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Kinematic effects of subthalamic stimulation on reach-to-grasp movements in Parkinson's disease

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A B S T R A C T

Background: Parkinsonian patients demonstrate particular difficulties when performing sequential motor tasks compared to simple movements indicating an important role of the basal ganglia in switching between different motor programs.
Objective: To investigate the impact of subthalamic stimulation on the kinematics of composed reach-to-grasp movements and on isolated movement segments.
Methods: 11 age matched controls and 16 PD patients with subthalamic stimulation were examined without medication with stimulation switched on and off. All subjects were instructed to perform three different externally cued hand movements: 1) The complete reach-to-grasp movement consisting of hand transport to and precision grip around a target. 2) The isolated reach movement to the grip device 3) The isolated precision grip and button press. Kinematic data were recorded with a 3D ultrasound movement analysis system (CMS 70 P4-V5, Zebris, Germany).
Results: The effect of subthalamic stimulation was accentuated during the reach phase compared to the grip formation during the composed movement. Stimulation induced kinematic changes of the composed movement were comparable to those of both isolated submovements.
Conclusion: Subthalamic stimulation improved certain aspects of all three hand movement types but did not differentially impact the composed reach-to-grasp task compared to the simple submovements. We assume that the complete reach-to-grasp task is encoded in a single generalised motor program which is affected by stimulation.

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1. Introduction

In Parkinson's disease (PD), bradykinesia is one of the defining symptoms. One particular quality of bradykinesia is an additional time requirement when executing sequential [1] or simultaneous [2] motor actions as compared to the sum of the individual movements [1–3]. This is caused by an increased interonset interval between segments of a composite movement and interpreted as a deficit to switch from one motor program to another in PD [1–3].

Prehension movements represent functionally relevant movements in daily routine which are ideally suited to test motor execution difficulties. The reach-to-grasp motor task consists of two coordinated submovements, the transport of the hand toward the target, mainly executed by proximal muscles of the upper limb, and the grasp including the formation of a grip adapted to the spatial properties of the object and exerted by distal hand muscles [4]. The different phases of the prehension movement are assumed to be controlled by two separate brain circuits, the dorsomedial loop involving the superior parietal and dorsal premotor cortex being active controlling the transport-phase and grip formation and the dorsolateral circuit including the inferior parietal and ventral premotor cortex governing predominantly the grasp formation [5,6].

In untreated PD patients, reach-to-grasp movements are disturbed in several kinematic aspects. Compared to controls, the total transport time is prolonged [7,8], the relative time to maximum deceleration and maximum elbow velocity is premature [8], the grip formation relative to the ongoing transport phase is delayed [8–10], the transport path is segmented and slowed [9], and the automaticity of grasp formation is lost [11].

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According to the current model of basal ganglia dysfunction in PD, the disturbed firing pattern, rate and synchronisation of the subthalamicus nucleus (STN) and altered basal ganglia output within individual, segregated motor subcircuits resulting in disturbed interference of the basal ganglia and cortical premotor and motor areas hallmark the pathophysiology of bradykinesia [12–14]. Evidence for the central role of STN-dysfunction in bradykinesia evolved from microrecordings of STN and basal ganglia during prehension movements in non-human primates [15–18]. Indirect evidence for the role of the STN in bradykinesia evolved in kinematic analyses in PD patients with chronically implanted electrodes for deep brain stimulation (STN-DBS). By switching STN-DBS ON or OFF, investigators have linked the kinematic parameters of proximal and distal motor performances to the different functional states of the STN [19–22].

The goal of the present study was twofold. On the one hand we aimed to elucidate a particular impact of STN-DBS on the composed reach-to-grasp movement compared to its subcomponents, the isolated transport or isolated grasp movement. On the other hand we were interested in the differential control of STN-DBS on proximal and distal components of the reach-to-grasp motor task.

2. Methods

2.1. Subjects

16 PD patients (9 women, 7 men; age 64.3 ± 6.6 years; disease duration: 15.9 ± 3.2 years) treated by STN-DBS (time after surgery: 28.4 ± 18.7 months) and 11 age matched healthy controls (7 women, 4 men, mean age 66.4 ± 4.4 years) were enrolled in this study after providing informed consent. The study protocol had been approved by the ethical committee of the Kiel Medical Faculty.

Clinical characteristics of the PD patients are detailed in Supplemental Table 1. All patients had been operated at the Kiel Neurocenter using MRI, microelectrode recordings and microstimulation for verification of a correct electrode placement within the STN. Inclusion criterion for surgery was an excellent responsiveness of motor symptoms to levodopa challenge. Patients with severe hand tremor were excluded from this study to avoid an interference with the requirements of the motor task. All patients exhibited an excellent response to STN-DBS with an average 55% reduction of motor symptoms (STIM OFF MED OFF mean score UPDRS part III: 37.7 ± 15.8; STIM ON MED OFF mean score UPDRS part III: 17.5 ± 8.2).

