rehabilitation regimen, such as providing choices in therapeutic exercise selection and setting goals collaboratively with patients, to enhance the training effects for people with PD.

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Figures

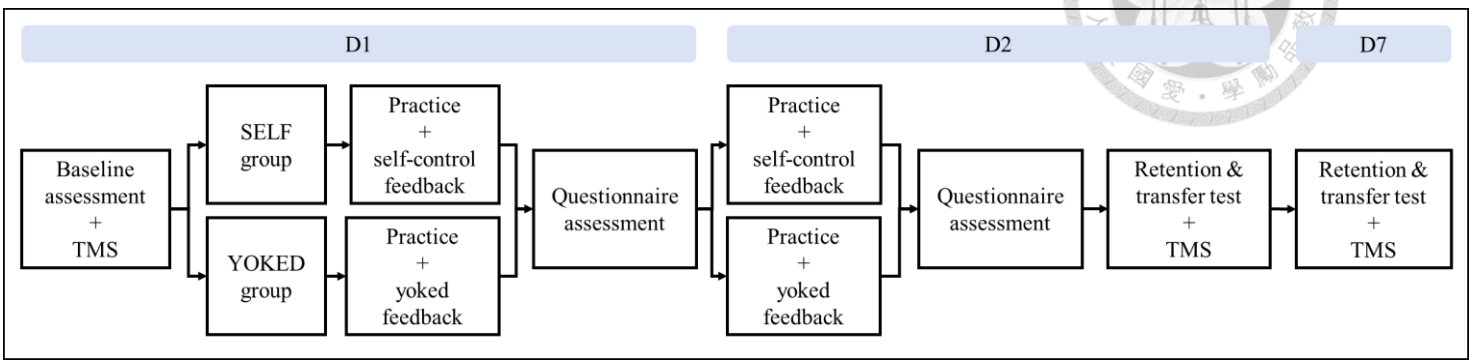

Figure 1. Study procedure of the experiment

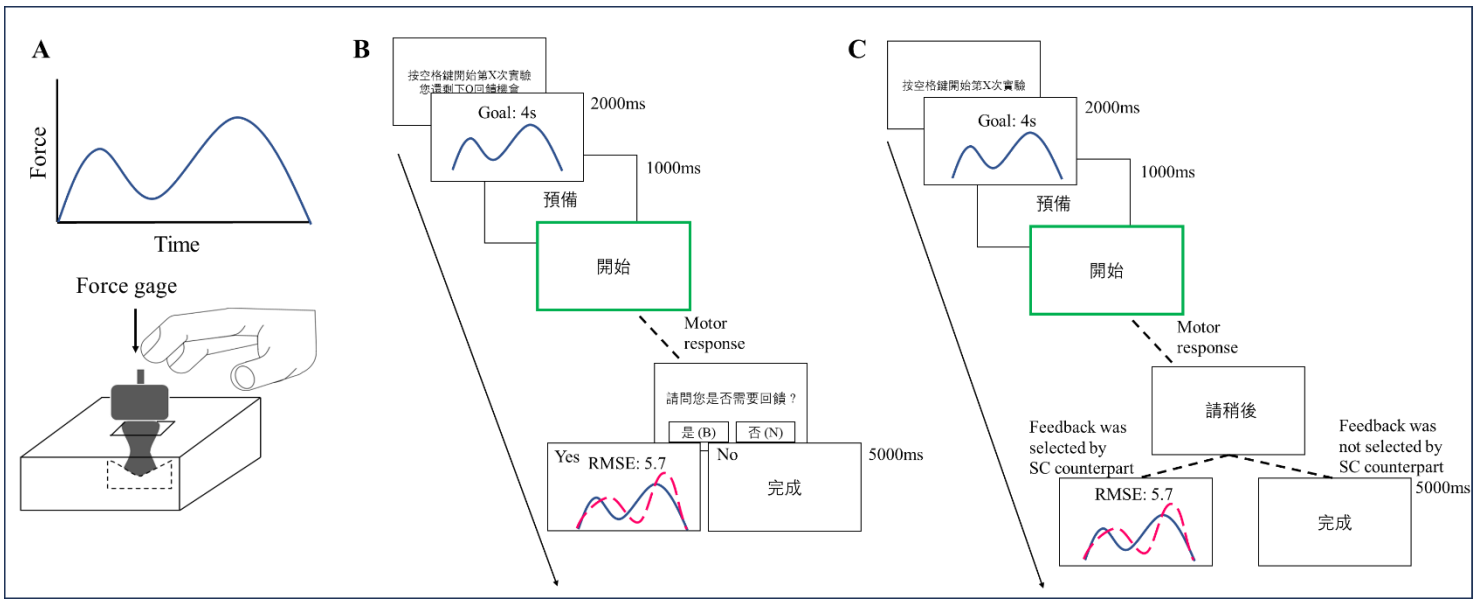

Figure 2. Schematic representation of the finger-pressing trajectory-matching task. **A** The participants reproduced the waveform trajectory with two rapid fingers downward pressing. **B** The sequence of events during the acquisition phase for the self-control group. **C** The only difference for the yoked group is that no feedback selection was provided. The feedback will be shown in a manner that corresponds to their counterpart in the self-control group.

