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RESEARCH ARTICLE

Relations between Sensorimotor Integration and Speech Disorders in Parkinson's Disease

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Abstract: ***Background:*** Sensorimotor integration mechanisms can be affected by many factors, among which are those involving neuromuscular disorders. Parkinson's disease (PD) is characterized by well-known motor symptoms, among which lately have been included motor speech deficits. Measurement of the acoustic startle reflex (ASR) and its modulations (prepulse inhibition and prepulse facilitation, PPI and PPF respectively) represent a simple and quantifiable tool to assess sensorimotor function. However, it remains unknown whether measures of the PPI and PPF are associated with motor speech deficits in PD.

Methods: A total of 88 subjects participated in this study, 52 diagnosed with PD and 36 control subjects. After obtaining written informed consent, participants were assessed with PPI at several interstimulus intervals, and PPF at 1000 ms using the SRH-Lab system (San Diego, CA). Percentage of change in the amplitude and latency of the ASR was analyzed between groups. Voice recordings were register of a specific text given to the subjects with a professional recorder and temporal patterns of speech were analyzed.

Results: Statistical analysis conducted in this study showed differences in PPI and PPF in subjects with PD compared to controls. In addition, discriminative parameters of voice abnormalities were observed in PD subjects related to control subjects showing a reduction in phonation time, vowel pulses, breaks, breakage and voice speech periods.

Conclusions: PD presents a disruption in sensorimotor filter mechanisms and speech disorders, and there is a relationship between these alterations. The correlation between the PPI and PPF with an alteration of the voice in PD subjects contributes toward understanding mechanism underlying the neurophysiological alterations in both processes. Overall, easy and non-invasive tests such as PPI, PPF together with voice analysis may be useful to identify early stages of PD.

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1. INTRODUCTION

Parkinson's disease (PD) belongs to a group of conditions called motor system disorders, which results from the damage of dopaminergic neurons in the substantia nigra pars compacta [1]. PD is difficult to diagnose accurately as early symptoms occur gradually and differ among patients that experience motor problems after 50% of the dopaminergic neurons deteriorate and die [2]. Motor abnormalities lead to the diagnostic criteria that include bradykinesia, rigidity, resting tremor or postural instability.

In addition to the hallmark symptoms of PD [3, 4] patients show significant and progressive manifestations in the phonatory system that frequently results in debilitating communicative deficits [4].

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The speech and voice deterioration in PD can be explained by a sensory processing deficit related to speech [5, 6]. Patients are often described as having a high-pitched, monotone, and monoloud voice with a restricted range pitch when compared with normal subjects [7, 8]. Vocal impairment may be amongst the earliest PD symptoms, detectable up to five years prior clinical diagnosis [9, 10]. The loss of dopaminergic input to the striatum and subsequent deregulation of the basal ganglia produce motor deficits that adversely affect all the subsystems related to speech motor control. Any alteration in one of these systems affects the voice and the proper coordination of speech [11]. The acoustic measurements of the human voice reflect the three dimensions of sound: amplitude, pitch and time structure. Disturbances in the phonatory system affect the vibrational rate of the vocal cords, causing changes in the fundamental frequency (F0), which is the main parameter of acoustic analysis

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Disturbances in motor control can be assessed through the analysis of electromyographic activity and movement, abnormal reflex reactions can be an expression of disturbed neuronal excitability, and may be assessed by measuring the size and latency of reflex responses [12]. The acoustic startle reflex (ASR) is a fast muscular contraction that follows a specific sequential pattern elicited by a sudden and intense auditory stimulus and constitutes a tool to evaluate mechanisms of sensorimotor plasticity [13]. The response pattern of the ASR reflects a protective behavior against injury and the magnitude of the response can be modulated by external and internal conditions [14]. Prepulse inhibition (PPI) is the reduction of the magnitude of ASR when the startle stimulus is preceded by a week non-startling stimulus (prepulse) by 30-500 ms [15]. The PPI is an operational measure of sensorimotor gating and reflects a protector mechanism where the information carried by the prepulse is analyzed early avoiding the interference of other stimuli, which limits the ingress of trivial stimuli to cognitive centers or motor output pathways [16]. When the prepulse-to-pulse intervals are longer than 500 ms, the phenomenon is known as prepulse facilitation (PPF) [17] and reflects sensory enhancement and selective attention [18, 19].

