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Short Communication

Steadiness of syllable repetition in early motor stages of Parkinson's disease

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ABSTRACT

Patients with Parkinson's disease (PD) show characteristic abnormalities in the performance of simple repetitive movements which can also be observed concerning speech rate and rhythm. The aim of the current study was to survey if patients with early PD already feature impairments of steady vocal pace performance based upon a simple syllable repetition paradigm. $N = 50$ patients with PD with mild to moderate motor impairment and $n = 32$ age-matched healthy controls were tested. Participants had to repeat a single syllable or a pair of alternating syllables in a self chosen steady pace or in a given pace of 80/min. The coefficient of variance was taken as measure of stability of repetition. As main and novel result, vocal pace performance was observed to be irregular in all patients, even in the subgroup of PD patients with only very mild motor impairment (Hoehn&Yahr stage 1), although the capacity of rapid syllable repetition was preserved. Weak correlations were found between the maximum repetition rate (but not with steadiness of repetition) and some distinctive Parkinsonian motor features as speech impairment and gait.

Assumed that subsequent studies are able to confirm these preliminary results, analysis of steadiness of syllable repetition might be a promising non-invasive tool for detection of subtle abnormalities of motor speech performance even in the early motor stages of PD.

1. Introduction

Parkinson's disease (PD) is a chronic progressive neurodegenerative neurological disease with a variety of motor and non-motor symptoms. According to the prevailing concept of the Braak stages, Lewy bodies as the neuropathological hallmarks of neurodegeneration in PD can initially be found in the olfactory bulb and lower brain stem nuclei years before the involvement of the dopamine producing cells in the substantia nigra pars compacta [1]. In these "premotor" stages a subtle acquisition of the patient's medical history might reveal early symptoms as hyposmia, constipation or REM sleep behavior disturbance and mood disorders [2], however, these symptoms are unspecific and not always present. Furthermore, they occur in an otherwise "neurologically healthy" population and systematic collection of these symptoms is difficult, although attempts to meet this goal are actually underway [e.g. 3]. But, at present, the clinical diagnosis of PD still depends on the identification of a combination of the cardinal motor features of bradykinesia, rest tremor and rigidity. The diagnosis can be assured by a favorable response to dopaminergic medication and additional clinical signs as asymmetry of motor symptoms [4]. However, despite these criteria, the diagnosis of PD in its "early motor" stages is still challenging and often inaccurate [5]. Nonetheless, the first motor signs of PD which could allow a clinical diagnosis based upon accepted criteria do not occur until a substantial number of dopaminergic midbrain neurons are already degenerated [6]. And even in these early motor stages of PD, the clinical signs are often subtle and inconclusive leading to a delay of the diagnosis and of the initiation of treatment [7].

On the other hand, early diagnosis of PD is desirable to provide appropriate information and management of patients, the more so, as some studies suggest that early treatment may lead to a better outcome [8,9], although real neuroprotective or disease modifying therapeutic strategies are still not available. Therefore, there is an urgent need for the establishment of meaningful and easily applicable clinical tests to facilitate an early diagnosis of PD.

Abbreviations: PD, Parkinson's disease; H&Y, Hoehn and Yahr classification of the stage of Parkinson's disease; UPDRS III, Unified Parkinson's Disease Rating Scale, Part III (motor section); SD, standard deviation; VKT, vowel keeping time (in milliseconds); maxSylRep, maximum syllable repetition rate (in syllables per second); IntDur, interval duration; avIntDur, average interval duration; COV, coefficient of variance; %PA, percentual pace acceleration; fMRI, functional magnetic resonance imaging.

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Table 1
definition of Hoehn&Yahr stages [13].

Stage 0	No motor signs
Stage 1	Symptoms on one body side only (purely unilateral motor signs)
Stage 1.5	Symptoms unilateral and also involving the neck and spine
Stage 2	Symptoms on both sides (bilateral) but no impairment of balance
Stage 2.5	Mild bilateral symptoms with recovery when the 'pull' test is given *(the doctor stands behind the person and asks them to maintain their balance when pulled backwards)*
Stage 3	Balance impairment. Mild to moderate disease. Physically independent
Stage 4	Severe disability, but still able to walk or stand unassisted
Stage5	Needing a wheelchair or bedridden unless assisted

However, first motor symptoms of PD as slightly reduced arm-swing while walking or mild deterioration of dexterity are often unspecific, especially in elder persons with co-existing morbidity, and therefore often enough do not suffice to establish the diagnosis of PD based upon conventional clinical/neurological examination. Accordingly, easy applicable tests with high sensitivity would be helpful to gain more diagnostic certainty already in the stages with subtle motor symptoms.

