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Paradoxical kinesia in Parkinson's disease revisited: Anticipation of temporal constraints is critical

Michael Distler [a,1], Johannes CM Schlachetzki [b,1], Zacharias Kohl [b], Jürgen Winkler [b], Thomas Schenk [c,*]

[a] Department of Neurology, University Hospital Erlangen, Friedrich-Alexander Universität Erlangen-Nürnberg, Germany
[b] Department of Molecular Neurology, University Hospital Erlangen, Friedrich-Alexander Universität Erlangen-Nürnberg, Germany
[c] Clinical Neuropsychology, Department Neuropsychology, Ludwig-Maximilians University, Munich, Germany

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ABSTRACT

Slowness of movement, called bradykinesia is the cardinal symptom of Parkinson's disease. Under distinct but not yet well-defined circumstances, patients with Parkinson's disease are able to overcome bradykinesia. One common hypothesis for this phenomenon termed *paradoxical kinesia* in Parkinson's disease postulates that the presentation of external sensory triggers is pivotal to elicit significant increase of motor velocity. In the present study, we examined an alternative hypothesis, namely that an internal cue in the absence of sensory cues are linked to paradoxical kinesia.

To test this alternative hypothesis, patients with Parkinson's disease and healthy age-matched controls (n=9 per group) performed two movement tasks. In the stationary-object prehension task, subjects had to pick up a stationary target object. For the escaping-object task, the participants had to pick up the target object before it moved out of reach. The time available to reach for the object was adjusted individually to ensure comparable difficulty across participants. Reaction time, movement duration, and maximum velocity were assessed for both movement tasks.

In Parkinson's disease patients and healthy controls, anticipation of the imminent movement of a target object significantly decreased reaction time, movement duration, and increased maximum movement velocity. The increase of maximum movement velocity in the escape-condition was significantly more pronounced for Parkinson's disease patients as compared to healthy controls. We provide evidence that internal cues such as temporal constraints are sufficient to diminish the cardinal clinical symptom of bradykinesia in Parkinson's disease. Our results suggest that expectations rather than sensory cues are critical for the emergence of paradoxical kinesia and we discuss the implications of our findings for an account of paradoxical kinesia.

1. Introduction

Bradykinesia, slowness of movement, is one of the cardinal symptoms in Parkinson's disease (PD). Under certain circumstances, however, PD patients are able to perform sudden and effective movements despite bradykinesia. This effect has been termed 'paradoxical kinesia' and has puzzled neuroscientists for decades (Babinski et al., 1921; Souques, 1921). However, the phenomenon of paradoxical kinesia is rare and has so far only been examined in a few controlled studies. The presentation of external sensory cues has been repeatedly shown to effectively improve motor velocity and performance in PD patients. In particular, extraordinary real life events such as a missile attack, earthquake or car accidents elicit remarkably fast motor responses in PD patients (Bonanni et al., 2010a, 2010b; Daroff, 2008; Schlesinger et al., 2007). In laboratory settings, presentation of visual or auditory stimuli were used to trigger fast motor responses in PD (Asmus, Huber et al., 2008; Azulay, et al., 1999; Freeman et al., 1993; Jiang and Norman, 2006; Thaut, et al., 1996). All of these studies have in common that an external sensory cue was necessary to improve motor performance. This led to the hypothesis that sensory cues are pivotal to provoke paradoxical kinesia (Glickstein and Stein, 1991). More specifically, the authors Glickstein and Stein argued that in particular visual motion signals are effective triggers for paradoxical kinesia. They speculated that such motion signals are preferentially processed in cerebellar structures. Presumably, cerebellar circuits allow the motor system to bypass the compromised basal ganglia network, leading to near-normal motor performance in PD patients. This notion has been

* Corresponding author.
E-mail address: thomas.schenk@psy.lmu.de (T. Schenk).
[1] These authors contributed equally to the manuscript.

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supported by the hypothesis that, besides basal ganglia, the cerebellar circuitry plays an important role in motor control and performance (Ballanger et al., 2008; Glickstein and Stein, 1991; Goerendt et al., 2004; Hanakawa et al., 1999).

A typical example for a study demonstrating paradoxical kinesia in PD patients can be used both to illustrate the *prima facia* plausibility of Glickstein and Stein's hypothesis, but also its limitations. Majsak et al., (1998) asked their patients to reach for a target object (Majsak et al., 1998). In one condition the object remained stationary and patients were instructed to reach as rapidly as possible. In the second condition, the object was rolling down a slope and in this condition PD patients reached significantly faster than in the stationary condition. More to the point, the patients' reaching speed was much closer to normal levels in the moving-object condition than in the stationary condition. In line with Glickstein and Stein's hypothesis, it could be argued that the critical factor is the presence of a salient visual motion cue present only in the moving-object condition, but not in the stationary condition. Alternatively, it could be argued that it is not the motion-cue per se, but its meaning and implication for the future of the object that is critical to its success as a trigger of paradoxical kinesia. In particular, it could be argued that seeing the rapidly moving object induces the expectation that the object will only be successfully caught if a very rapid reaching movement is performed. Thus according to this latter interpretation, it is the perceived requirement for a rapidly accelerated movement or the perceived imposition of a temporal constraint that might in fact be the critical factor distinguishing between the fast movement in the moving-object condition and the comparatively slow movement in the stationary object condition.