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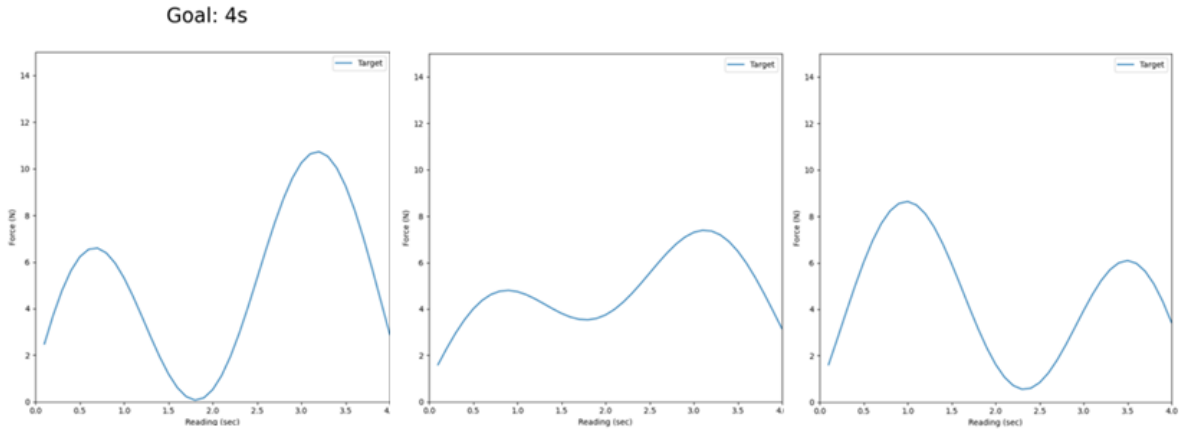

Figure 3. Illustration of the experiment waveforms. In each trial, one of the three template trajectories with specific time and force requirements in each was displayed to the participant.

