Neuropsychologia 51 (2013) 392–399

Contents lists available at SciVerse ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Using a startling acoustic stimulus to investigate underlying mechanisms of bradykinesia in Parkinson's disease

Anthony N. Carlsen [a,*], Quincy J. Almeida [b], Ian M. Franks [c]

[a] School of Human Kinetics, University Ottawa, 352-125 University Private, Ottawa, ON, Canada K1N 6N5
[b] Sun Life Financial Movement Disorders Research and Rehabilitation Centre, Wilfrid Laurier University, Waterloo, ON, Canada
[c] School of Kinesiology, University British Columbia, Vancouver, BC, Canada

ARTICLE INFO

Article history:
Received 15 August 2012
Received in revised form
23 October 2012
Accepted 19 November 2012
Available online 27 November 2012

Keywords:
Parkinson's disease
Basal ganglia
Startle
Reaction time
EMG

ABSTRACT

Delays in the initiation of a movement response and slowness during movement are among the hallmark motor symptoms in patients with Parkinson's disease (PD). These impairments may result from deficits in neural structures related to perception, response programming, response initiation, or a combination of all three. However, the relative impact of each process on movement control in PD is still unclear. The present study investigated which processes might be responsible for the observed slowness. Patients performed a simple reaction time (RT) task involving arm extension where the normal 82 dB acoustic "go" signal was unexpectedly replaced with a 124 dB startling acoustic stimulus (SAS) on selected trials. The SAS was used as a probe of motor preparatory state since it has been shown to act as a subcortically-mediated involuntarily trigger for actions that are sufficiently prepared and waiting to be initiated by normal cortical processes. It was expected that release of the voluntary response by startle would not occur in PD patients if bradykinetic symptoms were attributable primarily to motor programming deficits. In contrast, results clearly showed that when a SAS was presented, the prepared response was elicited at a significantly shorter latency. In addition, the amplitude and timing pattern of EMG output appeared to be improved compared to control, resulting in a faster, more normalized movement. These results suggest that in PD patients motor programming processes are relatively intact, while the dysfunctional basal ganglia likely assert an inhibitory effect on the thalamo-cortical connections responsible for the initiation of motor acts.

1. Introduction

One of the most commonly associated symptoms of Parkinson's disease (PD) is bradykinesia, which is clinically described as a general poverty of movement in terms of speed and amplitude once it is underway (Berardelli, Rothwell, Thompson, & Hallett, 2001; Jankovic, 2008). Bradykinetic symptoms are often found to be much more debilitating to patients than more widely publicized motor dysfunctions such as resting tremor and resistance to passive movement, or rigidity (Gauntlett-Gilbert & Brown, 1998). This bradykinesia has been consistently identified in reaction time studies revealing both response delays of 70–100 ms (e.g., Johnson, Vernon, Almeida, Grantier, & Jog, 2003) and subsequent slowness in carrying out the response (Bloxham, Dick, & Moore, 1987; Brown, Jahanshahi, & Marsden, 1993; Hallett, 1990; Sheridan, Flowers, & Hurrell, 1987). However, it is currently unclear which neural processes predominantly contribute to these bradykinetic symptoms and which processes are relatively intact. In particular, in an information processing framework, the task of responding with a fast movement after a "go" signal in a typical RT task can be conceptualized to include a number of processes, each of which may be differentially affected in PD. These processes may be related to detecting and recognizing the "go" stimulus, preparing a response, and executing (or "initiating") the motor act (Donders, 1969; see also Kiencke, Majjad, & Kramer, 1999 for a graphical representation of these processes).

Several studies have indicated that RT slowness exhibited by PD patients could be at least partially attributed to impaired stimulus processing (Bachmann et al., 1998; Giaschi, Lang, & Regan, 1997; Johnson et al., 2004; Jordan, Sagar, & Cooper, 1992). Importantly however, an investigation using an inspection time paradigm showed that although stimulus processing deficits existed, these were not significantly improved with levodopa treatment, whereas some of the motor impairments were ameliorated (Johnson et al., 2004). This suggests that while stimulus recognition processes were impaired, subsequent processes were also affected in PD.

