Parkinsonism and Related Disorders xxx (2015) 1–6

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

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

Parkinson bradykinesia correlates with EEG background frequency and perceptual forward projection

M. Beudel*, E. Roosma, O.E. Martinez Manzanera, T. van Laar, N.M. Maurits, B.M. de Jong

Department of Neurology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

ARTICLE INFO

Article history:
Received 12 February 2015
Received in revised form
21 April 2015
Accepted 4 May 2015

Keywords:
Parkinson's disease
Timing
Motor velocity
EEG
Bradykinesia

ABSTRACT

Background: To deal with processing-time in the nervous system, visuomotor control requires anticipation. An index for such anticipation is provided by the 'flash-lag illusion' in which moving objects are perceived ahead of static objects while actually being in the same place. We investigated the neurophysiological relation between visuomotor anticipation and motor velocity in Parkinson's disease (PD) and controls.

Methods: Motor velocity was assessed by the number of keystrokes in 30s ('kinesia score') and visuomotor anticipation in a behavioural flash-lag paradigm while electroencephalography data was obtained. PD patients (n = 24) were divided in a 'PDslow' and a 'PDfast' group based on kinesia score.

Results: The PDslow group had a lower kinesia score than controls (resp. 40.3 ± 1.7 and 64.9 ± 4.6, $p < 0.001$). The flash-lag illusion was weaker in the PDslow group than in controls (resp. fractions 0.32 ± 0.04 and 0.50 ± 0.09 of the responses indicating perceived lagging, $p = 0.03$). Furthermore, the magnitude of the flash-lag illusion correlated with the kinesia score ($cc = 0.45$, $p = 0.02$). Finally, electroencephalography background frequency was lower in the PDslow group than in controls (resp 8.24 ± 0.24 and 9.1 ± 0.32 Hz, $p = 0.01$) and background frequency correlated with the kinesia score ($cc = 0.58$, $p = 0.001$).

Conclusions: The decreased flash-lag illusion and lower electroencephalography background frequency in more bradykinetic PD patients provides support for disturbed visuomotor anticipations, putatively caused by reduced, sub-cortically mediated, network efficiency. This suggests a link between anticipation in early-stage visual motion processing and motor preparation.

1. Introduction

To deal with the delay of processing-time in the nervous system, effective visuomotor control requires *anticipation* in a dynamic environment. To make such anticipations, the timing of movements needs to be adjusted to the velocity of moving objects. We recently demonstrated a striatal role in such velocity estimations [1] while such estimations were impaired in Parkinson's disease (PD) [2], a condition of striatum dysfunction. Moreover, severity of PD bradykinesia correlated with an experimental measure for visuomotor anticipation [3], suggesting that perception of visual motion *and* the actual velocity of movements are controlled by a similar cortical processing mechanism.

The aspect of perceptual anticipation in visual motion is illustrated by the flash-lag illusion (FLI), i.e. the illusion that a moving object is perceived ahead of a stationary flash when they are in the same location [4]. Transcranial Magnetic Stimulation (TMS) applied over the visual motion area (V5/MT+) has been shown to reduce this illusion [5]. FLI might reflect the neuronal mechanism of anticipation which already starts during early stage visual motion processing. Interestingly, V5/MT + showed increased functional connectivity with the pre-supplementary motor area (SMA) in PD [6] suggesting a link between anticipations in early-stage visual motion processing and motor preparation. With the finding of disturbed cortical and subcortical neural oscillations in PD [7], these oscillations might provide further insight in cortical processing mechanism involved in both perception of visual motion *and* the actual velocity of movements.

PD bradykinesia is inversely correlated with the power [8] of *beta* (13–30 Hz) oscillations in the basal ganglia (BG) and frontal cortex [9]. Disturbed *alpha* (8–13 Hz) oscillations also occur in PD,

* Corresponding author. Department of Neurology, University Medical Center Groningen, 9700 RB, The Netherlands.
E-mail address: m.beudel@umcg.nl (M. Beudel).

http://dx.doi.org/10.1016/j.parkreldis.2015.05.004
1353-8020/

while the dynamics of subcortico-cortical alpha coupling in posterior regions [9], which is related to ON and OFF dopaminergic medication, correlates with bradykinesia scores [10]. In addition, decreased alpha power during movement preparation also correlates with bradykinesia scores [11]. Furthermore, alpha background activity is decreased in non-demented PD patients [12] and correlates with motor scores [13]. Decreased connectivity between cortical regions with alpha activity also negatively correlates with motor scores [14]. Such alpha oscillations are traditionally associated with cognitive and attentional capacities [15,16]. This raises the question whether background alpha activity reflects the system activity responsible for both the velocity of perception and the velocity of movements required for facilitating sensorimotor integration and possibly other cognitive computations.

We tested this hypothesis by assessing visuomotor performance and EEG background velocity in healthy volunteers (HV) and non-demented PD patients, groups which are characterised by different motor velocities. Two key hypotheses were that frequency of the dominant EEG background activity would correlate with motor velocity and that the latter would correlate with the strength of visual anticipation represented by the visual illusion of projecting a moving stimulus forward on its trajectory compared to a concurrent stationary flash, i.e. the FLI.

