Brain and Cognition 81 (2013) 271–282

Contents lists available at SciVerse ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Impact of Parkinson's disease and dopaminergic medication on adaptation to explicit and implicit visuomotor perturbations

David Mongeon [a,d], Pierre Blanchet [b,c], Julie Messier [a,d,*]

[a] Département de Kinésiologie, Université de Montréal, Montréal, Québec, Canada
[b] Département de Stomatologie, Université de Montréal, Montréal, Québec, Canada
[c] Services de neurologie du Centre Hospitalier de l'Université de Montréal, Montréal, Québec, Canada
[d] Institut universitaire de gériatrie de Montréal, Université de Montréal, Montréal, Québec, Canada

ARTICLE INFO

Article history:
Accepted 2 December 2012
Available online 8 January 2013

Keywords:
Visuomotor learning
3D reaching movements
Virtual reality
Basal ganglia

ABSTRACT

The capacity to learn new visuomotor associations is fundamental to adaptive motor behavior. Evidence suggests visuomotor learning deficits in Parkinson's disease (PD). However, the exact nature of these deficits and the ability of dopamine medication to improve them are under-explored. Previous studies suggested that learning driven by large and small movement errors engaged distinct neural mechanisms. Here, we investigated whether PD patients have a generalized impairment in visuomotor learning or selective deficits in learning from large explicit errors which engages cognitive strategies or small imperceptible movement errors involving primarily implicit learning processes. Visuomotor learning skills of non-medicated and medicated patients were assessed in two reaching tasks in which the size of visuospatial errors experienced during learning was manipulated using a novel three-dimensional virtual reality environment. In the explicit perturbation task, the visuomotor perturbation was applied suddenly resulting in large consciously detected initial spatial errors, whereas in the implicit perturbation task, the perturbation was gradually introduced in small undetectable steps such that subjects never experienced large movement errors. A major finding of this study was that PD patients in non-medicated and medicated conditions displayed slower learning rates and smaller adaptation magnitudes than healthy subjects in the explicit perturbation task, but performance similar to healthy controls in the implicit perturbation task. Also, non-medicated patients showed an average reduced deadaptation relative to healthy controls when exposed to the large errors produced by the sudden removal of the perturbation in both the explicit and implicit perturbation tasks. Although dopaminergic medication consistently improved motor signs, it produced a variable impact on learning the explicit perturbation and deadaptation and unexpectedly worsened performance in some patients. Considered together, these results indicate that PD selectively impairs the ability to learn from large consciously detected visuospatial errors. This finding suggests that basal ganglia-related circuits are important neural structures for adaptation to sudden perturbations requiring awareness and high-cost action selection. Dopaminergic treatment may selectively compromise the ability to learn from large explicit movement errors for reasons that remain to be elucidated.

1. Introduction

Our capacity for motor learning allows us to flexibly adapt movements to an ever-changing environment. The basal ganglia (BG) are a major site for adaptive plasticity (Kreitzer & Malenka, 2008; Pisani, Centonze, Bernardi, & Calabresi, 2005). In Parkinson's disease (PD), the functioning of the BG–cortical circuitry is strongly impaired due in part to the loss of dopaminergic neurons in the substantia nigra. If BG circuits are a fundamental neural system supporting movement adaptation, then BG dysfunction as in PD should affect adaptation learning. Psychophysical studies that tested the adaptation learning capabilities of patients with BG damage have yielded highly discordant results (Bédard & Sanes, 2011; Contreras-Vidal & Buch, 2003; Fernandez-Ruiz et al., 2003; Fucetola & Smith, 1997; Krebs, Hogan, Hening, Adamovich, & Poizner, 2001; Marinelli et al., 2009; Smith & Shadmehr, 2005; Stern, Mayeux, Hermann, & Rosen, 1988; Teulings, Contreras-Vidal, Stelmach, & Adler, 2002). Of particular interest, one study tested the motor adaption skills of PD patients using a multistage force field learning task (Krebs et al., 2001). Subjects were required to adapt to two opposite force fields presented in quick succession while

* Corresponding author. Address: Département de Kinésiologie, Université de Montréal, 2100, boul. Édouard-Montpetit, Bureau 8225, Montreal, QC H3T 1J4, Canada. Fax: +1 514 343 2181.
E-mail address: j.messier@umontreal.ca (J. Messier).

0278-2626/$ - see front matter © 2012 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.bandc.2012.12.001

reaching to visual targets with a robotic arm. PD subjects were more strongly impaired when they had to reverse the direction of the learned forces to successfully perform the task in the second field (reversal learning). Similar patterns of results were found using a multistage visuomotor learning task performed in a three-dimensional virtual reality environment: PD patients were more profoundly impaired when confronted with the second, reversed visuomotor dissociation (Messier et al., 2007). These results might reflect the selective difficulty of PD patients in remapping newly learned sensorimotor associations, i.e. to switch context (Krakauer et al., 2004; Monchi et al., 2004). An alternative and non-exclusive hypothesis is that PD patients are more strongly impaired when learning the second, opposite visuomotor mapping or force field because it introduced a double-sized error signal, i.e. an initial perturbation twice as large as the one experienced during initial learning. It has been recently suggested that distinct learning mechanisms operate during motor adaptation and treat small and large spatial errors differently (Contreras-Vidal & Buch, 2003; Kagerer, Contreras-Vidal, & Stelmach, 1997; Malfait & Ostry, 2004; Michel, Pisella, Prablanc, Rode, & Rossetti, 2007; Robertson & Miall, 1999; Criscimagna-Hemminger, Donchin, Gazzaniga, & Shadmehr, 2003). Large consciously-detected visuospatial errors would involve the formation and use of explicit cognitive strategies, whereas small spatial errors, often not consciously perceived, may use implicit automatic corrective mechanisms. Therefore, an interesting question is whether the size of visuospatial errors experienced during learning has a critical impact on motor adaptation skills of PD patients.

