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Review

Relearning of writing skills in Parkinson's disease: A literature review on influential factors and optimal strategies

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ABSTRACT

Patients with Parkinson's disease (PD) suffer from severe motor symptoms which can only be partly alleviated by means of dopaminergic medication. Motor rehabilitation, i.e. relearning of a known motor skill through intensive practice, can be an effective and lasting therapeutic supplement in chronic neurodegenerative diseases. Recent studies on motor learning in PD provide insights for the development of optimal motor rehabilitation strategies, with a particular focus on achieving consolidated learning and retention. In this review, findings from the last couple of years are discussed with specific interest in the potential benefits from cueing and feedback strategies as means to achieve lasting changes. In addition, current neuroscientific insights on the impact of dopamine and cognitive functioning on learning are summarized. Finally, the knowledge on these topics is combined to propose an optimal strategy for relearning of writing skills in PD, a frequently reported motor deficit also known as micrographia.

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1. Introduction

Parkinson's disease (PD) is a common neurodegenerative disorder caused by the loss of dopaminergic neurons in the pars compacta of the substantia nigra and other neurological systems, leading to a combination of motor and non-motor symptoms (Jankovic, 2008). One of the first symptoms often is micrographia. Wagle Shukla et al. (2012) defined it as '*an impairment of a fine motor skill manifesting mainly as a progressive reduction in amplitude during a writing task*'. Recently, it was shown by using objective criteria that 63% of patients with PD suffer from micrographia (Wagle Shukla et al., 2012). Fig. 1 shows a typical sample of handwriting impairments in PD, compared to a healthy person collected during our pilot experiments. Both participants were asked to copy as much as they could of a Dutch text on a blank page within

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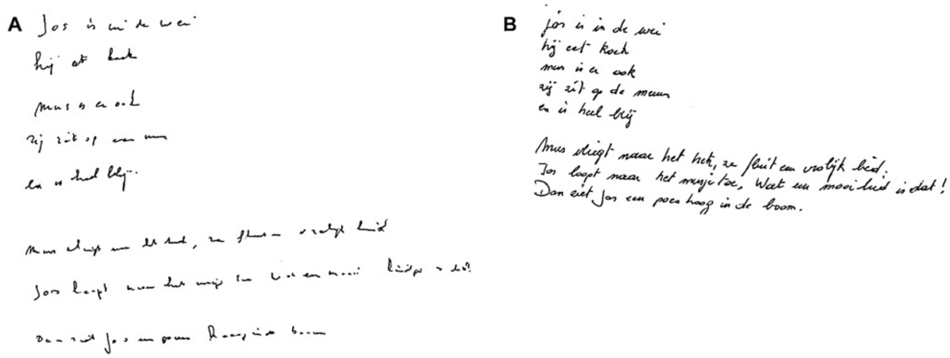

Fig. 1. Example of the handwriting of a PD patient and healthy control. (A) Writing example of a 54-year old male with idiopathic Parkinson's disease, Hoehn & Yahr stage III. Writing was performed while on dopaminergic medication and with deep-brain stimulator on. (B) Writing example of a 52-year old healthy female.

5 min. *Panel B* shows a healthy control who adopted a naturally small letter size. However, the handwriting is legible in contrast to the handwriting of the PD patient, as is shown in *Panel A*. Furthermore, it has been reported that writing velocity and sentence length are reduced in PD and that there is an increase in interruptions and variability of movement size (Broderick et al., 2009; Lange et al., 2006; Ponsen et al., 2008; Van Gemmert et al., 1999, 2003). It has been shown that dopaminergic medication and subthalamic nucleus stimulation can only partially improve these writing problems (Lange et al., 2006; Tucha et al., 2006), suggesting that additional therapeutic strategies are warranted. As an adjunct to pharmaceutical management of the disease, motor rehabilitation can play an important role in improving quality of life of PD patients (Goodwin et al., 2008; Keus et al., 2007, 2009). According to the World Health Organizations' (WHO) International Classification of Functioning, Disability and Health (ICF), rehabilitation can be considered as a health strategy that aims '*to enable people with health conditions, experiencing or likely to experience disability, to achieve and maintain optimal functioning in interaction with the environment*' (Stucki, 2005).