2. Materials & methods

Twenty-four patients with idiopathic PD, mean age (±SD) 64.2 ± 1.8 (13 men), and ten HV, mean age 65.2 ± 3.2 (6 men), were included (Table 1). Groups were matched for age, gender and cognition, the latter was quantified by the SCOPA-cognition test [17] (Table 1). Exclusion criteria were task-interfering neurological, psychiatric, ophthalmologic or upper extremity disorders. Participants provided written informed consent before testing. The study was approved by the local ethics committee.

2.1. Experimental procedure

PD patients were tested at the end of dose interval of their medication, approximating an OFF-state without actual medication withdrawal. HV were assessed at similar times of the day. To control for various dopaminergic states in patients, motor scores were obtained in the same dopaminergic state as the psychophysical task [3]. The experiment consisted of (i) motor assessment employing part three of the Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS UPDRS III) for PD patients, (ii) a short EEG recording, (iii) a quantitative bradykinesia task, (iv) a psychophysical paradigm evoking the FLI and (v) a cognitive assessment. These five parts (i-v) lasted approximately 70 min for PD patients while the four parts (ii-v) lasted about 60 min in HV.

2.2. Electroencephalography

EEG recordings were made with five unipolar electrodes over the occipital cortex and parieto-occipital junction (locations PO1/PO2, PO7/PO8, Oz in accordance with the extended international 10-20 system; Twente Medical Systems International BV, Oldenzaal, The Netherlands) [18]. EEG signals were amplified with a REFA amplifier (Advanced Neuro Technology BV, Enschede, The Netherlands) with a sampling frequency of 512 Hz employing an average reference and stored using Eemagine EEG software (Advanced Neuro Technology BV). An Ag/AgCI electrode attached to a wristband (Twente Medical Systems International BV) was used as ground. The dominant background frequency was obtained from a 60 s epoch with eyes closed in rest. For all five channels a fast Fourier transformation (FFT) enabled identification of the peak frequency in the dominant background alpha frequency (8–13 Hz range). For further analyses, the five peak-frequencies were averaged which resulted in a single background frequency per subject.

2.3. Manual motor velocity

Motor velocity was assessed using the kinesia score (KS) obtained from a computer keyboard-tapping task; the bradykinesia akinesia incoordination (BRAIN) task [19]. This recently validated BRAIN task strongly correlates with the bradykinesia items of the UPDRS [19]. Contrary to the UPDRS, this assessment is parametric and objective. The KS represents the number of keyboard key presses during 30 s and was assessed for both hands and subsequently averaged. Since our study was not full OFF medication and concerned relatively mildly affected patients, the PD group was divided into two groups based on the KS score for group comparisons. A 'PDslow' group concerned PD patients with KS scores lower than the median while the 'PDfast' group had KS scores above the median.

2.4. Flash-lag illusion

In the psychophysical paradigm, the FLI [4] was modulated in such a way that the stationary flash did not always occur at the time the ball passed its location. Given this variation, subjects had to indicate the position of the flash relative to the ball. The stimulus consisted of a circulating white ball and a white flash with the same shape and size on a grey background (Fig 1A). The moving ball made a circular clockwise movement (field of view: 6.10°) around a white fixation point with a velocity of 540°/s. It started at the twelve o'clock position (defined as 0°), made two full circles (720°) and disappeared at the subsequent three o'clock position (810°). Between ball positions 405° and 495°, a stationary flash appeared for 17 ms at the three o'clock position. During the stimulus trial, participants fixated on the central fixation point.

Table 1
Characteristics Participants. Characteristics of the groups of all patients with Parkinson's disease (PD) and healthy volunteers (HV) that participated in the study as well as PD subgroups and with the highest and lowest number of button presses on the BRAIN task (PD-fast and PD-slow, respectively). All values are means and standard error of the mean. Differences are expressed in *p*-values derived from 2 sample t-tests. y = years, # = number, Cog = cognition, UPDRS III = motor part of the unified Parkinson's disease rating scale.

	PD (n = 24)	HV (n = 10)	p − value PD vs HV	PDslow (n = 8)	PDfast (n = 8)	p − value PD − fast vs slow
Age (y)	64.2 ± 1.8	65.2 ± 3.2	0.77	62.5 ± 2.3	61.8 ± 3.9	0.89
Sex (# males & %)	13 (54%)	6 (60%)	0.77	5 (63%)	3 (38%)	0.61
SCOPA Cog (range 0–43)	29.8 ± 1.0	28.5 ± 1.44	0.47	30.1 ± 2.0	29.7 ± 2.0	0.89
Disease duration (y)	6.6 ± 1.1	–	–	6.12 ± 1.8	3.8 ± 0.8	0.24
UPDRS III (range 0–132)	21.0 ± 2.79	–	–	20.4 ± 5.14	20.8 ± 5.37	0.94
Bradykinesia subscore (UPDRS III items 3.4–3.8)	6.1 ± 1.1	–	–	7.4 ± 2.1	6.1 ± 1.6	0.30

Please cite this article in press as: M. Beudel, et al., Parkinson bradykinesia correlates with EEG background frequency and perceptual forward projection, Parkinsonism and Related Disorders (2015), http://dx.doi.org/10.1016/j.parkreldis.2015.05.004