Characterizing tongue tremor in Parkinson's disease using EMA

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Abstract

Resting tremor is a cardinal symptom of Parkinson's disease (PD) which has been well described in the limbs. Tongue tremor is less well understood, but is of particular interest since it is well known that PD patients experience articulation and swallowing difficulties resulting from atypical lingual function. To learn more about the nature and prevalence of tongue tremor in PD, we conducted an EMA study of 24 patients. Activity in two lingual sensors was tracked while the tongue was at rest in pre-speech intervals, and an algorithm was developed to automatically detect tremor from periodic components in the vertical tongue sensor signals. Tongue tremor was found in 17% of the speakers in our sample, indicating that it may be more prevalent than previously assumed. Results from this study have clinical relevance as tongue tremor may be one of the earlier symptoms of PD and may therefore be useful in the diagnosis of the disease.

Keywords: Parkinson's disease, tongue tremor, electromagnetic articulography, speech kinematics

1. Introduction

Tremor is a term that is used to describe the involuntary, periodic movement of a body part, and it is one of the three cardinal symptoms of Parkinson's disease (PD) (Poewe *et al*., 2017). It is estimated to occur in approximately 75% of all PD patients (Gironell *et al*., 2018). Although multiple forms of tremor have been identified in PD, a 'resting tremor' is the most common form. This tremor emerges when a body part is at rest and ceases as soon as the body part in question becomes actively used. Although resting tremor in PD is usually present in the upper and lower limbs, on the lips, on the jaw or in the larynx (e.g., Gironell *et al*., 2018; Perez *et al*., 1996), a small number of studies have also reported the presence of tremor in the tongue in PD (alternatively also referred to as 'lingual tremor'). Besides being less reported, tongue tremor is also considered rarer than limb tremor in PD (Jaulent *et al.,* 2015). One explanation for the lack of research on tongue tremor in PD may be the fact that patients are less concerned about tongue tremor and they may thus not report it as often as other symptoms (Fabri *et al.*, 2017). Experimental research on the prevalence of tongue tremor in PD is limited and inconclusive. Estimates of its occurrence in PD vary from 1% of PD patients in a study by Leopold and Kagel (1996) to 50% of patients in a study by Robbins *et al*. (1986). This difference might reflect methodological differences between the two studies. Where Leopold and Kagel examined the presence of a tremor through visual oral examination, Robbins *et al*. used videofluoroscopy to do so. A key difference between these methods is that in the first, patients have to lower their jaw and tongue to make it possible to observe tongue movement, whereas in the second, the vocal tract can remain at rest during the observation of the tongue. Especially when it comes to inspecting the posterior part of the tongue, these different methodologies may lead to different results. It is not unlikely that some patients only show a resting tremor while the vocal tract is fully at rest. Although tongue tremor does have a high prevalence amongst patients with Essential Tremor, this condition is generally considered to have its own distinct etiology and is therefore not comparable to PD (Lou & Jankovic, 1991; Shahed & Jankovic, 2007).

Past studies have shown that tongue tremor is often highly periodic, with frequencies ranging from 3 to 6 Hz (Hunker & Abbs, 1990; Toda *et al.,* 2017). These observations are comparable to what has been found for tremor in the limbs (Lee *et al.,* 2016). However, although tongue tremor can occur simultaneously with tremor in the limbs, it has also been observed on its own, suggesting that tongue and limb tremor may originate from different neural structures (Hunker & Abbs, 1990; Robbins *et al.,* 1986). Interestingly, previous work has described subjects for whom a tongue tremor was the first (Jaulent *et al.,* 2015) or among the first signs of PD (Delil *et al.,* 2015). This finding suggests that this symptom may be of interest with regard to the early diagnosis of the disease.