Motor learning entails an important component of rehabilitation. Doyon et al. (2009) described two types of motor learning: (i) motor sequence learning (MSL), which is a process by which a series of movement elements become an entity through practice; and (ii) motor adaptation (MA), which is a process that requires participants to adapt to environmental changes. The process of motor learning consists of several phases, starting with the acquisition of a motor skill, followed by automatization, transfer and retention of what was learned. These last three processes are considered hallmarks of consolidation of motor learning. Based upon brain imaging studies, Doyon et al. (2009) presented a model of normal motor skill learning. During the early acquisition phase of both MSL and MA, cerebral structures, i.e. the striatum, cerebellum, motor cortical regions, prefrontal cortex, parietal cortex and hippocampus, interact to establish the motor routines that are necessary for learning. The consolidation phase involves activation of the cortico-striatal circuit for MSL, whereas the cerebellum is no longer involved. For MA on the other hand, the cortico-cerebellar system is activated, but the striatum is no longer implicated.

From the model of Doyon et al. (2009) it is clear that the striatum is involved in almost all stages of motor learning, but particularly during consolidation of learned skills that have a sequencing component. This suggests that motor learning in PD will be affected throughout the learning process, but particularly during the consolidation phase, which raises the question whether PD patients are still capable of learning a motor skill. Recently, this question was addressed in two literature reviews, both showing that the capacity for motor learning is, at least partly, preserved in patients with PD (Felix et al., 2012; Nieuwboer et al., 2009a). However, both reviews mostly addressed the learning of novel motor tasks, and mainly considered learning that was guided by visual feedback. Compared to acquiring a novel motor task, improving the execution of an existing motor skill does not require the creation of a new motor program but instead engages previously established programs. We will refer to this type of learning as motor refinement, which is of particular importance when trying to regain movement coordination and control, which is lost due to the impact of a disease such as PD. As such, this question is highly relevant as it addresses the role of practice-induced functional neuroplasticity in the context of a chronic neurodegenerative disease.

1.1. Scope of this review

Few studies have been conducted on the optimal practice strategies to achieve motor refinement in PD. Therefore, the current review will consider what is known so far on the effectiveness of the relearning of an existing and automatic motor skill, such as handwriting, in PD. We will begin with discussing recent findings on general motor learning in PD, followed by the impact of external cueing and the application of feedback. This is followed by a review of the literature on several critical disease-specific motor learning problems caused by the impairments in the basal ganglia, namely the effect of dopamine and cognitive functioning. Finally, we will synthesize findings from a more focused review of the literature regarding relearning of writing skills in PD. To investigate the effects of both cueing and visual feedback on handwriting we conducted a systematic literature review using PubMED. Search terms to examine the effects of cueing included 'Parkinson's disease', 'micrographia', 'writing', 'drawing', 'cueing' and 'motor learning'. To investigate the effect of visual feedback we included 'Parkinson's disease', 'motor adaptation', 'distorted feedback' and 'writing' as search terms. Articles retrieved were screened based on the title, abstract and full content.

2. Motor learning in Parkinson's disease

To investigate motor learning, it is important to make a distinction between immediate improvements (early phase) in motor performance during acquisition and long-term motor learning (late phase). Because motor learning cannot be measured directly, retention and/or transfer tests are necessary (Salmoni et al., 1984). A retention test will evaluate the strength of the motor memory representation over time, while a transfer test involves testing whether what was learned during practice can be generalized to another task (Kantak and Winstein, 2012). Retention and/or transfer tests can be performed immediately ($\leq$24 h) or after a delay ($\geq$24 h). However, immediate retention and/or transfer tests are not always good predictors for relatively permanent