Similarly, several studies have argued that motor preparatory processes are impaired in patients with PD. For example, it was shown that there were no RT differences between situations

* Corresponding author. Tel.: +1 613 562 5800x7081; fax. +1 613 562 5149.
E-mail address: tony.carlsen@uOttawa.ca (A.N. Carlsen).

0028-3932/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.neuropsychologia.2012.11.024

where the patients knew the required response in advance (fully cued) compared to when it was unknown (not cued). This would suggest that PD patients have an impaired ability to utilize information about the upcoming action to fully prepare (or program) a motor response in advance (Bloxham et al., 1987; Sheridan et al., 1987). Other investigations have argued that while PD patients are able to fully prepare a response, the time required to complete the programming processes are lengthened compared to healthy controls (Jahanshahi, Brown, & Marsden, 1992a,b). Specifically, RT differences appeared to diminish with increased time between the warning cue and "go" signal, however, others would argue that these interpretations might be flawed, with the results being influenced by other factors such as medication state and experimental methods (for a review see Gauntlett-Gilbert & Brown, 1998). Nevertheless, more recent research has established the profound impact that movement programming can have on severe motor deficits such as freezing of gait (Knobl, Kielstra, & Almeida, 2012).

Finally, RT deficits in PD have also been argued to be related to processes governing the initiation of a fully prepared action. For example, when TMS was applied over the primary motor cortex in PD patients, the time required to respond was decreased. It was argued that subthreshold TMS resulted in an increase in cortical excitability that led to a decrease in the time required for initiation (Pascual-Leone, Valls-Solé, Brasilneto, Cohen, & Hallett, 1994b). Additionally, some researchers have suggested that the bradykinetic features of movement production in PD can be attributed to negative impacts of the malfunctioning basal ganglia on both response preparation and response initiation (for a review see Berardelli et al., 2001).

From the above evidence it is clear that although both motor programming and initiation processes have been associated with slowed RTs in patients with PD, it is still unclear which of these processes contributes more to response delays and overall slowness. More specifically the amount of preparation in the motor system just prior to the "go" cue is unclear for PD patients performing a simple RT task. In order to probe the preparatory state of the motor system, a "startle" method has been recently used in humans preparing ballistic movements in RT tasks. This method relies on the observation that when a motor response is prepared and ready to be initiated, the presentation of a loud acoustic stimulus that is capable of eliciting a startle response appears to involuntarily trigger the prepared action (Carlsen, Maslovat, & Franks, 2012b; Valls-Solé, Kumru, & Kofler, 2008). For healthy control subjects performing simple RT tasks, the presentation of a startling acoustic stimulus (SAS) has resulted in mean premotor RTs of <80 ms, and several individual RTs of <60 ms (e.g., Carlsen, Chua, Inglis, Sanderson, & Franks, 2004b; Valls-Solé, Rothwell, Goulart, Cossu, & Muñoz, 1999; Valls-Solé et al., 1995), suggesting that normal cortical stimulus processing pathways were bypassed. Importantly, in situations where limited response preparation occurs, (e.g., some choice RT tasks) no response was elicited by the SAS (Carlsen et al., 2008; Carlsen, Chua, Inglis, Sanderson, & Franks, 2004a). Thus, this method provides a convenient way to determine whether a response is sufficiently prepared and ready to be initiated via normal cortical processes depending on whether or not the voluntary response is triggered early by the SAS. Moreover, since the SAS has been hypothesized to act to trigger the response via non-traditional subcortically-mediated ascending pathways, this method may be able to elucidate the neurophysiological mechanisms of response execution in patients with PD.

