Abstract

As the population is growing older, we face new challenges to cope with an increased number of people with neurodegenerative neurological diseases. Parkinson's disease (PD) is the second most common neurodegenerative disorder, characterized by pathological deposits of α-synuclein that lead to the loss of dopaminergic neurons in the substantia nigra, which is the direct cause of principal motor manifestations, including bradykinesia, rigidity, and resting tremor. Unfortunately, no sufficiently accurate biomarkers are available to detect PD prodromally, differentiate it from other types of parkinsonism and measure its disease progression. As the most complex human motor skill involving numerous muscles, speech is a sensitive marker of damage to neural structures engaged in motor system control. This dissertation aims to explore the potential of objective acoustic evaluation of vowel articulation in comparison with other measures of speech dysfunction as a surrogate biomarker of α-synucleinopathies. To achieve this aim, we collected speech data from patients with isolated rapid eye movement sleep behavior disorder (iRBD), a special case of prodromal PD, de-novo PD, advanced PD, atypical parkinsonian syndromes, and other progressive neurodegenerative diseases, as well as healthy control speakers. We discovered that vowel articulation impairment was already affected in iRBD, especially in patients with hyposmia before nigrostriatal dopaminergic transmission was affected, suggesting that speech production is already slightly affected very early in the synucleinopathology process. We found distinct speech adaptation in atypical parkinsonian syndromes and other progressive neurodegenerative diseases compared to PD, reflecting sensitivity variations in vowel articulation in disease pathophysiology. Also, we showed that vowel articulation is age-independent. The findings of this thesis imply that vowel articulation may provide a robust digital speech biomarker for early presymptomatic diagnoses, differential diagnosis, and disease progression, bolstering its use in future clinical trials for developing neuroprotective therapies.

Keywords: Speech impairment; Dysarthria; Vowel articulation; Acoustic analysis; Automated Vowel Articulation Analysis; Parkinson's disease; Isolated REM sleep behaviour disorder; Atypical parkinsonian syndromes; Neurodegenerative disorders