Neurophysiologic tests such as ASR, PPI and PPF provide quantifiable data, are not expensive, are safe and can be used without adverse effects to the subjects. Thus, it is possible to use these tests for the evaluation of the alterations in brainstem circuits and their neurotransmitters. Based on the anatomical connections between structures belonging to sensory filtering circuit, substantia nigra (SN) and basal ganglia, we hypothesized that the dysfunction between these circuits affects the sensorimotor gating in PD. If so, it is possible to assess the alteration in sensorimotor filtering using the ASR and its modulation through the PPI and PPF and correlated with temporal speech patterns affected in PD.

2. MATERIALS AND METHOD

2.1. Participants

After obtaining permission of the local Ethics Committee, and written informed consent, the procedures were performed in accordance with the ethical standards laid down in the 2013 Declaration of Helsinki. A total of 88 Spanish subjects participated in the study. PD subjects were clinically diagnosed according to the criteria of the London Brain Bank [20]. They were outpatients from the Neurology Service of the University Hospital of Salamanca, who were seen by at least two senior neurologists experienced in movement disorders. Fifty-two subjects (mean age, 68.44 ± 9.89) formed the PD group and were clinically evaluated using Unified Parkinson's Disease Rating Scale [21] and, Hoehn and Yahr scale [22]. The study was conducted in the morning at the time of their medication's minimal effect. The control group was formed by 35 subjects, and recruited from the general community in recreational centers for elderly people (mean age, 72.14 ± 14.09). Exclusion criteria included: threshold hearing for 1 kHz greater than 30 dB, neurological disorders other than PD, head injury, psychiatric disorder other than minor depression assessed through Geriatric Depression Scale (GDS), and frequent use of illicit substances or alcohol consumption. Cognitive state of all subjects was evaluated with the Minimental State Examination (MMSE) [23]. Table **1** shows gender distribution.

2.2. Auditory Startle Reflex Measurement

Subjects remained comfortably seated in a chair with armrests for the duration of the 15-minute test. The binaural auditory stimulation is provided through headphones (Sony MDR-V6) connected to the reflection measurement device (SRH-LAB trending system), and electromyographic registration of the right orbicularis oculi was done using two small silver electrodes filled with conductive paste placed beneath the right eye and the ground electrode placed in the right mastoid. The test starts after acclimation period of 4 minutes with background noise (70 dB white noise), which is maintained during the entire test. ASR trigger pulses are bursts of 40 ms of white noise with an intensity of 115 dB. The prepulse, a non-startling stimulus, have duration of 20 ms and intensity of 85 dB white noise. Intertrial intervals (ITIs) were assigned with durations of 9 to 23 ms to avoid habituation. The session had four blocks of pulse and prepulse with interstimulus intervals (ISIs) of 60, 120, and 1000 ms. The initial and final blocks were composed of single pulses (5 in each block). The second and third block, each one contained 6 pulses alone and 9 prepulse-pulse with ISI of 60 ms, 9 prepulse-pulse with ISI of 120 ms and 9 prepulse-pulse with ISI of 1000 ms in order to asses PPF.

The latency was measured in ms from the acoustic stimulus to the beginning of the maximum amplitude response (in microvolts), that occurs within 18-120 ms. PPI and PPF were calculated using the mathematic formula:

PPI or PPF % = 100 X [(amplitude ASR without prepulse - amplitude ASR after prepulse) / amplitude ASR without prepulse].

Table1. Gender distribution of the sample of study.

Sample characteristics	Control		Parkinson	
	Women	Men	Women	Men
N	18	17	24	28
(age ± SD)	71.45±18.78	72.56±10.12	69.08±10.03	68.14±10.05
MMSE	27.2±0.6		26.5±0.4	
GDS	6.6±1.8		10.7±1.0	

N, number of subjects. MMSE, Minimental-State. GDS, Geriatric Depression Scale.