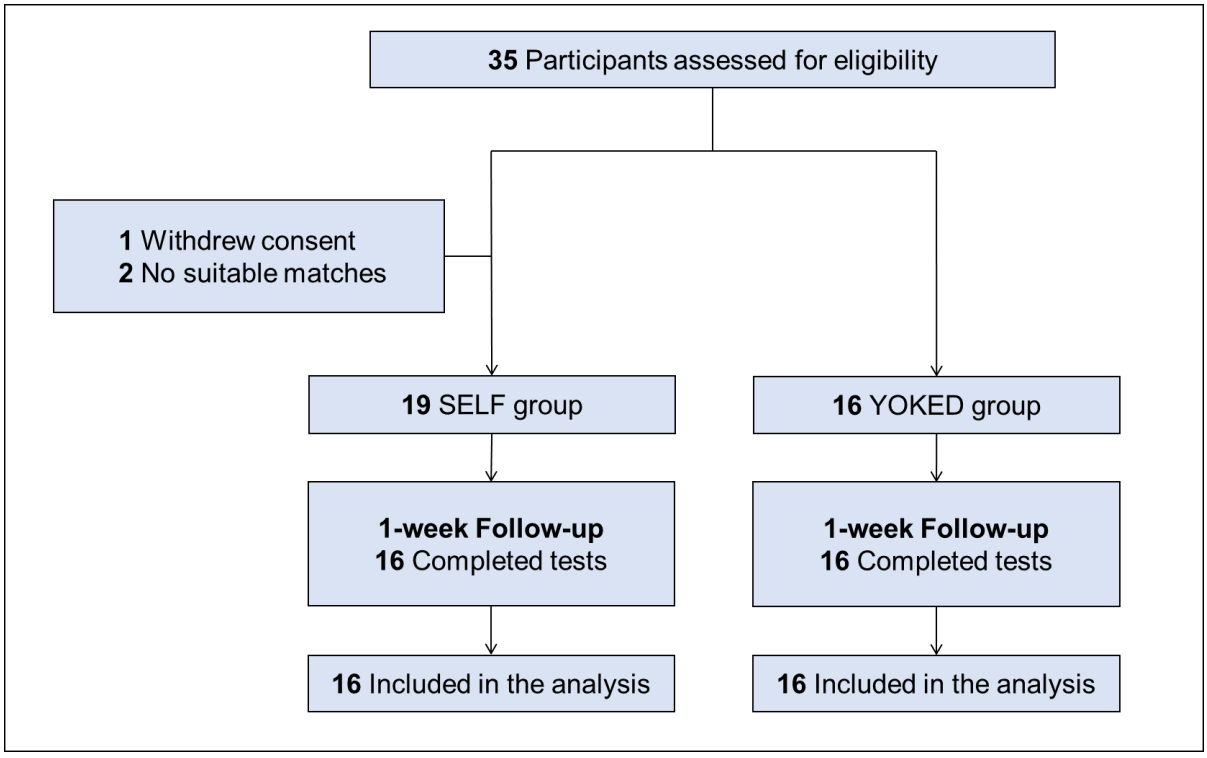

Figure 4. Flow chart of the study

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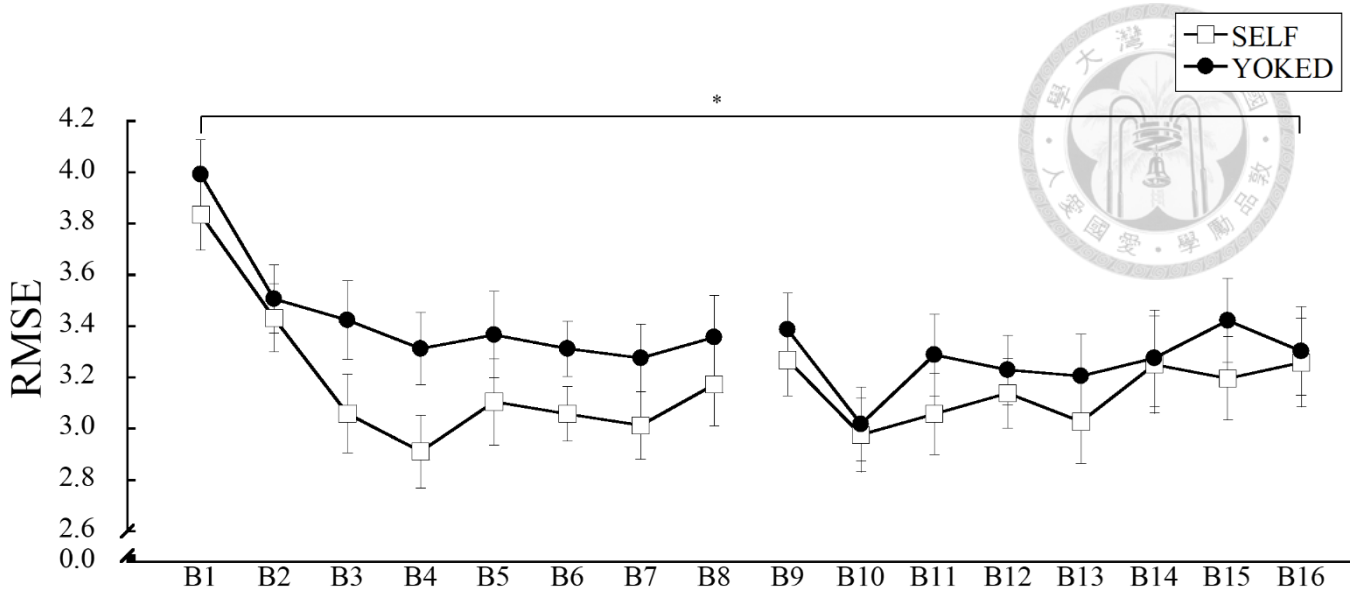

Figure 5. RMSE of practice performances of both groups. The range bar represents standard error. $^{*}p < 0.05$ of main time effect.

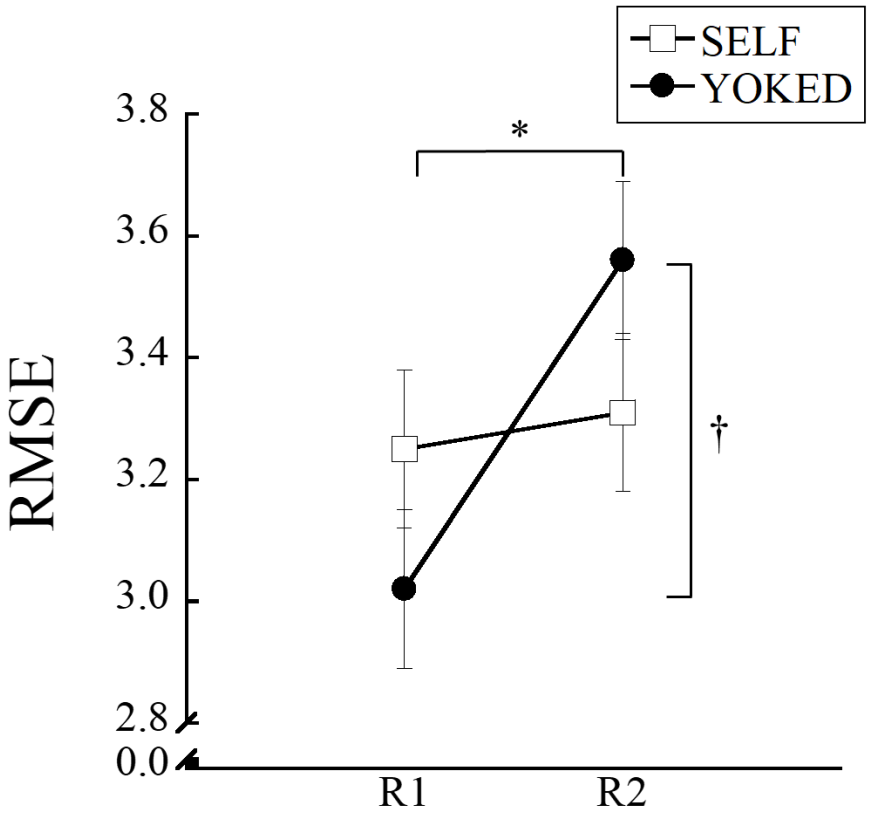

Figure 6. RMSE of retention performances of both groups. The range bar represents standard error. $^{*}p < 0.05$ of main time effect. $^{\dagger}p < 0.05$ of group-by-time interaction.