The aim of the present study was twofold. First, the study demonstrates how electromagnetic articulography (EMA) can be used to study tongue tremor in PD in new detail and in ways not previously possible using existing methods. EMA provides data on the state of the vocal tract while all articulators are at rest: information which is not typically available when examining a patient's body only from the outside. In addition, EMA provides detailed information about the frequency and the temporal characteristics of the tremor. Our study is the first to employ EMA to study tongue tremor. Second, our study proposes an automated method to detect tongue tremor from kinematic signals. Automated methods such as these might eventually help clinicians to diagnose tongue tremor on the basis of articulatory data. Our algorithm has been written on the basis of tongue tremor data that was observed in a large samples of PD patients. To demonstrate our approach, we describe two subjects with different pathologies for whom a tremor was detected.

2. Method

Twenty-four patients diagnosed with idiopathic Parkinson's disease took part in this study. Speakers were not selected on the basis of their symptoms, but speakers with severe swallowing problems were excluded from taking part in the study to avoid any risk associated with the sensor adhesion procedure. All speakers were on dopaminergic (Levodopa) medication during the experimental procedure. Before taking part in the experiment, they completed Part II of the International Parkinson and Movement Disorder Society UPDRS (Goetz *et al.,* 2008), including question 2.10 regarding tremor: "Over the past week, have you usually had shaking or tremor?" Subjects rated their tremor on a 5-point scale ranging from 0 ("Not at all. I have no shaking or tremor") to 4 ("Shaking or tremor causes problems with most or all activities"). The study was approved by the Medical Ethics Review Board of the University Medical Center Groningen (UMCG) under number NL66063.042.18.

Subjects were asked to read aloud carrier phrases containing target words which were constructed for other purposes than the present study. EMA recordings were started two seconds prior to stimulus presentation and thus prior to the initiation of speech. Two sensors were placed on the dorsal midline of the tongue, one sensor was placed on each lip at the vermillion border, and to track JAW movement a sensor was placed either below the lower incisors (subject A) or on the chin (subject B). The posterior tongue sensor (TB) was located by using dental color transfer applicators to stain the palate and determining the mark left on the tongue dorsum after the participant produced [k]. The anterior tongue sensor (TT) was placed 1 cm posterior to the tongue's apex (see Rebernik *et al*. (forthcoming, 2021), for a more detailed description of our procedure).

Kinematic analysis was performed in MATLAB (R2017b). Sensor vertical movement trajectories were smoothed using a robust discretized smoothing spline (Garcia, 2010), followed by an 8th order high-pass IIR filter with a cutoff frequency of 1 Hz to remove the DC component. In order to identify tremor on the resting tongue, the first two seconds of every recording were analyzed, prior to speech activity. Because no methods have previously been described for automatic analysis of tongue tremor in PD, we explored different signal processing methods capable of capturing the tongue tremor observed in these data; the algorithm presented here represents an initial attempt at automatic detection of tongue tremor which will require further refinement.

Power spectra were generated for the sensor signals of interest, calculated using a 1024-pt Fast Fourier Transform over the entire two second pre-speech time interval. Periodic articulator movement was identified from peaks in each power density spectrum, and peaks exceeding 75% of the maximum intensity were flagged as potential tremor frequencies. Additionally, the RMS energy of the entire two second pre-speech interval was computed. Signals characterized by a marked spectral peak between 3-6 Hz (see **Figure 1**) and for which the RMS amplitude of the original EMA trace was higher than 0.2 mm were classified as showing tremor. The 3-6 Hz range was chosen to conform with frequencies identified in previous studies of limb tremor (Hunker & Abbs, 1990; Toda *et al*., 2017), and the 0.2 mm threshold was determined to be the most effective level for robustly distinguishing between trials with and without tremor. Settings were refined through repeated visual inspections of the data, ensuring that visually observed tremor was detected by the algorithm in as many trials as possible, while random noise was not identified as tremor. This procedure was applied to the TT, TB and JAW signals. The script can be downloaded from here.