2.3. Voice Analysis

The recordings were obtained with a portable professional voice recorder (Sony PCM-M10), in an isolated sound room, placing the microphone at 8 cm and an angle of 45° from the mouth to prevent aerodynamic noise. The speech task consisted of asking subjects to read on a screen (48-point font size and multiple lines to facilitate reading), the first paragraph of the novel "Don Quixote" by Miguel de Cervantes (405 syllables): "In a village of La Mancha, the name of which I have no desire to call to mind, there lived not long since one of those gentlemen that keep a lance in the lance-rack…" (English translation of Don Quixote by John Ormsby, 1885). This paragraph is well known by all Spanish speakers. Recording voice patterns was performed by Praat 5.1.42 [24] program applied to the recordings obtained, according to the methodology described in previous studies [25]. Analysis focused on common acoustic measures of speech, including temporal aspects of the speech sample, pitch or fundamental frequency (F0), volume (intensity), and voice quality. To characterize the fluctuations in the amplitude of sound, we computed the intensity in dB of voice and unvoiced signals, and measured phonatory stability shimmer period perturbation stability (short term, cycle to cycle, perturbation in the amplitude of the voice): local shimmer (shimmer loc) and shimmer amplitude perturbation quotient 3 (shimmer apq3). Prosodic patterns were quantified by automatic prosodic transcription of a recording, using the algorithms implemented by Mertens [26] on the Praat program [24]. To characterize the temporal aspects of the speech sample, we computed the duration of the voice sample used (total duration of the paragraph from Don Quixote, the phonation time, and the reading and articulation speed), the interruption of sound (proportion and number of pauses of voice, percentage of the recording without voice, and number and percentage of voice breaks), and the periods of voice (number of pulses analyzed as voice, and mean number of periods of voice). To characterize the F0, we analyzed the mean F0, maximum and minimum values of F0, high and low global pitch and autocorrelation measures. Detection range of 65-650 Hz for F0, on windows of 0.005 s duration; for automatic segmentation threshold intensity was used in the styling of the algorithm that determines the presence of a vowel (Glissando = $0.32/T^2$ semitones / s, DG = 30, dmin = 0.05). While the standard psychoacoustic threshold for isolated voice is G = 0.16/T2, during natural speech voice flow is rarely linear, so that the value assigned is the better-modeled prosodic voice variables. Finally, we computed measures of the speaker's voice quality, and one spectral noise measure, the noise-to harmonics ratio (NHR).

2.4. Statistical Analysis

All statistical analyzes were performed using SPSS (IBM version 20.0 for Windows; SPSS Inc., Chicago, Illinois, USA). The description of the data was performed using the mean ± standard error of the mean (SEM) for continuous variables.

Results were analyzed using Pearson's correlation (and its corresponding linear regression model) to determine the relationship or covariance between different quantitative variables. For comparisons between two groups, the Student t test or the Mann-Whitney was used for the purpose of comparing the average values in quantitative variables in different pairs of groups.

The level of statistical significance, in all cases, was $p < 0.05$.

3. RESULTS

3.1. Acoustic Startle Reflex, PPI and PPF in PD Subjects and Healthy Controls

Our results showed that there were no significant differences in ASR amplitude and latency between PD subjects and control subjects (Table **2**), although the latency had a tendency to be higher in PD. Previous studies have reported sex differences in ASR in normal subjects, with women exhibiting lower response than men [27]. Thus, we examined sex differences across groups and within each group. We found no significant gender differences in ASR, amplitude and latency, between subjects (Table **2**). Therefore, we grouped men and women together for the analysis.

We analyzed the PPI at different interstimulus intervals (PPI_{60} and PPI_{120}) and the PPF (Fig. **1**).

The measures revealed an overall increase of the PPI and PPF in PD subjects relative to the control group.

