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Dopaminergic contributions to distance estimation in Parkinson's disease: A sensory-perceptual deficit?

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ABSTRACT

Recent research has found that perceptual deficits exist in Parkinson's disease (PD), yet the link between perception and movement impairments is not well understood. Inaccurate estimation of distance has the potential to be an underlying cause of movement impairments. Alternatively, those with PD may not be able to perceive their own movements accurately. The main objectives of these studies were to evaluate (1) whether distance estimation is influenced by static perception compared to perception during movement in PD, (2) how visual motion processing contributes to distance estimation during movement, and (3) how dopaminergic medication contributes to these distance estimation deficits. Thirty-seven participants (19 individuals with PD, 18 age-matched healthy control (HC) participants) estimated distance to a remembered target in a total of 48 trials, in 4 randomized blocks. Estimation conditions included: (i) static perception (laser): participants pointed with a laser, (ii) active dynamic perception (walk): participants walked to the estimated position, (iii) passive dynamic perception (wheelchair): participants were pushed in a wheelchair while they gave their estimate. PD patients completed this protocol twice; once OFF and once ON dopaminergic medication. Participants with PD and HC did not differ in judgment accuracy during the static perception (laser) condition. However, those with PD had greater amounts of error compared to HC participants while estimating distance during active dynamic perception (walk). Interestingly, those with PD significantly underestimated the target position compared to healthy control participants across all conditions. Individuals with PD also demonstrated greater variability in their judgments overall. There was no significant influence of dopaminergic medication in any of the conditions. Individuals with PD demonstrated distance estimation deficits only when required to actively move through their environment. In contrast to estimations made with movement, neither static perception (laser) nor passive dynamic perceptions (wheelchair) revealed significant differences in the magnitude of error between the two groups. Thus perceptual estimation deficits appear to be amplified during movement, which may be suggestive of an underlying sensory processing deficit which leads to a problem integrating vision and self-motion information.

1. Introduction

The basal ganglia (BG) are an important part of a complex neural network that processes and integrates various sensory inputs in order to produce and modulate motor outputs (Contreras-Vidal, 1999; Graziano & Gross, 1993; Houk & Wise, 1995; Nagy, Eordegh, Paroczy, Markus, & Benedek, 2006). Boecker and colleagues termed the BG a "sensory analyser" engaged in central somatosensory control, suggesting interconnections between the cortex, BG and thalamus that make up an indirect BG-sensory loop (Boecker et al., 1999b). In Parkinson's disease (PD) there is a degeneration of dopaminergic neurons in the BG, which impairs the basal ganglia–cortical circuitry. This results primarily in motor symptoms; however implications of BG damage on sensory processes has remained uncertain. Many researchers have examined sensory and perceptual capabilities in PD to try and explain common motor deficits such as hypometric movements, increased number of falls, poor balance and freezing of gait. Although a sensory-perceptual origin for motor deficits has been hypothesized (Almeida & Lebold, 2010), the manner in which visual perception is integrated with proprioceptive processing in order to produce accurate movements through an environment remains unclear.

Researchers have investigated whether those with PD are impaired in perceiving their visual environment. Studies measuring target pointing errors or verbal estimates of depth perception

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found that PD participants had a significantly more errors during the pointing task compared to healthy control participants (Maschke, Gomez, Tuite, Pickett, & Konczak, 2006). Some researchers have even suggested that individuals with PD demonstrate a perceptual asymmetry that distorts their visual representation of the environment. Large leftward deviations during a straight ahead pointing task (Wright, Gurfinkel, King, & Horak, 2007) and compressed body-scaled judgments of aperture width (Lee, Harris, Atkinson, & Fowler, 2001) have provided support for this hypothesis. However, a recent study had participants make perceptual height judgments of an obstacle in their environment and found that those with PD did not differ from healthy control participants in their perceptual judgment accuracy (Martens & Almeida, 2011). Similar results were found when judging the passability of an aperture (Cohen, Chao, Nutt, & Horak, 2011). Taken together, there appears to be some evidence of a visual processing impairment of the environment in PD; however when tested in an ecologically valid setting (i.e., prior to crossing an obstacle, or after passing through a doorway), there does not seem to be clear evidence of a perceptual deficit in this sensory domain within PD. Therefore, a visual perceptual mechanism should not be ruled out since it has only been tested in various forms of a static judgment task (i.e., after participants have walked through the doorway, or standing judgments of obstacle height). It is also possible that those with PD are unable to process other sensory information about movement, such as optic flow (i.e., visual information about movement direction) or self-motion which may lead to subsequent movement impairments.