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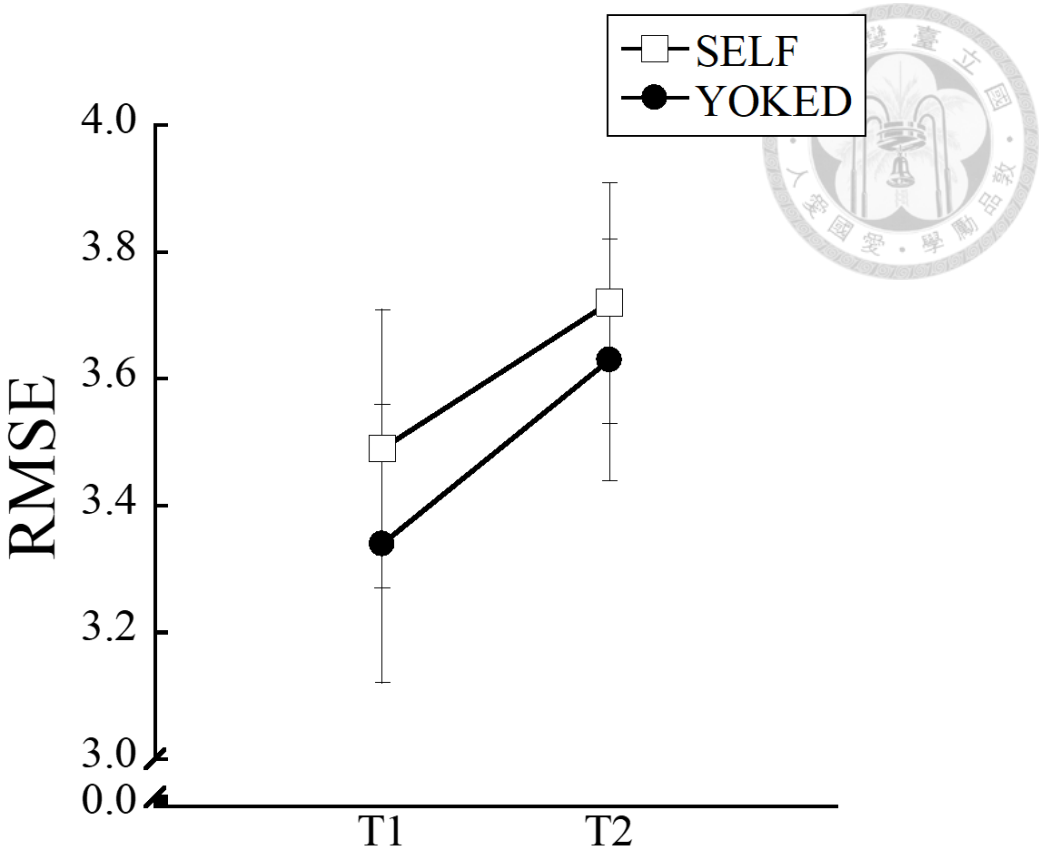

Figure 7. RMSE of both groups at the transfer tests. The range bar represents standard error.

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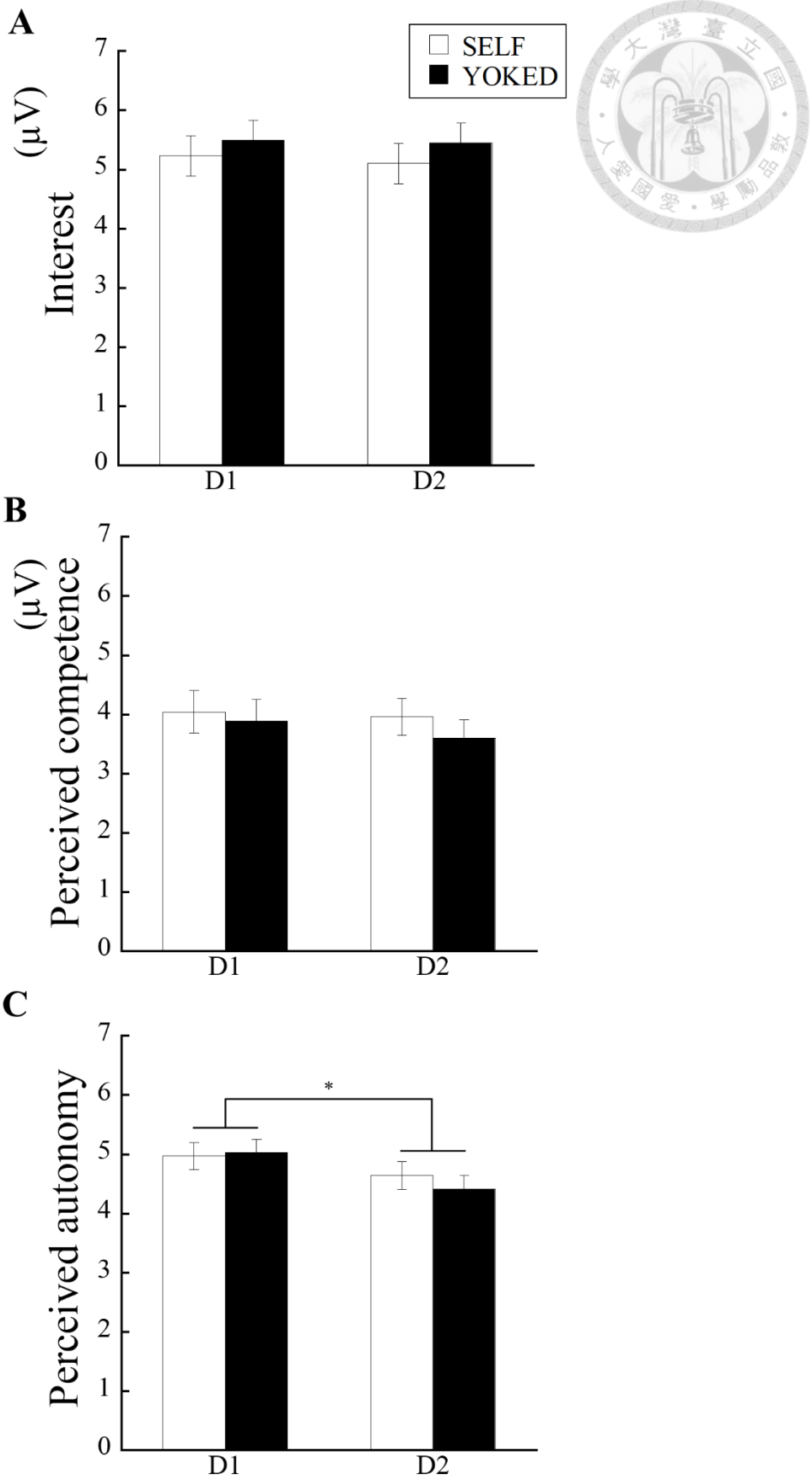

