Journal of Clinical Neuroscience 30 (2016) 49–55

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

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

Clinical Study

Finger tapping analysis in patients with Parkinson's disease and atypical parkinsonism

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ARTICLE INFO

Article history:
Received 20 October 2015
Accepted 27 October 2015

Keywords:
Atypical parkinsonism
Hypokinesia
Kinematic analysis
Progressive supranuclear palsy
Repetitive finger tapping

ABSTRACT

The goal of this study was to investigate repetitive finger tapping patterns in patients with Parkinson's disease (PD), progressive supranuclear palsy–Richardson syndrome (PSP-R), or multiple system atrophy of parkinsonian type (MSA-P). The finger tapping performance was objectively assessed in PD (n = 13), PSP-R (n = 15), and MSA-P (n = 14) patients and matched healthy controls (HC; n = 14), using miniature inertial sensors positioned on the thumb and index finger, providing spatio-temporal kinematic parameters. The main finding was the lack or only minimal progressive reduction in amplitude during the finger tapping in PSP-R patients, similar to HC, but significantly different from the sequence effect (progressive decrement) in both PD and MSA-P patients. The mean negative amplitude slope of −0.12°/cycle revealed less progression of amplitude decrement even in comparison to HC (−0.21°/cycle, p = 0.032), and particularly from PD (−0.56°/cycle, p = 0.001), and MSA-P patients (−1.48°/cycle, p = 0.003). No significant differences were found in the average finger separation amplitudes between PD, PSP-R and MSA-P patients ($p_{msa\text{-}pd}$ = 0.726, $p_{msa\text{-}psp}$ = 0.363, $p_{psp\text{-}pd}$ = 0.726). The lack of clinically significant sequence effect during finger tapping differentiated PSP-R from both PD and MSA-P patients, and might be specific for PSP-R. The finger tapping kinematic parameter of amplitude slope may be a neurophysiological marker able to differentiate particular forms of parkinsonism.

1. Introduction

Progressive supranuclear palsy (PSP) is the second most common form of neurodegenerative parkinsonism after Parkinson's disease (PD). Its classical clinical presentation, known as Richardson syndrome (PSP-R), is characterized by early gait instability with falls, vertical supranuclear gaze palsy, symmetrical akinetic-rigid syndrome, cognitive and behavioral changes, and death within 7–8 years of initial symptom onset [1].

Akinetic-rigid parkinsonian syndrome in PSP-R is predominantly axial, and sometimes out of proportion to limb tone which may be relatively spared [2]. Bradykinesia, defined as "slowness of initiation of voluntary movement with progressive reduction in speed and amplitude of repetitive action" (also known as sequence effect [SE]) [3], is controversial in PSP patients. A study of 75 pathologically proven PSP patients identified bradykinesia in only 22% of patients in the first disease year [4], in contrast to more recent studies where early bradykinesia was reported in 88% and 75% of pathologically confirmed PSP cases [5], [6]. Recently, Ling et al. objectively assessed repetitive finger tapping (FT) in PSP-R and PD patients and age- and sex-matched healthy controls (HC), and found that PSP-R patients had small finger separation amplitude (<50% of that in controls and PD patients) without progressive decrement (that is, without SE) [7]. Therefore, they concluded that "the severe hypokinesia (small amplitude movements) irrespective of disease severity and the lack of a sequence effect" were useful in discriminating PSP-R from PD patients and HC, suggesting also that features identified in PSP-R might not adhere to the definition of bradykinesia in PD [3].

We studied the differences in the pattern of repetitive FT in patients with PD, PSP-R, and multiple system atrophy of

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http://dx.doi.org/10.1016/j.jocn.2015.10.053
0967-5868/

predominantly parkinsonian subtype (MSA-P), and compared them with HC.

2. Methods

2.1. Participants

This study comprised of four groups of right-handed participants recruited from the Movement Disorders Unit at the Clinic of Neurology, Belgrade: (1) 13 patients with PD diagnosed according to the UK Queen Square Brain Bank Criteria [3]; (2) 15 PSP-R patients diagnosed according to the criteria of Litvan et al. [5]; (3) 14 MSA-P patients, fulfilling the criteria of Gilman et al. [8]; and (4) 14 HC with no history of neurological or psychiatric disease (Table 1). HC were age- and sex-matched with the overall patient group.

Patients with tremor/dyskinesia and hand dystonia, as well as any disability of the extremities that might interfere with motor tasks, were excluded from the study. Other exclusion criteria in PD patients were: (1) scores of <26 on the Mini Mental Status Examination [9] or <15 on the Frontal Assessment Battery [10]; (2) score $\geqslant$14 for the Hamilton Depression Rating Scale [11]; and (3) history of psychosis or major medical disease.

Disease staging was assessed according to the Hoehn and Yahr system [12] and motor disability using the Unified Parkinson's Disease Rating Scale (UPDRS III) [13]. Levodopa equivalent dose was also calculated [14]. All the tests, including FT performed in accordance with the recommendations for FT assessment, were conducted in the morning after an overnight treatment withdrawal of at least 12 hours where applicable (patients with PD were tested during "off" time) [15].