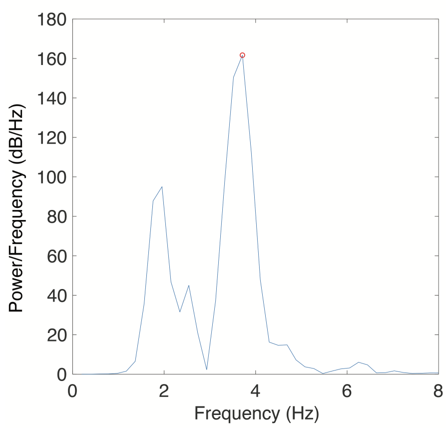

Figure 1: *Power Density Spectrum of the vertical component of the TB signal in a trial classified as showing tremor. The strong spectral peak at approximately 4 Hz is characteristic of tremor observed on speech articulators in the participants in this study.*

3. Observations

Our algorithm detected tremor in one or more trials for four of the twenty-four PD patients (16.7%) included in our study. The acoustic and articulatory activity in each trial that was automatically flagged using the algorithm, was examined closely by a trained phonetician in order to ensure that the repetitive activity was not associated with speech movements, noise, or other potentially confounding factors. Each of the automatically identified trials showed clear evidence of tongue tremor. We present data from two patients to illustrate the utility of this method: one showing both tongue as well as jaw tremor, and one who reported being unaware of any shaking or tremor.

3.1. Subject A

Subject A is a 73-year-old male, diagnosed with PD 12 years ago, who reported experiencing articulatory difficulties. For question 2.10 of the UPDRS he reported a 1, stating that shaking or tremor occurred, but did not lead to any problems. Tongue tremor was identified in the TB signal for 55 of 80 trials (69%) (mean tremor frequency = 3.7 Hz (SD = 0.3); RMS tremor amplitude = 1.7 mm (SD = 0.5)). Tremor was identified in the TT signal in 53 of 80 trials (66%) (mean tremor frequency = 3.7 Hz (SD = 0.3); RMS tremor amplitude = 0.9 mm (SD = 0.3)). In 38 of 80 trials (48%) an additional jaw tremor was observed with a more variable frequency than the tongue tremor (mean tremor frequency = 4.7 Hz (SD = 1.8); RMS tremor amplitude = 0.9 mm (SD = 0.8)). Example tremors in two trials by Subject A are illustrated in **Figure 2**.

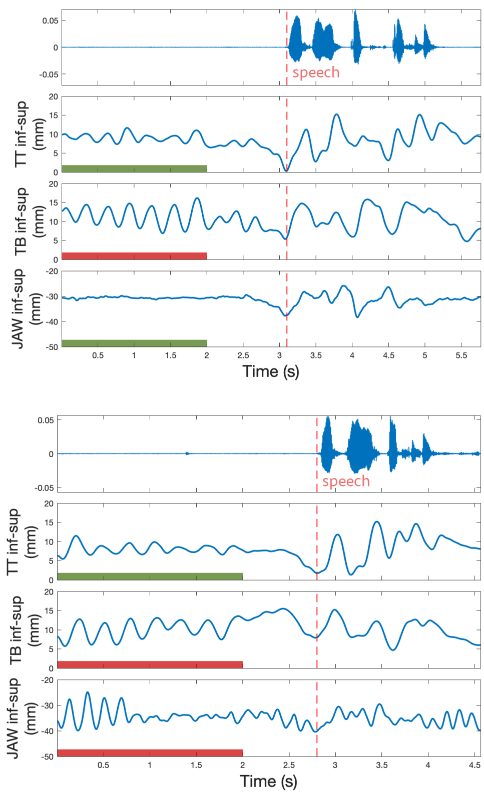

Figure 2: *Tongue trajectories for Subject A during two trials. Vertical trajectories of TT (2nd row), TB (3rd row) and JAW (bottom row) are shown over time. The waveform is shown in the top row. Trajectories for which a tremor was detected are marked with a red bar at the bottom of the row. Trajectories for which no tremor was detected are marked with a green bar. For the TT trajectories, the marked spectral peaks had frequencies between 2-3 Hz, which were just below the 3-6 Hz range of the tremor detection algorithm. Note that in the bottom graph, an additional jaw tremor can be observed with higher frequency and amplitude than the tongue tremor.*

