Parkinsonism and Related Disorders 19 (2013) 300–305

Contents lists available at SciVerse ScienceDirect

Parkinsonism and Related Disorders

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

The pattern of attentional deficits in Parkinson's disease

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ARTICLE INFO

Article history:
Received 13 June 2012
Received in revised form
30 October 2012
Accepted 8 November 2012

Keywords:
Attention
Parkinson's disease
Executive functions
Flexibility

ABSTRACT

Background: Cognitive impairment without dementia is frequent in Parkinson's disease. It often presents as a dysexecutive syndrome with deficient attentional resource allocation. The nature of attention deficits in Parkinson's disease has rarely been investigated with robust, theory-based tasks. The main objective of the present study was to investigate attention disorders in Parkinson's disease patients by applying a paradigm based on a model of attention. We also sought to identify the main demographic and clinical characteristics associated with attention deficits in Parkinson's disease.
Methods: Eighty non-demented Parkinson's disease patients and 60 healthy controls participated in the study. Attention was assessed in a computer-controlled reaction time paradigm. The test session comprised a simple reaction time task and four choice reaction time tasks: a go/no-go task, a one-dimension, focused-attention task, a two-dimension, divided-attention task and an alternating task. Performance was assessed by composite measures: (i) cognitive reaction time, corresponding to the difference between the simple reaction time and the choice reaction time in the given condition, and (ii) reaction time variability, corresponding to the sum of the coefficients of variance of the reaction times. Accuracy was also considered.
Results: Apart from an overall slowing and greater reaction time variability, Parkinson's disease patients were only significantly impaired in the alternating condition. This set-shifting impairment was associated with their performance in the go/no-go and divided-attention conditions.
Conclusion: Our systematic assessment of the different attentional subcomponents revealed that mental flexibility is particularly impaired in non-demented Parkinson's disease patients.

1. Introduction

Cognitive impairment without dementia is frequent in Parkinson's disease (PD), even in early-stage disease [1]. It often presents as a dysexecutive syndrome in which impairments in attentional resource allocation are considered to play a central role [2].

Attention is a complex neurocognitive process that can be divided into several components. Van Zomeren and Brouwer [3] have suggested distinguishing between two main attentional axes. Firstly, "intensity" corresponds to sustained attention and encompasses the ability to maintain overall response readiness (tonic alertness) or response readiness after a warning stimulus (phasic alertness). Secondly, "selectivity" includes focused-attention (the ability to detect and process a specific stimulus or a dimension of a stimulus while ignoring the others) and divided-attention (the ability to share attentional resources between two or more stimuli or two or more dimensions of a stimulus). Current models usually add an executive component with a supervisory attentional system [4] that corresponds to the voluntary control needed to manage conflicting information, overcome routines, detect errors and apprehend new or unfamiliar situations. These subcomponents are mediated by large cortical and subcortical networks and are related to specific neuromodulators [4,5]. In PD, disruption by dopamine depletion of the associative and limbic circuits connecting the striatum to the frontal and prefrontal areas (namely the anterior cingulate, medial frontal and lateral prefrontal cortex), is often considered as the main cause of attention and executive function impairments [6,7].

Very few studies have assessed systematically the different attentional components to investigate the nature of attention deficits in PD. Most of the theory-based studies focused on a single

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http://dx.doi.org/10.1016/j.parkreldis.2012.11.001

attentional subcomponent and reported deficits in sustained [8], focused [9–12] or divided [13] attention. Several investigations based on set-shifting tasks have also evidenced impairments in the voluntary control of attention in PD patients [7,14,15].

The main objective of the present study was to investigate the nature of attention disorders in PD patients by using a paradigm based on the model of Van Zomeren and Brouwer [3]. We sought to assess in the same patient group the different attentional subcomponents and determine which were impaired or unaffected. We assumed that PD patients would be more impaired than healthy controls in attention tasks but that this impairment would depend on the subcomponent involved. We expected to see more marked impairments in tasks involving divided and flexible attention than in tasks involving focused-attention.

2. Methods

2.1. Population

Eighty patients with probable PD participated in the study. They were prospectively recruited from outpatients attending the Movement Disorders Department at Lille University Medical Center. PD was defined according to international criteria [16]. None of the patients was suffering from a neurological disease other than PD. None was suffering from depression (as defined by the DSM-IV criteria) or dementia (as defined by the Movement Disorders Society criteria [17]).

All patients were treated and assessed after receiving their usual anti-parkinsonian medication. Treatment details are shown in Table 1.

Sixty healthy controls also participated in the study and were matched as closely as possible to patients in terms of age, gender and the duration of formal education. They were recruited among the patients' spouses. None of the controls had a personal history of neurological or psychiatric illness. Subjects with a Mini Mental State Examination (MMSE) score < 27 were excluded.

Table 1
Demographic and clinical data (means and standard deviations) and details of treatments in the healthy control and Parkinson's disease (PD) patient groups.

