Neuroscience 254 (2013) 205–221

PARKINSON'S DISEASE PATIENTS SHOW IMPAIRED CORRECTIVE GRASP CONTROL AND EYE–HAND COUPLING WHEN REACHING TO GRASP VIRTUAL OBJECTS

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Abstract—The effect of Parkinson's disease (PD) on hand–eye coordination and corrective response control during reach-to-grasp tasks remains unclear. Moderately impaired PD patients ($n = 9$) and age-matched controls ($n = 12$) reached to and grasped a virtual rectangular object, with haptic feedback provided to the thumb and index fingertip by two 3-degree of freedom manipulanda. The object rotated unexpectedly on a minority of trials, requiring subjects to adjust their grasp aperture. On half the trials, visual feedback of finger positions disappeared during the initial phase of the reach, when feedforward mechanisms are known to guide movement. PD patients were tested without (OFF) and with (ON) medication to investigate the effects of dopamine depletion and repletion on eye–hand coordination online corrective response control. We quantified eye–hand coordination by monitoring hand kinematics and eye position during the reach. We hypothesized that if the basal ganglia are important for eye–hand coordination and online corrections to object perturbations, then PD patients tested OFF medication would show reduced eye–hand spans and impoverished arm-hand coordination responses to the perturbation, which would be further exasperated when visual feedback of the hand was removed. Strikingly, PD patients tracked their hands with their gaze, and their movements became destabilized when having to make online corrective responses to object perturbations exhibiting pauses and changes in movement direction. These impairments largely remained even when tested in the ON state, despite significant improvement on the Unified Parkinson's Disease Rating Scale. Our findings suggest that basal ganglia-cortical loops are essential for mediating eye–hand coordination and adaptive online responses for reach-to-grasp movements, and that restoration of tonic levels of dopamine may not be adequate to remediate this coordinative nature of basal ganglia-modulated function.

Key words: reaching, grasping, online corrections, dopamine-replacement, eye–hand coordination.

INTRODUCTION

The ability to continuously adapt motor commands to meet task demands is essential to successful interactions in dynamic environments. Online correction of hand movements to grasp a moving object requires complex eye–hand coordination. The brain must analyze visual input about the object and the environment, analyze proprioceptive input from the limb, head, and eyes, update its representations in relation to dynamic changes of the environment and the arm, and issue appropriate and precisely timed motor commands. Parieto-frontal circuits mediate reaching (Marconi et al., 2001) and grasping (Rizzolatti and Matelli, 2003). The posterior parietal cortex is critical for on-line visuomotor control (Frey et al., 2005; Rice et al., 2006), particularly in response to perturbations either of a target to be reached for (Desmurget et al., 1999; Torres et al., 2010) or an object to be grasped (Tunik et al., 2005, 2008a,b). Disruption of activity within the anterior intraparietal sulcus (aIPS) by transcranial magnetic stimulation, for example, selectively interferes with subjects' ability to adjust their grasp to sudden perturbations in an object's size or orientation (Tunik et al., 2005). However, the role of basal ganglia-cortical circuits and dopaminergic pathways in such on-line visuomotor control is poorly understood. Evaluating the behavioral output of Parkinson's disease (PD) patients presents a unique opportunity to indirectly investigate these issues, since death of midbrain dopaminergic cells results in marked alterations in basal ganglia modulation of frontal cortical activity, leading to the core deficits in motor planning and execution seen in PD (Rodriguez-Oroz et al., 2009).

Two deficits particularly implicated in PD are the inability to assemble complex motor actions that include multiple movement components and the difficulty in producing accurate movements that are internally generated rather than visually guided (Rodriguez-Oroz

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Abbreviations: aIPS, anterior intraparietal sulcus; ANOVA, analysis of variance; EEG, electroencephalographic; PD, Parkinson's disease; UPDRS, Unified Parkinson's Disease Rating Scale.

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http://dx.doi.org/10.1016/j.neuroscience.2013.09.026

et al., 2009). Previous work has shown that PD patients exhibit deficits in the generation of intentional saccades to targets (Crawford et al., 1989; Briand et al., 1999) and difficulties in the initiation and precise control of internally driven arm movements (Flowers, 1976; Georgiou et al., 1993; Adamovich et al., 2001). Moreover, the temporal coupling of the hand and arm is impaired in PD during reaching for and grasping objects differing both in size and shape (Castiello and Bennett, 1994; Schettino et al., 2004, 2006). These deficits are exacerbated when vision of the hand is blocked (Schettino et al., 2006; Rand et al., 2010; Lee et al., 2013).