The aim of the current investigation was to determine whether presenting a SAS in a RT task would result in the involuntary and early triggering of a prepared movement in patients with PD and a normalization of movement speed. Unlike previous studies of startle in PD (e.g., Valldeoriola et al., 1998), the current investigation was designed to specifically determine the effect of startle on the initiation and execution of the voluntary movement. It was hypothesized that if abnormally long RTs are attributable to motor programming deficits, release of the fully planned voluntary response by startle would not occur. However, if bradykinetic symptoms (including slow response initiation and execution) are due to a diminished cortical initiation signal, early release of a more normalized movement would be seen at short latency following the SAS since the regular response initiation pathways would be bypassed.

2. Material and methods

2.1. Participants

Twenty four individuals with idiopathic Parkinson's disease were recruited from the patient database at the Sun Life Financial Movement Disorders Research and Rehabilitation Centre (MDRC) at Wilfrid Laurier University, Canada. Participants were tested both "OFF" and "ON" anti-Parkinson's treatment. "OFF" involved voluntary withdrawal from their medication for an average of 15.7 h. Upon arrival in the OFF state, participants were evaluated using the motor examination subsection of the Unified Parkinson's Disease Rating Scale (UPDRS-III) to determine the severity of their motor symptoms. After a first round of testing in the RT task (see Section 2.2) while OFF medication, participants were instructed to take a regular dose of their PD medication and then waited a minimum of 70 min for the medication to take effect. Participants were re-evaluated on the UPDRS-III to confirm dopa-responsiveness of motor symptoms. Participants were excluded from data analysis if they did not appear to be dopa-responsive, as indicated by a minimum 5-point improvement on the UPDRS-III evaluation. As such, seven participants were excluded from analysis due to a lack of symptom improvement from OFF to ON medication state. Data from seventeen individuals (12M/5F; mean age = 64.7 years; age range 52–76 years, see Table 1) are included in the current analysis. All participants gave written informed consent and the study was approved by the ethics committee at Wilfrid Laurier University in accordance with the 1964 Declaration of Helsinki. All participants were right handed, and if a tremor was present, it was left side dominant to avoid any EMG signal disturbance. All participants were free from any sensory disorders, joint replacement or disease, significant visual or hearing impairment, as well as any obvious upper body abnormalities that would affect their performance in a RT task.

2.2. Participant set-up and task

Participants sat upright in a comfortable, height-adjustable chair. The chair was placed in front of a computer monitor, so that the participants could receive feedback during the experimental procedure. The right forearm was secured in a pronated position with the palm down, to a custom-made aluminum manipulandum that moved in the horizontal plane with an axis of rotation about the elbow. The home position (90 deg of flexion at the elbow with the shoulder flexed and abducted 30 deg) was indicated by a physical stop (see Fig. 1).

Participants performed a simple RT task requiring extension of the elbow in a quick movement to a fixed target located at 20 deg from the home position in response to an auditory "go" signal. Instructions emphasized quick reactions following the "go" signal, and participants were asked to try to perform the extension movement as quickly and accurately as possible. Feedback about reaction time and movement accuracy was provided following each trial; however, ongoing instructions emphasized speed of reaction over accuracy.

Real-time position feedback was provided during trials with a 1 cm wide yellow horizontal line on a computer screen whose vertical movement within a 15 cm tall $\times$ 1 cm wide box corresponded directly to movement of the manipulandum (0.5 cm/deg). The starting (home) position for the marker was at the bottom end of the box (see Fig. 1). The fixed target was represented with a similar 1 cm wide marker line (blue, located 10 cm vertical to the start position). Participants were allowed to practice the task prior to testing to familiarize themselves with the equipment and were instructed that the loudness of the "go" stimulus would be variable. Prior to performing each task, participants received a single block of 10 practice trials.

2.3. Instrumentation and stimuli

Each trial started with a visual "get ready" warning signal in addition to a short acoustic warning tone (100 ms, 300 Hz, 80 dB) which was followed immediately by a random foreperiod of 2–3 s. Following the foreperiod, a computer program generated the imperative "go" stimulus consisting of a narrow band noise pulse (1 kHz, 40 ms duration) that was amplified and presented via a loudspeaker (M58H, MG Electronics) placed directly behind the head of the participant with an intensity of either 82 dB (Control) or 124 dB (Startle) SPL