	Controls	PD
Number	60	80
Age (years)	60.53 (9.39)	60.93 (9.17)
Gender (M/F)	31/29	40/40
Duration of formal education (years)[a]	12.47 (2.98)	11.14 (3.34)
Disease duration (in years)	–	9.74 (8.26)
MADRS score (out of 60)	–	6.91 (6.14)
MMSE score (out of 30)[a]	29.08 (1.28)	28.00 (1.80)
Mattis Dementia Rating Scale score (out of 144)	–	137.36 (5.33)
UPDRS I (mentation, behavior, mood) (out of 16)	–	1.98 (1.71)
UPDRS II (ADL) in the "On" state (out of 52)	–	9.65 (5.97)
UPDRS II (ADL) in the "Off" state (out of 52)	–	14.36 (8.95)
UPDRS III (motor) in the "On" state (out of 108)	–	24.83 (10.83)
UPDRS IV (complications of therapy) (/23)	–	3.28 (3.18)
Axial subscore in the "On" state (out of 20)	–	4.81 (3.61)
Mean (*SD*) levodopa equivalent daily dose (mg/day)	–	787.81 (*759.20*)
Dopaminergic agonists	–	54 (67%)
Monoamine oxidase inhibitors	–	9 (11%)
Amantadine	–	6 (7%)
Subthalamic nucleus deep brain stimulation	–	31 (39%)
Benzodiazepines	5 (8%)	11 (14%)
Hypnotics	7 (12%)	15 (19%)
Serotonin reuptake inhibitors	1 (2%)	14 (17%)

MADRS: Montgomery and Asberg Depression Rating Scale; MMSE: Mini Mental State Examination; UPDRS: Unified Parkinson's Disease Rating Scale; ADL: activities of daily living.

[a] Indicates a significant effect of group ($p < 0.05$).

All participants gave their informed consent to participation in the study. The study protocol was approved by the local institutional review board (*Comité de Protection des Personnes de la région Nord-Ouest IV*, reference 2008-008210-38).

The participants' main demographic and clinical characteristics are shown in Table 1.

2.2. Assessments

Disability was rated using the four parts of the Unified Parkinson's Disease Rating Scale (UPDRS) [18] and an axial score summing the subscores at items 18, 27, 28, 29 and 30 of the UPDRS part III.

Severity of depressive symptoms was rated on the Montgomery-Asberg Depression Rating Scale (MADRS) [19]).

Overall cognitive status was assessed in terms of the MMSE score and the Mattis dementia rating scale (DRS) score [20].

Attention was assessed by performance in a computer-controlled reaction time paradigm designed to measure the different attentional subcomponents while controlling for visuospatial processing (uniform central presentation) and motor participation (a single key response). The experimental program was written with E-Prime Professional software (version 2.0, Psychology Software Tools, Sharpsburg, PA, USA).

Fig. 1 depicts the task stimuli and the time course of events.

Participants were seated in front of a 15-inch color monitor. They were instructed to fix a grey square (2.5×2.5 cm) in the center of the screen and to press the response key with their preferred hand as soon as the target stimulus appeared. The task comprised five levels:

- A simple reaction time task (SRT): at irregular intervals (1750-3750 ms with an average of 2750 ms) the color of the central square changed and became green, blue or red. The subject was required to press the response key as quickly as possible when the color changed. Thirty trials (10 with each color) were administered in random order. This baseline condition was intended to measure processing speed.
- A go/no-go choice reaction time task (GNG): the material was the same as in the SRT condition but the subject was required to press the response key as quickly as possible when the central square turned blue only. Ninety trials (30 with each color) were administered in random order. This condition was intended to measure single stimulus discrimination.
- A one-dimension, focused-attention choice reaction time task (FOC): the blue, red or yellow squares appeared on the screen (as in the GNG task) but were now surrounded by a varying number (0, 2 or 5) of green rectangles (measuring 0.1×0.5 cm). Subjects were instructed to ignore the green rectangles (considered as distracters) and respond as in the GNG, i.e. by pressing the response key as quickly as possible when the central square turned blue, regardless of the number of distracters. Ninety trials (30 with each color, including 10 with 0 distracters, 10 with 2 distracters and 10 with 5 distracters) were administered in random order. This condition was intended to assess the subject's ability to focus his/her attention on a one-dimensional stimulus.
- A two-dimension, divided-attention choice reaction time task (DIV): material was identical as the FOC condition but the distractors became relevant, requiring the subject to attend simultaneously to the color of the square and the number of rectangles. Subjects were instructed to respond as quickly as possible only when a blue square appeared surrounded by two green rectangles. One hundred and ten trials (including 30 target stimuli) were administered in random order. This condition was intended to assess the subject's ability to divide his/her attention between two stimulus dimensions.
- An alternating choice reaction time task (ALT): the material was the same as in the FOC condition. In the first phase of the task (30 trials), the instructions were the same as in the FOC condition, i.e. the subject had to press the response key as quickly as possible when the central square turned blue, regardless of the number of distracters. Then, the instructions changed; the subjects were instructed to consider only the number of rectangles and to respond as quickly as possible when there were 2 rectangles (regardless of the color of the square). Four blocks of 30 trials (each including 10 targets) were administered with alternate instructions in each block. Performance was only calculated for the last three blocks, since the first phase was not subject to alternation. This task condition was intended to measure the flexibility of attention.

The stimuli remained on the screen for 2 s at most or until a response was recorded during that time. A practice block preceded each level of the assessment. The SRT condition was always performed first and the order of presentation of the four other conditions was counterbalanced to limit order effect.

The mean response time (in ms), the number of misses and the number of false alarms (except for the SRT condition, in which false alarms were not possible) were recorded for each condition. Composite measures were then extracted. Firstly, the cognitive reaction time (CRT) corresponded to the difference between the SRT and the choice reaction time in the given condition. The CRT thus reflects the cognitive processing required to decide whether the presented stimulus is a target or not.