Furthermore, the interplay of reaching and grasping with gaze behavior and eye–hand coordination is unknown. Patterns of eye–hand coordination become particularly important when subjects must adapt their hand movements during the reach to a perturbation of the object to be grasped. Boisseau et al. (2002) suggested that the nature of eye–hand coordination control was no different between PD patients and controls after finding no performance differences in a pointing task. However, they did not directly record eye movements and the movement profiles of the hand in space were not reported. While eye–hand coordination and intersegmental coordination are considered central features of cerebellar function (Thach et al., 1992; Miall and Reckess, 2002), basal ganglia circuits may also play a very important role. Differentiated, parallel, and largely segregated cortical-subcortical reentrant circuits link specific cortical areas with their corresponding regions in the basal ganglia (Alexander et al., 1986; Alexander and Crutcher, 1990). Precise, differentiated function within and across these topographically separated circuits may facilitate the integration of different brain regions needed for coordinated motor output. The integrity of these circuits also may be critical for gating afferent input to cortical motor areas in a context-sensitive manner (Schneider et al., 1982; Lidsky and Manetto, 1987; West et al., 1987) and, thus, critical for the context-dependent adaptive control of movement. Under conditions of dopamine depletion, fronto-basal ganglia circuits become pathologically synchronized and "locked-in" at the beta band frequency (Jenkinson and Brown, 2011), potentially reducing the ability of the circuits to appropriately update an ongoing action in response to an environmental perturbation.

Dopaminergic therapy is the most common and effective treatment for motor deficits in PD (Sage and Mark, 1994; Hagan et al., 1997). Previous electrophysiological data have shown that increasing tonic dopamine levels improves the desynchronization of activity over cortical motor areas prior to and during hand and arm movements, correlating with increases in movement speed (Wang et al., 1999). However, our lab and others have found that dopaminergic therapy does not have a unidimensional effect on movement but rather reverses deficits in what we have termed 'intensive' aspects of movement (e.g., speed or amplitude) to a greater extent than deficits in 'coordinative' aspects such as hand–arm coordination (Johnson et al., 1994, 1996; Schettino et al., 2006; Levy-Tzedek et al., 2011), hand-posture coordination during trunk-assisted reaching (Tunik et al., 2007; Rand et al., 2010), and multi-segmental coordination during walking while holding an object (Albert et al., 2010). It is currently unknown, however, what effects dopamine repletion may have on visuomotor online corrective responses to object perturbations and on associated eye–hand coordination for reach-to-grasp movements.

To examine the effect of PD on eye–hand coordination and online corrective responses, we compared PD patients and age-matched controls in reaching for and grasping a virtual rectangular object with visual and haptic feedback, while simultaneously recording finger, thumb, and eye movements. On a subset of trials, the to-be-grasped object rotated mid-reach such that subjects had to dynamically adapt their finger trajectories to successfully grasp the object. In addition, on half of the trials, visual feedback of finger positions disappeared during the feedforward phase of movement, forcing reliance on internal rather than external guidance of the movement.

We hypothesized the following: First, that healthy subjects would rapidly and smoothly alter their finger trajectories to enable a successful grasp in the face of unexpected perturbations of the object. In contrast, if the basal ganglia are critical nodes in a network mediating the flexible and adaptive visuomotor responses to altered environmental contexts, perturbation of the object should have a detrimental effect on the finger trajectories of the PD patients. Second, we hypothesized that due to PD patients' over-reliance on visual feedback to monitor and correct movement errors, their gaze would be aligned with their finger positions to a greater extent than in the control group. Given this reliance on visual feedback, we also hypothesized that blocking vision of the hand would have a much more detrimental effect on the movements of the PD patients than on the control subjects. Finally based on prior results, we hypothesized that increasing tonic dopamine levels through dopaminergic therapy would increase reach speed and aperture of hand opening (i.e., intensive measures), but would not reverse online grasp correction deficits or deficits in eye–hand coordination (i.e., coordinative measures).

EXPERIMENTAL PROCEDURES

Participants

Nine PD patients (six female) and 12 age-matched normal older adults (four female) participated in this study (Mean ± SD age: PD patients, 62.8 ± 8.4 years; controls, 65.7 ± 9.8 years; $t = 0.72$, $p > 0.05$). All patients had mild to moderate clinically typical PD (Hoehn and Yahr (1967) stages 2 and 3), and their motor disabilities were responsive to anti-Parkinsonian medications. No patient had marked resting tremor, action tremor, or dyskinesias. Moreover, no patient had dementia or major depression (screened with the