Evidence of a visual processing deficit has been hypothesized (Castelo-Branco et al., 2009; Silva et al., 2005), since peripheral vision is known to be altered in PD by an abnormality of dopaminergic amacrine cells (Bodis-Wollner & Paulus, 1999). There has been some support for this hypothesis since studies have shown that those with PD have difficulty identifying the direction or speed of movement when relying solely on moving visual stimuli in their periphery (Mosimann et al., 2004; Trick, Kaskie & Steinman, 1994). When a low-level of motion discrimination is available, PD do not demonstrate any visual processing deficits, however perception of motion coherence has been reported to be impaired specifically during tasks with high demands on motion integration (Castelo-Branco et al., 2009). Researchers have also argued that the dorsal stream, which has been known to integrate visuospatial information into motoric actions may also be impaired in those with PD (Lord, Archibald, Mosimann, Burn, & Rochester, 2012). It remains unclear whether movement impairments are the result of inaccurate processing of visual information during movement, but this has yet to be determined.

Accurate movements also depend on one's ability to track displacement through space using path integration (i.e., using sensed motion to update the current position and orientation of one's body relative to a starting position) (Durgin et al., 2005; Rieser, Pick, Ashmead, & Garing, 1995). The somatosensory system is very important when moving through an environment since it stores proprioceptive information generated from the trunk and legs during locomotion, which is then integrated with vestibular information to compute current position (Barlow, 1964). Therefore, it is essential to consider the role of proprioception in motor production and control.

Proprioceptive deficits are well documented in PD (Klockgether, Borutta, Rapp, Spieker, & Dichgans, 1995; Schneider, Diamond, & Markham, 1987; Zia, Cody & O'Boyle, 2000), although similar to visual perception, their contribution to movement impairments remains unclear. Studies have shown that individuals with PD have abnormal processing of sensory information, specifically proprioceptive inputs (Klockgether et al., 1995; Rickards & Cody, 1997; Schneider et al., 1987; Zia et al., 2000). Abnormal vibration-induced movement errors have been observed in PD during joint flexion-extension tasks (Rickards & Cody, 1997; Schrader et al., 2008), and PET imaging studies of passive finger vibration have demonstrated a reduction in sensory evoked brain activations in the cortical (parietal and frontal) and subcortical (BG) areas of the brain (Boecker et al., 1999a). During limb position tasks, individuals with PD demonstrate greater errors in matching static limb position, detecting limb displacements, or using the lower limbs to estimate the size of an object (Martens & Almeida, 2011; O'Suilleabhain, Bullard, & Dewey, 2001; Zia et al., 2000). Similarly, tasks involving reaching and pointing to remembered targets have found that PD patients exhibit significantly large errors when locating the original target (Keijsers, Admiraal, Cools, Bloem, & Gielen, 2005; Klockgether et al., 1995), especially when patients are unable to see their hand (Mongeon, Blanchet, & Messier, 2009) or in the complete absence of visual information (Keijsers et al., 2005). Adamovich, Berkinblit, Hening, Sage, & Poizner (2001) showed that reaching accuracy of PD deteriorated selectively when two sources of sensory information needed to be integrated with one another (i.e., visual–proprioceptive integration), which presented uncertainty as to whether spatial errors of PD arise from deficits in proprioceptive processing or from difficulty in visual–proprioceptive integration (Adamovich et al., 2001). There is converging evidence that undoubtedly points to a proprioceptive deficit in the upper limbs; however, very few studies have investigated whether these movement impairments translate into the lower limbs.

Proprioceptive feedback is just as important in the lower limbs since it modulates balance, locomotion and navigating through an environment which are much more continuous, repetitive and coordinated movements. Thus, one might expect that the lower limbs may be more dependent on proprioception since vision is less involved in guiding movements compared to the upper limbs. Therefore, movement impairments might be anticipated in PD as a consequence of poor proprioceptive processing. One study, investigating the influence of visual and proprioceptive information in locomotion and target accuracy in PD, showed that when PD patients performed the task 'off' their medication, they moved to the target (in the dark) with less accuracy than healthy control participants, especially when proprioception was the primary source of feedback (Almeida et al., 2005). These findings support the hypothesis that locomotion may be heavily dependent on proprioception which is impaired in PD. Jacobs and Horak (2006) employed a similar paradigm measuring compensatory stepping behaviours in PD. They found that individuals with PD made larger errors when stepping to a target and that those with severe PD were particularly disadvantaged when they were prevented from seeing their legs (Jacobs & Horak, 2006). Jacobs and Horak noted however, that even when participants were allowed full vision, step accuracy was still compromised. This suggested that, in severe PD, visual input could not fully compensate for a proprioceptive deficit. However, it has yet to be determined whether self-motion deficits can be overcome by visual feedback during movement through a regular environment, especially since the majority of the previous work has focused on proprioceptive deficits and movement impairments in complete darkness. The current research will attempt to replicate real world situations where vision and proprioception are both used to move through an environment, to see whether it becomes clear which sensory system might be contributing to movement impairments experienced in PD.

The overall goal of the current study was to examine sensory perceptual deficits across all sensory modalities in PD to gain a better understanding of the underlying causes of movement problems. Previous methods of examining sensory perceptual deficits have used distance estimation paradigms, and assess the accuracy of judgments made with different types of sensory information available. Thomson (1983) showed that it was possible to walk to a target accurately, with only a short visual presentation and no further subsequent visual input necessary. He noted that individuals must calibrate the visual representation