When examined the differences between the two experimental groups, PD and control subjects, using ANOVA (group ~ inter-stimulus interval) with repeated measures, no differences in PPI levels as effect of group were found at PPI_{60}. Moreover, there were significant differences between controls and PD subjects when the interstimulus interval was 120 ms (PPI_{120}) ($F_{1, 83} = 8.52$, p = 0.005) or 1000 ms (PPF) ($F_{1, 83} = 13.6$; $p = 0.000$).

Table 2. Mean ASR amplitude (in arbitrary units) and latency (s) (± S.E.M.) in Parkinson disease (PD) and controls subjects.

ASR variables	PD	Controls	PD		Controls	
			Men	Women	Men	Women
Startle Amplitude	75.2±6.9	62.8 ± 8.4	68.9 ± 9.4	81.5±10.1	68.0±12.0	57.5±11.7
Startle Latency	88.3 ±10.1	74.7 ±12.2	97.7±13.7	79.0±14.8	79.6±17.6	69.9±17.0

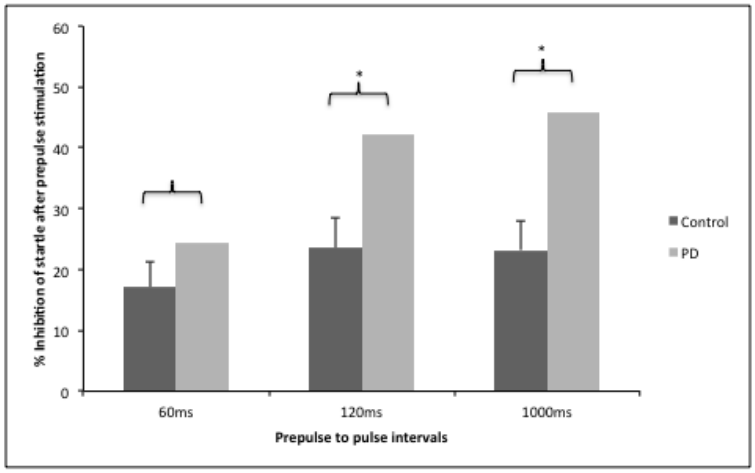

Fig. (1). Mean PPI and PPF values of the experimental groups, control and Parkinson disease (PD). Columns represent the mean percentage of startle amplitude inhibition at different interstimulus intervals, 60 ms, 120 ms and at 1000 ms. Error bars hemi S.E.M. (*) indicate a significant ($p < 0.05$) increase of PPI in PD group.

Table 3. Voice parameters measures in Parkinson disease (PD) subjects and Controls. *p < 0.05 and ** p < 0.01 indicate the differences between Control and PD subjects.

Voice Analysis	Parameters	Control	PD
		(Mean ± SEM)	(Mean ± SEM)
Temporal aspects of the speech sample	Total duration (s)*	56.60 ± 4.84	41.78 ± 2.39
	Phonation time (s)**	39.53 ± 2.65	30.61 ± 1.68
	Speech rate, syllable/s	3.43 ± 0.22	3.22 ± 0.11
	Articulation rate, syllables/s	4.46 ± 0.14	4.15 ± 0.08
Analysis of Fundamental frequency (F0)	Mean F0, (Hz)	156.74 ± 5.25	153.09 ± 5.51
	Minimum F0 (Hz)*	66.37 ± 0.88	72.17 ±1.26
	Maximum F0, (Hz)	520.53 ± 26.27	543.06 ± 16.33
Acoustic Parameters	NHR**	0.21 ± 0.02	0.13 ± 0.10
Analysis of periods of voice	Pulses, (n)*	4791.69 ± 319.29	3832.36 ± 215.17
	Periods, (n)*	4684.50 ± 314.08	3750.26 ± 213.81
Voice intensity	Shimmer loc*	15.49 ±.95	12.43 ±.63
	Shimmer apqu3*	6.68 ± .51	4.83 ± .33
	Voice (dB) *	71.22 ± .54	79.19 ± 2.64
Interruption of Sound	Without voice, (%)	37.20 ± 2.38	34.65 ± 1.23
	Voice breaks, (n)*	95.46 ± 6.54	70.58 ± 3.45
	Pauses, (n)*	22.96 ± 3.12	15.72 ± 1.68