Figure 8. Motivation questionnaire scores of both groups. The range bar represents standard error. $^{*}p < 0.05$ of main time effect.

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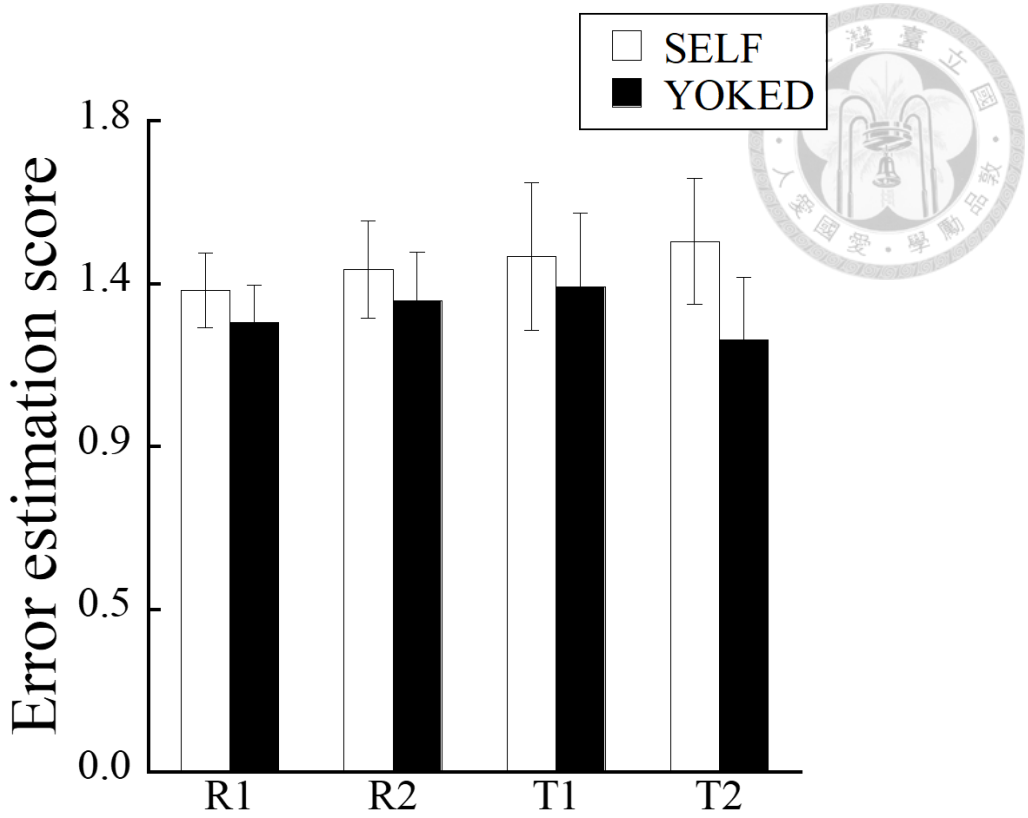

Figure 9. Error estimation scores of both groups. The range bar represents standard error.