3.2. Subject B

Subject B is a 72-year-old male, diagnosed with PD 3 years before participating in the study, who also reported experiencing articulatory difficulties. For question 2.10 of the UPDRS he reported a 0, indicating that he experienced no shaking or tremor. Nevertheless, a tremor was observed in the TB signal for 27 of 81 trials (33%) (mean tremor frequency = 3.7 Hz (SD = 0.3); RMS tremor amplitude = 1.5 mm (SD = 0.5)), and in the TT signal for 16 of 81 trials (20%) (mean tremor frequency = 3.9 Hz (SD = 0.5); RMS tremor amplitude = 0.2 mm (SD = 0.1)). The tremor emerged when the tongue was raised and disappeared when it was lowered. In 16 trials, a relatively weak tremor was observed for the jaw as well (mean tremor frequency = 4.7 Hz (SD = 0.9); mean RMS amplitude = 0.3 mm (SD = 0.03)). Characteristic tremors observed for Subject B are illustrated in two trials in **Figure 3**.

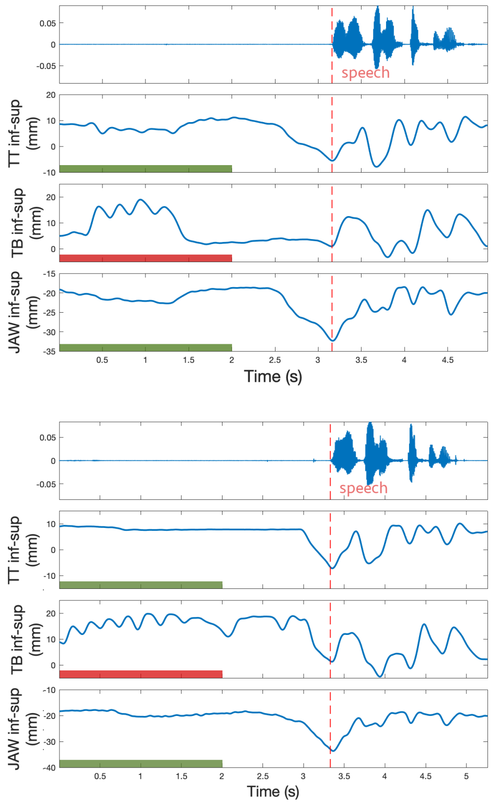

Figure 3: *Tongue trajectories for Subject B during two trials. Vertical trajectories of TT (2nd row), TB (3rd row) and JAW (bottom row) are shown over time. The waveform is shown in the top row. Trajectories for which a tremor was detected are marked with a red bar at the bottom of the row. Trajectories for which no tremor was detected are marked with a green bar. In the top graph, the tremor emerges with TB raising and dissolves as soon as it is lowered. In the bottom graph, TB is kept in a high position and therefore shows a continuous tremor.*

3.3. Tremor during speech

Because the intrinsic frequencies of articulatory gestures during speech were close to those of the tremors observed in these data, our method was not able to disentangle tremor from speech articulation and robustly assess whether tremor also occurred during speech. More detailed analyses might be developed to automatically identify tremor during speech once more data are available to better characterize each signal component and facilitate signal separation.

4. Discussion and conclusion

The purpose of this study was to examine tongue tremor in PD using a modern articulatory method (i.e., EMA) and to propose an automated algorithm to detect tremor from (the first two seconds of) a kinematic signal. The algorithm that we developed successfully identified tremor in 16.7% of PD patients included in this study. These data suggest that tongue tremor in PD might not be as rare as has previously been claimed (Toda *et al.,* 2017). Although we found several cases showing tongue tremor, its true prevalence is possibly even higher. First, our algorithm only identified evident cases of tongue tremor, which could also be visually observed. A more refined algorithm may detect an even higher number of cases, including more subtle manifestations of tremor. Second, the speakers in our study were all in the ON (Levodopa) state, meaning that a potential mediating effect of Levodopa may have influenced our results. Limb tremor often wears off after dopaminergic treatment (Fahn, 2006; Zach *et al.,* 2017), and also tongue tremor has been found to respond well to dopaminergic treatment in a speaker with PD (Jaulent *et al.,* 2015). Thus, we cannot exclude the possibility that tongue tremor of some patients may have been attenuated, suppressed, or absent as a direct result of Levodopa intake. Finally, the fact that speakers with severe swallowing difficulties were excluded from our study may have biased our sample. The prevalence of tongue tremor may be even higher in this group of patients, and perhaps even related to control of their tongue during swallowing (Robbins *et al.,* 1986).