2.2. Experimental procedures

Patients were tested after overnight withdrawal of antiparkinsonian medication (MED OFF) in randomized sequence either with (STIM ON) or without STN-DBS (STIM OFF). After changing the stimulation output, a waiting period of at least 30 min was maintained [23]. All subjects performed the motor tasks with the right hand at their own pace. The session started with a few practice trials to familiarize the subject with the task. Subjects were seated in a comfortable chair in front of the target board which was individually adjusted in height and distance (0.30–0.40 m) to allow a comfortable reach. The board (0.35 m × 0.35 m) carried a central light-emitting diode (LED) and four cubic grip objects (0.02 m × 0.045 m × 0.085 m) with response buttons and target LEDs. The central light was illuminated for 3 s as a warning cue at the start of each trial. Illumination of the target LED and dimming of the central LED was the starting cue for each movement. A successful button press was acknowledged by turning off the target LED (Supplemental Figure 1). Subjects were instructed to perform the movements fast but without rushing.

20 repetitions of three different types of hand movements were performed in a randomized sequence: 1. Reach-to-grasp movement, 2. Pointing movement, 3. Grasp movement (Supplemental Figure 1).

1. Reach-to-grasp movement

The subjects placed the palm of the right hand on a marker on the table with the tips of the thumb and the index finger touching each other. They were instructed to reach to the upper left cube (indicated by an illuminated LED) after the go cue, to grasp the object between thumb and index finger and to press the response button within the recessed grip.

2. Pointing movement

The hand was placed on the start marker as described above. After the Go-signal the subject was asked to point to the grip device and touch it with the outstretched index finger without grasping the response button. This task intended to test the reaching movement in isolation.

3. Grasp movement

The subjects leaned slightly forward with the elbow supported on the table with the cube between thumb and index finger opened to a comfortable grasp aperture. Upon the go cue they were asked to close the grip and to press the response button. This task intended to test the grasp movement in isolation.

2.2.1. Data recording

An ultrasound movement analysis system (CMS 70 P4-V5, Zebris, Germany) recorded the hand movements. The system consists of small ultrasound emitting markers (diameter 5 mm), which were fixed to the tip of the thumb and index finger, the radial styloid process, the lateral epicondyle of the elbow and the acromion of the shoulder, and a recording panel of three microphones measuring the marker movements in 3D space. Positional data were sampled at a frequency of 40 Hz with a spatial resolution of 1/10 mm and stored on a portable Windows PC for off-line analysis (Windata 2.19.3×). The cebris system and the lightning of the LEDs of the experimental board were externally triggered, synchronised and governed by a master script of the spike 2 program of the CED 1401 system (Cambridge electronic design, UK).

2.3. Data analysis

Off-line analysis was performed using custom made software (Greifanalyse V2.0.87), which reconstructs the position and velocity curves of the wrist marker and the kinematics of the grasp movements as indicated by the distance between the thumb and index markers in the sagittal plane (Supplemental Figure 1). The software automatically identifies the following time markers in each movement: (1) movement onset (first time point in which the wrist velocity exceeded 0.05 m/s), (2) peak velocity of the wrist movement and (3) end of movement (first time point in which the wrist velocity fell below 0.05 m/s). From these time markers the following kinematic parameters of the reaching movement are determined: (1) acceleration time (MT ACC), the duration from movement onset to peak velocity; (2) deceleration time (MT DEC), the duration from peak velocity to the end of movement; (3) total movement time (Total MT) from the beginning to the end of the movement. MT DEC and MT ACC were also expressed as proportions of Total MT (in %). Reaction time (RT) was defined as the time from the go cue to movement onset of the reach-to-grasp and pointing movement. In the grasp condition RT was defined as the time from the go cue to the onset of a decreasing index-thumb distance. Since the definition of RT differed across conditions we did not compare this variable between the isolated grasp condition and the composed movement.

As parameters of the grasp movement we determined the maximal (PGA) and minimal distance (MGA) between thumb and index finger marker (in mm) and calculated the relative grip aperture as the difference between PGA and MGA (distance PGA-MGA). Besides we analysed the duration from movement onset to maximal grip aperture (MT PGA) and the duration of grip closure from maximal to minimal grip aperture (MT MGA). Artefact contaminated trials due to temporarily concealed ultrasound markers were rejected or manually corrected.

2.4. Statistics

Group data are reported as mean ± standard deviation if not stated otherwise. After testing for normal distribution by Kolmogorov–Smirrnoff testing, pairwise comparisons between patients and controls or between the two treatment conditions (STIM ON/OFF) within the patient group were conducted using *t*-tests. The focus of interest was the investigation of PD specific changes of movement characteristics compared to controls and differences between stimulation induced improvements of the three different movement types. The level of significance for all statistical tests was set to $p < 0.01$ (two-tailed). Statistical analyses were performed with SPSS (version 18).

3. Results

3.1. Kinematic analysis of hand movements in healthy controls

Table 1 summarizes the kinematic data of the different hand movements in normal controls. The individual movement paths revealed a highly invariant temporal coupling between the transport and grasp phase in the combined motor task. The acceleration phase of hand transport (0.28 ± 0.04 s) was shorter than the deceleration phase (0.45 ± 0.07 s) leading to a skewed velocity profile with a peak at 39 ± 5% of the total movement time. The grip formation for the button press evolved in parallel to the transport

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