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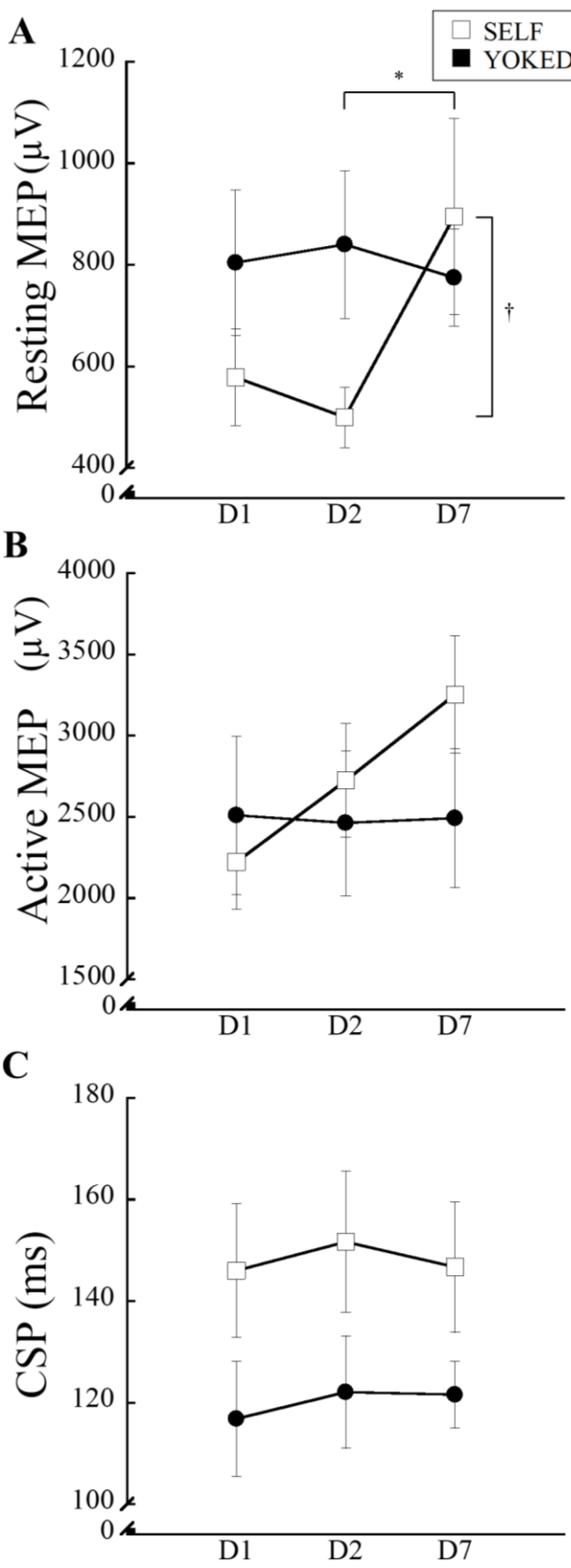

Figure 10. Single pulse TMS of MEP in both groups. The range bar represents standard error**.** *$p < 0.05$ of main time effect. †$p < 0.05$ of group-by-time interaction.

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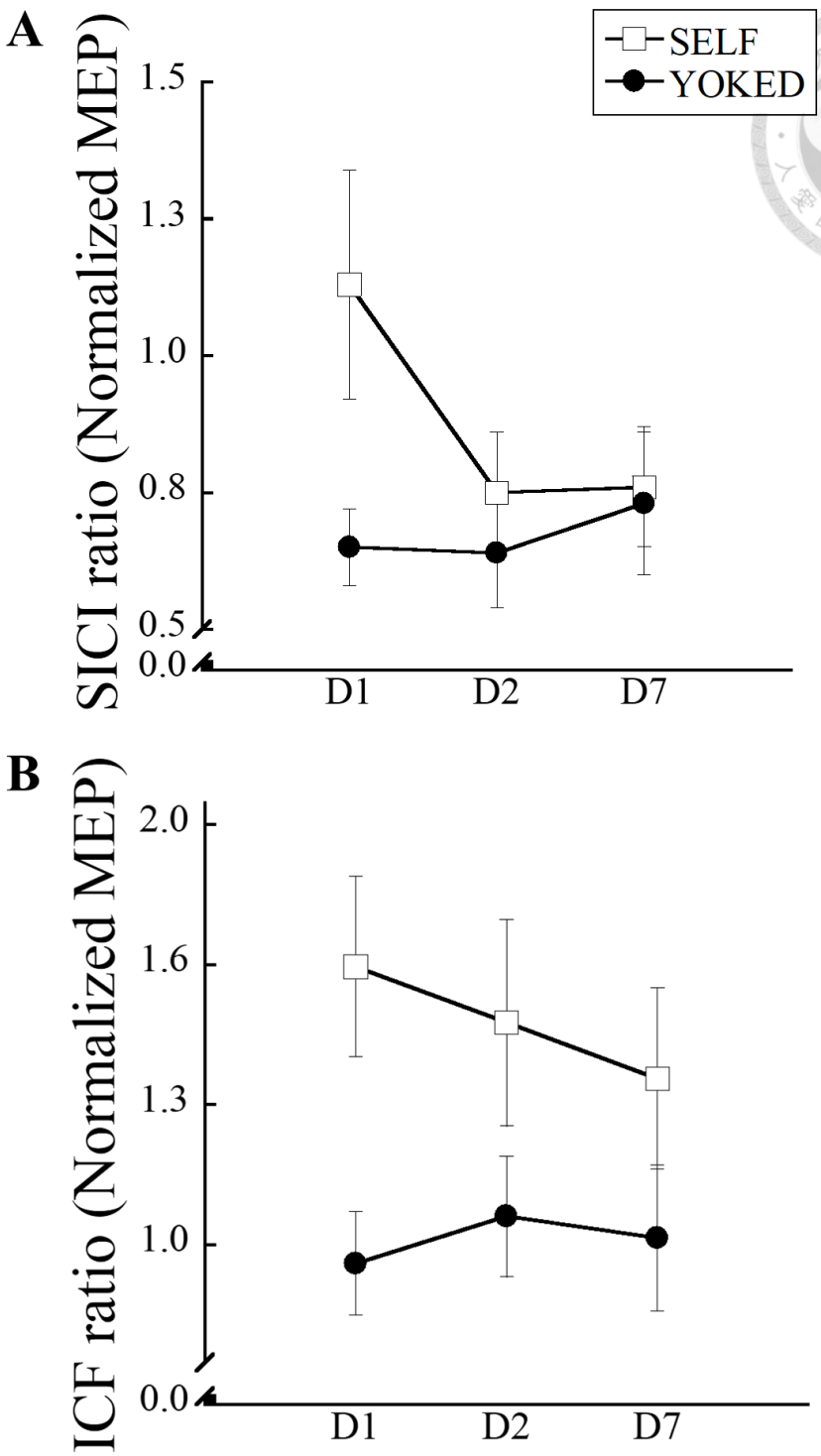