The research was approved by the Ethical Committee of the School of Medicine, University of Belgrade, and written informed consent was obtained from each participant.

2.2. Experimental setup and testing protocol

The system included two inertial measurement sensor units which acquired signals and wirelessly transmitted to a remote computer [16].

The PD group included only patients with predominantly right sided affliction and data were obtained from the right hand.

The participants were asked to sit comfortably and were asked to hold their hand in front of them. Participants were instructed to repeatedly tap the index finger and thumb as rapidly and as widely as possible for 15 seconds (the same acoustic signal was used for "start" and "stop" commands), with a 1 minute pause between trials. Each of the three consecutive trials began and ended with fingers closed (zero angle).

2.3. Kinematic parameters

Angle amplitude in degrees (°), cycle duration (ms), and speed (°/s) were measured for each cycle of FT from one index finger–thumb separation to the next [7]. Signals were processed by custom-made software [16].

Tapping amplitude was defined as the angle between the long axes of the thumb and index finger. Mean speed was the mean rate of change in aperture regardless of whether the aperture was opening or closing. Closing and opening velocities (°/s) were the peak velocities of aperture closure and opening within a cycle, respectively.

The coefficients of variation (CV) of amplitude and speed across the tap trials were calculated [17]. High values of CV illustrated irregularities of kinematic parameters.

Progressive changes in amplitude, duration and speed across a 15 s FT trial were represented by the slope of the fitted linear regression line as shown in Figure 1. The slope of change in amplitude was used to assess progressive hypokinesia or "decrement". The slope of change in speed that encompassed both amplitude and duration was used to assess progressive slowing of movement.

2.4. Statistical analysis

All groups were compared according to their mean values, using parametric one-way analysis of variance (ANOVA) (or Welch ANOVA when group variances were non-equal), and Kruskal–Wallis one-way analysis as a non-parametric test. For parameters with statistically significant differences among groups, we performed multiple comparisons between each two groups (Tukey test within one-way ANOVA, Games-Holwell test within Welch ANOVA, or Holm test within Kruskal–Wallis). Comparisons of slopes of kinematic parameters were carried out by univariate analysis of covariance (ANCOVA) with sex, age and disease duration as covariates. UPDRS total, UPDRS III and disease duration were analyzed with the t-test for two independent samples or Mann–Wilcoxon test. Sex and Hoehn and Yahr score were analyzed with chi-squared or Fisher's test. The coefficient of Spearman's correlation (ρ) was used to quantify correlation between kinematic parameters and clinimetric scores.

The Statistical Package for the Social Sciences version 17.0 (IBM, Armonk, NY, USA) and R-studio (2014) version 0.98.976 (Boston, MA, USA) were used for statistical analysis.

Table 1
Demographic and clinical features of patients with PD (n = 13), PSP (n = 15), MSA (n = 14) and HC (n = 14)

Parameters	HC	PD	PSP	MSA	All groups (p-value)	HC–PD	HC–PSP	HC–MSA	PSP–MSA	PD–MSA	PSP–PD
Age, years	56.8 ± 9.0	60.9 ± 9.9	65.8 ± 8.7	58.0 ± 4.5	0.074	–	–	–	–	–	–
Female/Male	8/6	6/7	6/9	9/5	0.626	–	–	–	–	–	–
Disease duration, years	–	4.6 ± 4.5	5.2 ± 2.4	3.5 ± 1.3	0.259	–	–	–	–	–	–
LED, mg/day	–	664 ± 531	746 ± 175	541 ± 306	0.149	–	–	–	–	–	–
Hoehn and Yahr stage	–	2.1 ± 0.9	3.8 ± 0.8	2.0 ± 2.6	0.032	–	–	–	–	–	–
UPDRS total	–	47.1 ± 18.9	81.7 ± 17.6	78.5 ± 12.5	p < 0.001	–	p < 0.001	–	–	–	p < 0.001
UPDRS motor part	–	27.2 ± 10.3	46.7 ± 10.7	45.7 ± 8.3	p < 0.001	–	p < 0.001	–	–	–	p < 0.001
MMSE	29.4 ± 0.9	28.8 ± 1.1	24.1 ± 3.6	27.5 ± 1.9	p < 0.001	p < 0.001	p < 0.001	p = 0.016	p = 0.002	–	–
HDRS	4.0 ± 2.1	8.2 ± 4.7	13.2 ± 6.3	16.5 ± 6.3	p < 0.001	p = 0.023	–	p < 0.001	p < 0.001	p < 0.001	p = 0.023
FAB	17.9 ± 0.3	15.5 ± 1.3	8.9 ± 3.6	14.4 ± 2.6	p < 0.001	p < 0.001	p < 0.001	p < 0.001	p < 0.001	–	p < 0.001

Data are presented as mean ± standard deviation.
FAB = Frontal Assessment Battery, HC = healthy controls, HDRS = Hamilton Depression Rating Scale, LED = levodopa equivalent dose, MMSE = Mini Mental Status Examination, MSA = multiple system atrophy of parkinsonian type, PD = Parkinson's disease, PSP = progressive supranuclear palsy, UPDRS = Unified Parkinson's Disease Rating Scale.