3.2. Acoustic Parameters of Voice

We analyzed the alteration in temporal speech parameters in PD subjects and controls subjects (Table **3**). In the prosodic parameters analyzed, we found significant differences between control subjects and PD subjects in the total duration (p=0.01), phonation time (p=0.01), voice pulse numbers (p=0.05), voice period number (p=0.05), voice break number (p=0.01), and the number of pauses (p= 0.05). In the acoustic parameters, we found differences in the Minimum F0 between PD subjects and control subjects (p= 0.01), and NHR (p=0.01). As for the intensity of speech, we found differences in the intensity of pronunciation (dB Voice) (p=0.05) in Shimmer loc (p=0.05) and Shimmer apq3 (p=0.05).

In summary, prosody in PD subjects is faster and exhibits a reduction in phonation time, vowel pulses, breaks, breakage and voice speech periods. Also, PD subjects display less

use of low frequencies, resulting in a lower voice vowel sound. Their voice is more intense, but there is no change between pulses or voice prosody relative to the control subjects.

3.3. Relationship between Prepulse Inhibition and Prepulse Facilitation Scores and Voice Acoustic Parameters

To determine the relationship between PPI and PPF scores and speech parameters, we performed a Pearson correlation between the ASR modulations and the temporal aspects of the speech sample, volume (intensity), and voice quality in subjects with PD regarding the control group (Table **4**).

There is a significant correlation between total duration of voice, pauses numbers, unvoiced percentage and PPI and PPF in PD that is not present in controls. Thus, as linguistic prosody parameters in PD, there is a negative relationship between total duration of voice and PPI (prepulse-to-pulse interval 60 ms). A negative correlation was also found between unvoiced percentage and PPI (prepulse-to-pulse intervals 60 and 120 ms) and pauses number (prepulse-to-pulse interval 120 ms) in PD subjects. Regarding the PPF, we found an inverse relationship between this paradigm and unvoiced percentage and number of pauses.

This pattern was not observed in controls subjects in which a positive relationship between the number of periods of voice, number of pulses, and the number of voice breaks was found at prepulse-to-pulse intervals of 120 ms. There was a positive correlation between PPF and period number of voice and pulses number.

4. DISCUSSION

Our results showed that the amplitude and latency of the ASR was not significantly different between PD and control subjects. PD patients present comorbidity with depression that this could affect the reflex responses, but our participants had a GDS value 10.7±1.0, nearly normal [31]. There were differences in PPI values between groups at prepulse-to-pulse intervals of 120 ms. Our study also showed a significant difference in PPF between subjects. The voice analysis findings showed speech impairment in PD subjects compared to control subjects. Thus, subjects with PD have slower language syllabic and prosodic articulation than healthy controls. The correlations analyses also suggest a relationship between PPI, PPF and voice disorders.

There were limitations to the present study that need to be acknowledged. Our relatively small sample size may limit the generalizability to all subjects with PD. Despite this, here we addressed the question of whether subjects with PD exhibit disturbances in sensorimotor gating, and this inhibitory process is related to acoustic and prosodic parameters, such as control of the low frequencies of the voice and the emission ratio of vowel sounds.

4.1. Prepulse Inhibition and Prepulse Facilitation in PD

In the present study, we found that PD and control subjects had ASR with similar amplitudes and latencies. However, PD subjects exhibited a tendency to have longer onset latencies when compared to controls. Supporting this, several authors [28-30] described longer latencies in orbicularis oculi muscle in PD, which was prolonged in ON states and in sitting positions. Our results were also consistent with the literature [19, 32-34] and showed low ASR amplitude values at older ages, a variable that affects healthy and PD subjects. Our study showed that the ASR amplitude was higher in women than in men, a result that was in line with those previously published by Kofler and coworkers [35].