Figure 11. Paired-pulse TMS of SICI ratio in both groups. The range bar represents standard error**.**

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Tables

Table 1. Demographic characteristics of participants in both groups

	SELF group (n=16)	YOKED group (n=16)	Statistics
Age (years)	67.7 ± 1.75	67.9 ± 2.00	$p = 0.944$
Gender (M/F)	(10/6)	(10/6)	$p = 1.000$
Disease duration (years)	6.2 ± 1.15	7.6 ± 1.44	$p = 0.447$
Modified Hoehn and Yahr stage	2.4 ± 0.1	2.6 ± 0.1	$p = 0.838$
More affected side (L/R)	(4/12)	(8/8)	$p = 0.144$
UPDRS-III	22.3 ± 2.59	23.0 ± 2.65	$p = 0.854$
Levodopa equivalent dosage (mg)	611.6 ± 117.82	476.9 ± 83.89	$p = 0.359$
HADS-A	1.2 ± 0.51	3.1 ± 0.78	$p = 0.057$
HADS-D	3.4 ± 0.76	4.8 ± 0.51	$p = 0.145$
MoCA	28.2 ± 0.37	27.5 ± 0.40	$p = 0.214$

Abbreviations: UPDRS-III, Part III of the Unified Parkinson's Disease Rating Scale; HADS-A, Anxiety subscale of Hospital Anxiety and Depression Scale; HADS-D, Depression subscale of Hospital Anxiety and Depression Scale; MoCA, Montreal Cognitive Assessment. Values are presented as mean ± standard error of mean for continuous variables and frequency for categorical variables.

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Table 2. Results of the interview regarding participants' strategy for requesting feedback

Groups	Number of responses	
SELF group (n=10)	**D1**	**D2**
您在練習過程中何時/為何請求回饋？		
a）大多數是在感知到良好的表現後	1	2
b）大多數是在感知到不好的表現後	2	0
c）在感知到良好和不好的表現後一樣	7	8
d）隨機	0	0
e）其他	0	0
您在練習過程中何時/為何沒有請求回饋？		
a）大多數是在感知到良好的表現後	0	1
b）大多數是在感知到不好的表現後	3	5
c）在感知到良好和不好的表現後一樣	0	0
d）隨機	0	0
e）其他	7	4
YOKED group (n=10)		
您是否認為在適當的嘗試之後（時機）接收到回饋？		
a）是	9	6
b）否	1	4
如上題為否，您希望在何時收到回饋？		
a）大多數是在感知到良好的表現後	1	2
b）大多數是在感知到不好的表現後	0	0
c）在感知到良好和不好的表現後一樣	0	2
d）隨機	0	0
e）其他	0	0

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Table 3. Corticomotor excitability measured by transcranial magnetic stimulation of the 2 groups.

Outcome	D1-test	D2-test	D7-test
Resting MEP (μV)			
SELF	578.56 ± 95.40	499.40 ± 59.03*	895.53 ± 192.86*
YOKED	804.28 ± 143.71	839.96 ± 146.21	774.92 ± 95.50
Active MEP (μV)			
SELF	2221.69 ± 291.78	2725.09 ± 349.13	*3254.34 ± 361.94*
YOKED	2510.21 ± 488.63	2462.09 ± 447.64	*2492.92 ± 427.56*
CSP (ms)			
SELF	146.03 ± 13.19	151.71 ± 13.88	*146.71 ± 12.86*
YOKED	116.82 ± 11.37	122.07 ± 11.07	*121.57 ± 6.59*
SICI ratio			
SELF	1.13 ± 0.21	0.75 ± 0.11	*0.76 ± 0.11*
YOKED	0.65 ± 0.07	0.64 ± 0.10	*0.73 ± 0.13*
ICF ratio			
SELF	1.49 ± 0.20	1.34 ± 0.22	*1.30 ± 0.18*
YOKED	0.84 ± 0.10	1.05 ± 0.17	0.84 ± 0.14

Abbreviations: MEP, motor evoked potentials; CSP, cortical silent period; SICI, short-interval intracortical inhibition; ICF, intracortical facilitation.
Values are presented as mean ± standard error.
*Significant time difference between D2 and D7 test ($p < 0.05$).