One recent study assessed the ability of PD patients to adapt movements to a visuomotor perturbation that is suddenly introduced which produced large initial spatial errors versus one that is introduced gradually over many trials which exposed subjects to only small errors (Venkatakrishnan, Banquet, Burnod, & Contreras-Vidal, 2011). In a similar manner as anterior studies in young healthy controls (Kagerer et al., 1997; Michel et al., 2007), PD patients better adapted their movements to the gradual than the sudden perturbation, when compared to age-matched healthy subjects. In that study, however, PD patients were tested only in the medicated state. Very little is known about the impact of dopaminergic medication on motor learning mechanisms and studies have reported them to be either beneficial (Paquet et al., 2008) or detrimental (Ghilardi et al., 2007; Kwak, Müller, Bohnen, Dayalu, & Seidler, 2010). Therefore, if degeneration of dopaminergic circuitry within the BG is responsible for the deficit in learning from large explicit spatial errors observed in PD or if this impairment results from a deleterious medication effect is an open question.

Of relevance, two studies evaluated explicit motor sequence learning and found reduced motor learning in medicated PD patients compared either to age-matched controls (Ghilardi et al., 2007; Kwak et al., 2010) or to their non-medicated state (Kwak et al., 2010). It was proposed that dopaminergic medication either does not restore or actually impair the specific BG functions that contribute to the cognitive processes required to learn new motor sequences. Another report indicated a beneficial effect of dopamine therapy on a mirror drawing adaptation task performed in two-dimensional space (Paquet et al., 2008). The amount of cognitive/strategic processing greatly varies across movement adaptation protocols. Given that medication degrades performance in explicit motor sequence learning as well as in several cognitive tasks (Cools (2006), for a review), dopaminergic medication might not produce a general positive effect on adaptation learning. Furthermore, motor adaptation during natural unconstrained movements within three-dimensional space requires compensation for gravitational forces which greatly depends on proprioceptive processing. Since proprioception is often impaired in medicated PD patients (Mongeon, Blanchet, & Messier, 2009; O'Suilleabhain et al., 2001), it is undetermined whether dopamine therapy improves motor adaptation skills of PD patients during natural three-dimensional movements similar to those performed in everyday motor activities.

The present study was designed to evaluate the impact of Parkinson's disease and dopaminergic medication on adaptation learning processes based on small unperceived or large spatial errors involving awareness of the visuomotor perturbation and cognitive strategies. We assessed the visuomotor adaptation skills of PD patients in two reaching tasks in which the size of visuospatial errors experienced during learning was manipulated using a three-dimensional virtual environment. In the explicit perturbation task, the visuomotor perturbation was applied suddenly resulting in large initial spatial errors, whereas in the implicit perturbation task, the visuomotor perturbation was gradually introduced such that subjects never experienced large movement errors. Furthermore, to assess the action of dopaminergic medication on adaptation learning, PD patients were tested twice, in the ON and OFF medicated states. To our knowledge, there is no information in the literature about the effect of dopaminergic medication on the ability of PD patients to learn from large consciously detected versus small unperceived spatial errors.

If there is a general deficit in sensorimotor learning in PD, then PD patients should be equally impaired relative to age-matched controls when exposed to both the sudden and gradual visuomotor perturbation paradigms. However, if the role of BG–cortical circuits in adaptation processes is restricted to situations with large sudden visuomotor perturbations, as recently suggested, non-medicated PD patients should exhibit impairments relative to aged-matched controls in the sudden explicit but not in the gradual implicit perturbation task. Furthermore, if dopamine replacement therapy impairs learning when new acquisition largely depends on awareness and cognitive strategies, then medicated PD patients should perform more poorly than non-medicated patients in the explicit perturbation task. Finally, if dysfunction of dopaminergic circuits within the BG is primarily responsible for the adaptation–learning deficits, then these deficits should be improved by dopaminergic medication.

2. Methods

2.1. Subjects

Thirteen individuals with PD (mean age = 65.5; range 49–76 years) and 10 neurologically healthy age-comparable controls (mean age = 65.4; range 50–75 years) participated voluntarily in this study. There was no significant difference in age between healthy controls and PD patients ($t = 0.018$; $p > 0.05$). All subjects were right-handed individuals and had normal or corrected-to-normal vision. Handedness was assessed using the Edinburg Handedness Inventory (Oldfield, 1971). Neuropsychological evaluations confirmed that PD patients were non-depressed and non-demented (assessed with the Beck Depression Inventory and the Mini-Mental State Examination, respectively). All PD subjects were treated with levodopa and other co-medications (see Table 1).

To assess the impact of dopaminergic medication on visuomotor learning, each PD patient was tested during two morning sessions 1 week apart, in the practically defined OFF state, i.e. at least 12 h after the last intake of medication, and in the ON state, 1–2 h after taking the first dose of antiparkinsonian medication of the day. The order of ON and OFF sessions was counterbalanced across patients. Immediately prior to each session, PD patients were evaluated by a movement disorders specialist (author P.B.) and were found to have mild to moderate PD (Hoehn and Yahr Stages II and III) and showed motor scores ranging between 5 and 33 points in the OFF state (mean of 16.3) and between 2 and