It is thus the aim of this study to examine whether the critical factor underlying paradoxical kinesia are visual motion signals or internally represented, *anti*cipated temporal constraints. To examine this, it is critical to use a condition where visual motion and temporal constraints are dissociated. In past studies, temporal constraints were introduced by a moving object (Majsak et al., 1998; Schenk et al., 2003). The object started to move rapidly thus signaling to the patient that a rapid reaching movement was required. Thus a visual motion signal was present prior to movement execution and arguable could have been responsible for triggering paradoxical kinesia. To clearly separate these cues we will reverse the sequence of object motion and reaching response. We will present a stationary object that remains stationary for a given time period but moves out of reach after that time has passed. This means that in the case of successful movements, the reaching movement has been completed before the object motion begins. In such a condition the motion signal comes too late to trigger a change in the movement. If paradoxical kinesia is observed in such a condition, it seems likely that the *anti*cipation of temporal constraints, not salient visual motion is critical for paradoxical kinesia.

2. Materials and methods

2.1. Subjects

The study was approved by the Medical Ethics Review Board of the Friedrich-Alexander-University Erlangen-Nürnberg. All subjects gave written informed consent prior to study participation. PD patients were recruited from the movement disorder outpatient center of the Department of Molecular Neurology, University Hospital Erlangen. All patients were diagnosed according to consensus criteria of the German Society of Neurology analogue to the National Institute of Neurological Disorders and Stroke (NINDS) diagnostic criteria for PD (Gelb et al., 1999). Disease staging was based on the Hoehn and Yahr Disability Scale (Goetz et al., 2004), motor impairment of PD subjects was assessed using the UPDRS motor score part III rating (Goetz et al., 2007). PD patients in an intermediate or advanced stage of the disease (i.e. H&Y 3–4) and without motor fluctuation were screened for the following inclusion criteria: ability to sit freely in front of the testing table, no orthopedic disabilities of the upper extremities, no visual and hearing impairment as well as no signs of cognitive impairment. For all PD patients, the total levodopa equivalent daily dose (LEDD) was calculated (Tomlinson et al., 2010). Nine PD patients and nine healthy age-matched control subjects with no medical history of neurological or orthopedic preconditions participated in our study.

Table 1
Study population.

	PD patients (N=9)	Healthy controls (N=9)
Age (years)	64.9 ± 11.7 [46–81]	67.2 ± 8.9 [49–79]
Gender (f/m)	2/7	4/5
Disease duration (years)	12.6 ± 3.8 [6–18]	
Hoehn and Yahr stage	3.4 ± 0.5 [3–4]	
UPDRS-III	34.1 ± 16.9 [12–68]	
LEDD (mg/d)	1299 ± 714 [510–2590]	
Calibration time (ms)	694.4 ± 278.9 [450–1150]	483.3 ± 50.0 [450–550]

Data presented as mean ± S.D.

Nine PD patients and nine age-matched healthy controls participated in this study (Table 1). PD patients were in an intermediate to advanced stage of the disease (H&Y 3–4). This was also reflected by the disease duration of 12.6 ± 3.8 years, the level of motor impairment based on the UPDRS (part III) and LEDD of 1299 ± 714 mg/day.

2.2. Apparatus

The test subjects were positioned at a table-like device, specifically developed to study interceptive behavior (Schenk, et al., 2003). The system (Servo-Object-Controller, SOC) moves a given object using two servomotors (x-and y-directions), controlled by a customized computer system (PC card and software by Parker Compumotor, USA, installed on a Pentium PC). A metal plate covers all motor-driven components. The motor-driven linear axes carry a sled onto which a magnet is mounted. On top of the metal plate another magnet is embedded in the object carrier. This arrangement ensures that the movement of the sled is transferred to the carrier. The target object is loosely attached to the carrier with the use of two further magnets. The target object is a black cylinder: weight 15 g, height 6 cm, and diameter 4 cm.

Reaching and grasping movements were recorded with a 3D movement registration system (CMS 70, Zebris, Isny, Germany) using a sampling frequency of 50 Hz and a spatial resolution of 0.1 mm. The CMS 70 employs active markers that emit ultrasonic signals detected by a fixed set of three microphones. To measure the reaching movement we used three markers with specified positions. The first marker was positioned on the top of the index finger, the second one on the tip of the thumb, and the last was attached to the wrist above the radial styloid process. Using three markers provides sufficient redundancy in case one of the markers does not provide a reliable signal in a given trial.

The system for movement registration and the SOC were electronically synchronized. The computer system also produces a sound to signal the start of the trial and received a signal from a start button to indicate whether the hand rests in the starting position or has been lifted off the button.

2.3. Experimental procedures

At the beginning of each session the subject sat in front of the table with his/her affected arm (for the control group the dominant arm) in a comfortable position resting on top of the start button (Fig. 1). The target object was positioned at a distance of 50 cm and either 25 cm to the left or 25 cm to the right of the start-position. A randomized sequence determined which target position was chosen; both positions appeared with equal frequency.

2.4. Stationary-object task

Subjects were instructed to reach as fast as possible. In the stationary-object condition (i.e. reaching task), an acoustic stimulus signaled the start of the reaching movement (Fig. 1(A)). After the object had been grasped, it was returned to the target position for the next trial. A total of 20 trials were presented: 10 targets on the right, 10 on the left. Variables of interest were reaction time, movement duration, and maximum velocity (Table 2). Target position did not affect any of the variables of interest (data not shown).

2.5. Escaping-object task

In this condition, the object was presented at the same positions as before. Again a tone signal indicated that the reaching movement should now be started. At a specified temporal interval after this tone signal, the target object moved out of