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Appendix

Appendix 1. Clinical Trial/Research Approval by the Research Ethics Committee of National Taiwan University Hospital

國立臺灣大學醫學院附設醫院C研究倫理委員會

Research Ethics Committee C
National Taiwan University Hospital
7, Chung-Shan South Road, Taipei, Taiwan 100, R.O.C
Phone: 2312-3456 Fax: 23951950

臨床試驗/研究許可書

許可日期：2023 年 5 月 29 日

倫委會案號：202304047RINC
計畫名稱：自主權對於巴金森氏症患者動作學習之影響。
試驗機構：國立臺灣大學
部門/計畫主持人：物理治療學系　李亞芸副教授
上述計畫業經 2023 年 5 月 29 日本院 C 研究倫理委員會第 168 次會議審查同意，符合研究倫理規範。本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。
本臨床試驗/研究許可書之有效期限為 1 年(自 2023 年 5 月 29 日至 2024 年 5 月 28 日止)，計畫主持人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，並應於到期日至少 6 週前提出持續審查申請表，本案需經持續審查，方可繼續執行。

主任委員 蔡甫昌

Clinical Trial/Research Approval

Date of approval: May 29, 2023

NTUH-REC No.：202304047RINC
Title of protocol：Influence of autonomy on motor learning in people with Parkinson's disease.
Trial/Research Institution：National Taiwan University
Department/ Principal Investigator：Department of Physical Therapy / Associate Professor Ya-Yun Lee

The protocol has been approved by the 168th meeting of Research Ethics Committee C of the National Taiwan University Hospital on May 29, 2023. The committee is organized under, and operates in accordance with, the Good Clinical Practice guidelines and governmental laws and regulations.

The duration of this approval is one year (from May 29, 2023 to May 28, 2024). The investigator is required to report Serious Adverse Events and Unanticipated Problems in accordance with the governmental laws and regulations and NTUH requirements and apply for a continuing review not less than six weeks prior to the approval expiration date.

Daniel Fu-Chang Tsai, M.D. Ph.D. Daniel Fu-Chang Tsai
Chairman
Research Ethics Committee C

1

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Appendix 2. Questions regarding the strategy of participants for requesting feedback

自主組

您在練習過程中何時/為何請求回饋？

a）大多數是在感知到良好的表現後

b）大多數是在感知到不好的表現後

c）在感知到良好和不好的表現後一樣

d）隨機

e）其他

您在練習過程中何時/為何沒有請求回饋？

a）大多數是在感知到良好的表現後

b）大多數是在感知到不好的表現後

c）在感知到良好和不好的表現後一樣

d）隨機

e）其他

共軛組

您是否認為在適當的嘗試之後（時機）接收到回饋？

a）是

b）否

如上題為否，您希望在何時收到回饋？

a）大多數是在感知到良好的表現後

b）大多數是在感知到不好的表現後

c）在感知到良好和不好的表現後一樣

d）隨機

e）其他

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Appendix 3. The motivation questionnaire

		完全不同意	不同意	稍微不同意	中立	稍微同意	同意	完全同意
1.	我認爲我在任務中表現良好。	☐	☐	☐	☐	☐	☐	☐
2.	在練習過程中，我能夠自由選擇並呈現我的想法。	☐	☐	☐	☐	☐	☐	☐
3.	我認爲我在任務中的表現比其他人好。	☐	☐	☐	☐	☐	☐	☐
4.	在練習過程中，我感到被控制。	☐	☐	☐	☐	☐	☐	☐
5.	完成任務後，我感到自己很能幹。	☐	☐	☐	☐	☐	☐	☐
6.	我喜歡這個任務。	☐	☐	☐	☐	☐	☐	☐
7.	我很滿意自己在任務中的表現。	☐	☐	☐	☐	☐	☐	☐
8.	在練習過程中，我沒有太多機會可以做選擇。	☐	☐	☐	☐	☐	☐	☐
9.	我很擅長這項任務。	☐	☐	☐	☐	☐	☐	☐
10.	這個任務很有趣。	☐	☐	☐	☐	☐	☐	☐
11.	我無法做好這項任務。	☐	☐	☐	☐	☐	☐	☐
12.	我覺得這是一個無聊的任務。	☐	☐	☐	☐	☐	☐	☐
13.	在練習過程中，我感到自己的選擇和想法有被納入考量。	☐	☐	☐	☐	☐	☐	☐
14.	這個任務無法吸引我的注意。	☐	☐	☐	☐	☐	☐	☐

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