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Vocal changed in Parkinson's disease patients

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Introduction

Background of PD

Parkinson's disease (PD) is a long-term degenerative disease of the central nervous system. It is the fastest growing disease and there will be more than 12 million patients until 2040 [1]. Due to its negative impact, which impairs patient's motor skill, language skills, and reduces the life quality rapidly. These will induce daily increased burden on our health care system and society [2].

Vocal changed in PD

The significant manifestation of PD is characterized by a resting tremor [3], rigidity [4], bradykinesia [4] and especially changes in voice and speech [5]. It is obvious that vocals are changed in PD patients in the second phase [6], which are caused by hypertension on muscles from facial, vocal and trunk part. Due to these reasons, the vocal manifestations of PD was mainly characterized by changed sound quality [7], poor articulation [8-10], dropping tone or rhythm [8,11], trembling voice, increased frequency and number of jitters [8,12] and reduced volume [13-15].

The most obviously phenomenon of vocal changed in PD patients is presented in declined sound quality and poor articulation. Early in 2004, Kawada, et al. used acoustic analysis to compare the vocalizations and speeches between PD patients and control. They found out that patients showed slow pronunciation speed [8]. In another cross-sectional study, Silva, et al., reported that the voice quality changed (details) in patient with PD [7]. Furthermore, in 2010, Alexander, et al. described the fluency of speech in patients with PD, indicating that PD patients' voices were disfluent and the rate of articulation was significantly reduced under clear speech conditions [9]. Similarly, Martínez-Sánchez et al. found that the speech and articulation rates of PD patients were also significantly reduced in 2016 [10].

Another vocal change displayed in decline tone or rhythm

Sabine, *et al.* performed a single syllable or a pair of alternating syllable repeating tests on PD patients in 2013, they inferred that the rhythm of speaking in PD patients was irregular, which can be found even in early stages of PD and correlate to axial motor symptoms [11]. In addition, Kawada, *et al.* suggested that when PD patients are reading the short sentences loudly, the tone of each syllable was flat, and the speech of a single syllable lacks articulation [8].

Moreover, Sound tremor, frequency and number of jitters presented increased

In 2005, Gómez-Vilda, *et al.* reported that vocal fold tremor is a specific marker that can be detected in approximately 60% of PD cases and is known to be distributed in a frequency band of 2-4 Hz (physiologic), 6-10 (nerve) or above 10 Hz (sometimes called dithering or dithering) [12]. In 2012, Silva, *et al.* conducted a cross-sectional study of PD patient sounds, they found out that the basic frequency and jitter of the PD patient's voice exhibited a higher value than health control [7].

Meanwhile, volume down presented decrease among them. In 2013, Sinclair, *et al.* suggested that the laryngeal dysfunction caused by motor-induced dysarthria in PD is manifested as glottic insufficiency caused by vocal cord paralysis, accompanied by atrophy, showing a decrease in voice volume and sound intensity [13]. In 2015, Harishchandra, *et al.* demonstrated that PD patients have decreased functional communication due to the presence of dysarthria, which can be characterized by not only a reduced loudness, but also monotonous tones (or fundamental frequencies), irregular speech, and imprecise consonants [14]. In 2017, Schalling, *et al.* proposed that the most common symptoms of PD patients were weak voice and inaccurate pronunciation [15].

Mechanism of dysphonia

The fine control on muscles present deficits due to partially damage on basal ganglia in PD patients [16]. Dysarthria can be the leading cause causing the muscle weakness, paralysis, or a lack of coordination of the motor-speech system [17]. Therefore, the muscles in speech-producing organ including face, moth, voice-box (larynx) and chest, present insufficient control during speaking process [18].

Date back to 1990, Murdoch pointed out that the main components of the extra-pyramidal system includes the basal ganglia in the cerebral hemisphere, and dysarthria may occur when muscle control is involved

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in the pronunciation mechanism [19]. Muscle dyskinesia occurred in mouth, throat and ankle, these induced the difficulty in pronunciation. These muscle dyskinesias may induced salivation, difficulty swallowing, slow speech rate and difficulty in pronunciation as well [20,21].

While muscle tone and tremor may be increased due to dyskinesia. In 2005, Widnell showed that increased muscle tone and tremor in patients with PD are associated with dopamine receptors [22]. When patients with PD have reduced dopamine receptors, their muscle tone and tremor will increase, their amplitude will decrease, and the frequency will increase, resulting in a series of bass, sound tremors and apathy [23].

Furthermore, the vocal cords are playing the crucial role in pronunciation [24]. The damage on vocal cord can caused dysphonia [25]. Early as 1978, Logemann, et al. studied the frequency of speech and vocal symptoms in patients with PD, as well as other vocaltract dysfunction, including laryngeal disorders, rate disorders, and hypernasality. The vocal-tract symptoms are mainly laryngeal dysfunction, back-tongue involvement, tongue-blade dysfunction, and labial misarticulations [26]. In 2002, Yücetürk, et al. performed video laryngoscopy on dopamine-treated PD patients and normal subjects to evaluate the parameters of vocal fold edges, glottal closure, and amplitude of vibration. The results showed that the PD group had a higher rate of abnormal video laryngoscopy. These parameters provide sufficient information for the diagnosis of vocal cord function in PD patients [27]. In 2015, Giovanni Defazio, et al. found that the vocal cords exhibited reduced elongation and limited/unstable adduction at the articulation level, which affected the quality and range of speech [28]. In 2016, Tsai, et al. found that vocal cord muscles dysfunction in PD patients may be associated with nigrostriatal dopaminergic dysfunction [29].

Perspective

The daily life was seriously affected by this disease directly and indirectly. This can lead to a serious financial burden on the patient's family. Therefore, early diagnosis of PD can improve their quality of life. Vocal changes in PD patients are a promising biomarker at the early stage of PD. Early identification of PD can increase the chances of earlier intervention and delay the onset of the disease.

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