Abnormalities of the steady performance of simple repetitive "automated" movements are well-known features of PD and can be identified in different motor modalities as hand and finger movements, gait and also in Parkinsonian hypokinetic dysarthria. This characteristic pattern of "motor instability" throughout the performance is thought to be induced by the complex dysfunction of planning, preparing, scaling and maintaining a once chosen simple motor program as a consequence of the underlying basal ganglia dysfunction [10]. Since speech can be subdivided down to the level of single utterances, one might expect abnormalities of vocal pace performance already on the level of very basic non-speech articulatory gestures. Indeed, in previous studies, our group had been able to show that patients in different stages of PD featured marked difficulties to steadily repeat a single syllable without changing the speed of the repetition [11,12]. However, the majority of these tested patients was in their rather moderate to advanced stages of PD and was affected by considerable co-existing voice and speech impairment as well. Up till now, it has not been investigated, if these abnormalities of steady vocal pace performance are already detectable in the very early motor stages of PD and if they occur somewhat independent from overall dysarthria.

2. Methods

$N = 50$ patients with PD (30 male) with mild to moderate motor impairment and $n = 32$ age-matched healthy controls (19 male) were tested. A group of $n = 20$ patients and $n = 16$ control speakers had already participated in a previous study of our group [12]. In the patients' group Hoehn&Yahr/H&Y stages ([13] see Table 1) ranged from 1.0 to 2 (average H&Y 1.70, standard deviation/SD 0.39) and the average Unified Parkinson's Disease Motor Score/UPDRS III was 14.90 pts. (SD 6.08). Moreover, the axial symptoms of the UPDRS III except item 18/speech were calculated separately (items 19 [facial expression], 20 [head tremor], 21 [neck rigidity], 27 [arising from chair], 28 [posture], 29 [gait] and 30 [postural stability]) and related to the entire UPDRS Motor Score (axial ratio = axial subscore/overall UPDRS III).

Participants' characteristics are listed in Table 2. At the time of examination, all patients were under stable but uncontrolled regimen of dopaminergic medication for at least four weeks. Speech and motor examinations were performed 60–90 min after the morning dose of medication to ensure the "on"-state.

Speech samples were digitally recorded and anonymized by a study nurse using a commercial audio software and a headset microphone. The speech task consisted of four subtests which have been described in detail in one previous study of our group [12]. Vowel keeping time/VKT (in milliseconds): Participants had to produce the German vowel/a/as long as possible with one single breath. Test 0: Participants had to reiterate the syllables /pa/ and /pa–ti/ as fast as possible for at least 5 s for the description of maximum syllable repetition rate (maxSylRep in syllables per second). Test 1: Repetition of the syllable /pa/ in a self chosen steady (isochronous) pace without acceleration or slowing articulatory velocity.

A subgroup of $n = 32$ patients with PD (20 male) and the entire control group performed two additional syllable repetition tasks (The results of this subgroup have already been presented on the MAVEBA conference 2013): Test 2: Repetition of the syllable /pa/ in a velocity of 80/min given by a metronome; participants had to listen to the pace first, then start with the syllable repetition; the metronome was stopped after four utterances, and participants had to keep the given pace. Test 3: Alternating repetition of the syllables /pa/ and /ti/ with the given metronome-based velocity of 80/min.

Each subtest was performed twice; the average values of first and second cycle were taken for the definite analyses. In each test the participants were asked to repeat the syllables at least 40 times (see Fig. 1). Only the first 30 utterances were taken for the definite analyses in order to avoid a modification of participants' articulatory velocity by the expectance of the imminent end of the task. Based upon the oscillographic sound pressure signal of the recorded audio material, the period from onset of one vocalization until the following vocalization was defined as "interval"; interval duration (IntDur) was measured manually in milliseconds (ms). Stability of pace of the utterances was defined as relative coefficient of variation (COV_{5-30}) calculated for the intervals 5–30 in relation to the average interval length of the first 4 utterances ($avIntDur_{1-4}$) following the formula: $COV_{5-30} = SD_{5-30}/[(avIntDur_{1-4})/\sqrt{26}] \times 100$. Additionally, the average interval length of the intervals 5–17 and of the intervals 18–30 were related to the reference interval ($avIntDur_{1-4}$); the difference of both average interval lengths (of the first and second half of the performance) in relation to the reference interval duration was defined as comprehensive measure of pace acceleration in the course of the repetition (%PA) with values greater than 0 indicating an acceleration. Furthermore, in test 3 (alternating repetition of a pair of syllables in a given pace), the

Table 2
Participants' characteristics definition.

	Entire PD group $n = 50$, 30 m Mean/SD/range	PD subgroup (test 2 + 3) $n = 32$, 20 m Mean/SD/range	Control group $n = 32$, 19 m Mean/SD/range
Age (years)	64.98/9.11/40–82	66.68/9.32/40–82	66.00/11.89/43–83
Disease duration (years)	3.54/2.12./1–9	3.71/2.30/1–9	
Hoehn&Yahr	1.70/0.39/1–2	1.82/0.24/1.5–2	
UPDRS III	14.90/6.08/5–25	12.74/4.29/5–21	
Axial UPDRS score	5.14/2.57/1–17	6.16/2.57/3–17	
Axial ratio	0.39/0.19/0.08–0.85	0.50/0.13/0.33–0.85	
UPDRS speech item	0.82/0.66/0–3	0.97/0.66/0–3	