Interestingly, tongue tremor is often not experienced as a burden to patients, which may partly explain why some have designated tongue tremor as a "forgotten clinical sign of PD" (Fabbri *et al.,* 2017, p. 274). In line with this, the patients in our study did not report to experience any (severe) tremor. Subject B even reported that he was not aware of any tremor at all, while his data was clearly showing the presence of it. The fact that patients do not experience the tremor as being problematic, does however not exclude the possibility that its presence may have serious consequences to actions that require tongue movement, such as swallowing or speaking. It is possible that the tremor may lead to muscle weakness, a process which has been suggested to occur in the upper limbs (Brown *et al.,* 1997). There is indeed some evidence that suggests diminished tongue strength in PD patients (Pitts *et al.*, 2018; Solomon *et al.*, 2000), which may in turn lead to speech and swallowing difficulties.

The frequencies of the tremors found in our study align closely with those previously reported for both limb as well as tongue tremor. However, it should be noted that the working of our algorithm was only evaluated by visual inspection of the data. A more systematic approach, in particular one in which the algorithm is tested on novel data, is required to both verify and replicate our results.

In the present study we have shown that EMA is an excellent tool to examine tongue tremor. The use of EMA allowed us to examine different articulators at the same time while the vocal tract was at rest. It also provided us with a detailed time course of the development of the tremor. To our surprise, Subject B seemed to suppress his tremor by actively pushing the tongue down. This is a coping strategy that has not been reported in previous reports. On the other hand, Subject A did not actively suppress the tremor, which is why it was present during the entire two-second interval. This may suggest that the lingual system is balancing the presence of tremor with active suppression. The fact that the tremor was not present in all trials for any of our speakers also points in this direction. Note that this balancing act must be an unconscious process, as our patients were not aware of the tremor.

Another benefit of using EMA in our study was that we were able to demonstrate, for the first time, a difference between the front and posterior part of the tongue. For both Patient A and Patient B, the tremor was most often detected on the posterior tongue sensor. Since the posterior part of the tongue may be hard to observe externally, the presence of tongue tremor may well be missed during a physical examination of the patient in the clinic. Especially since we have shown that patients do not always seem to be aware of its existence. We therefore suggest that EMA is a suitable technique to identify this type of tremor. In addition, EMA does not put any strain on the muscles once the participant has adjusted to sensor placement, in contrast to the general physical examination where a patient would at least have to actively lower the jaw for the tongue to be examined. Thus, it reduces the occurrence of false negative errors. Other than EMA, ultrasound tongue imaging (UTI) may also be a useful tool to quickly observe the presence or absence of tongue tremor in the clinic, as it is relatively inexpensive, less invasive, and easy to deploy. Since previous studies have found tongue tremor to be amongst the first signs of PD, an examination of the tongue in an early stage may be valuable in the diagnostic process of the disease.

To conclude, our study highlights the need for more articulatory research on tongue tremor in PD. We have shown that the occurrence of tongue tremor may be higher than is often assumed. Future studies may investigate this further by including patients in the OFF instead of in the ON state, and by also including patients who experience swallowing difficulties. In addition, we believe that the development of a more sophisticated algorithm than the one used in the present study may also be able to detect tremor when it is less pronounced in the data. Such an algorithm should be applied to a novel data set, especially one in which the researchers do not have any prior knowledge of the data. More knowledge on this topic is warranted, as it may be important for our understanding of tremor in general and may be valuable when it comes to an early and accurate diagnosis of the disease itself. Another open question is how tongue tremor relates to swallowing and speech difficulties. The data from the present study were not sufficient to answer this question, but this is likely of interest to anyone who works on speech and swallowing in PD. We therefore encourage future studies to pursue this matter further.

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