PPI circuits are controlled through the pedunculo-pontine tegmental nucleus, which regulates the excitability of the startle related structures of the reticular formation [36]. When compare to controls, PD subjects showed higher PPI at 120 ms, confirming our hypothesis that PD might exhibit disturbances in sensorimotor gating. Periol and coworkers [37] reported a significant difference in PPI at 120 ms in PD when compared to control subjects. In their study, they also compared subjects with Alzheimer's disease and Dementia with Lewy bodies and their results suggested an involvement of the dopaminergic subcortical-thalamocortical networks in the PPI regulation. Also, they showed more severe disruption of these networks in Dementia with Lewy's bodies than in PD. Consistently, Valls-Solé and coworkers [38] reported an increased PPI in PD subjects as well as an enhancement of the blink reflex, indicating an increased filtering of sensory

Table 4. Correlation between PPI measurements and temporal parameters of voice (non-significance is shown as blank spaces). R-value. Pearson correlation. ** Significant correlation level 0.01 (bilateral). *Significant correlation level 0.05 (bilateral).

Voice parameters	Control			PD Subjects		
Voice parameters	PPI 60	PPI120	PPF 1000	PPI 60	PPI 120	PPF 1000
Total Duration of Voice				-0.30*		
Periods number of Voice		0.41**	0.48**			
Pulses number		0.41**	0.47**			
Pauses number					-0.36**	-0.37**
Unvoiced percentage				-0.29*	-0.45**	-0.46**
Voice breaks number		0.41**				

information. Excessive sensory gating in PD may reflect impaired integration of sensory inputs that might generate alterations in movements [39]. Bradykinesia, one of the cardinal manifestations of PD, is the slowed movements or lack of movement that results from a failure in the neuronal mechanisms that prepare and execute the commands to move [40]. This can delay the time at which movement is detected and slow the initiation of any movement, as well as disruption of movements once they have been initiated [41]. The impairment of the sensorimotor regions such as basal ganglia, cerebral cortex, and other associated regions might account for errors in the initiation, timing and range of movement in PD patients [39]. The fact that PD patients frequently exhibit rigidity caused by involuntary increase in muscle tone and rigidity can reflect a tendency of the central nervous system to remain in a state of alert and movement preparation, while awaiting the arrival of the afferent signal, resulting in a delayed or aberrant transition to movement execution [39, 42].

The analysis of ASR facilitation (measured in percentage values PPF) also showed a significant difference between PD subjects and controls, showing PD subjects with disruption in the sensorimotor gating paradigms that were completely different when compared to controls. PPF is associated with alerting or orienting processes [43] as well as elective attention mechanisms [44]. According with Graham [44], the PPF reflects a generalized orienting or attention automatically elicited. The study published by Wynn [45] showed that schizophrenic patients and their siblings had lower PPF than controls, inferring this finding to an orienting deficit. Bowen and Ison [46] reported that PPF has a more peripheral motor consequence of a non-specific alerting reaction, suggesting that the pathways of the PPF may not depend on the sensorymotor processing [46]. In order to explain our results showing higher PPF in PD subjects, a cognitive evaluation of the PD and control participants should be necessary to evaluate any type of cognitive impairment or attention disorders.

4.2. Acoustic Parameters of Voice

We have analyzed the speech fluency, rate and articulation in subjects with PD. The results showed that PD is associated with a decrease in the speed of elocution and articulation.

The control of specific frequencies is learned in childhood and requires coordination of the acoustic resonances of the vocal tract [47-49]. This motor coordination in various structures along the vocal tract is affected in PD. Our results were consistent with previous studies [47-49] that showed significant differences in the acoustic parameters of voice between healthy controls and subjects with PD, and also with others neurological diseases with non-pathological senescence [50]. As reflected in studies of voice in the PD [7, 8, 51], we found that there were interruptions in the temporal aspects of the voice such as breaks in the prosody, poorly controlled phonation time, fewer pauses as well as voice breaks. Our results showed that PD subjects exhibited higher pitched-voice and less control of the low frequencies, that makes the characteristic sounds in the voice of elderly individuals disappear. Also, the lack of motor control in PD subjects increased the loudness of their voice, and resulted in a flat monotone voice due to the few accentual variations [52].

It was stated that motor disorders in PD affect the major elements of speech production, including the respiration, phonation and articulation [53] as a result of disruption of basal ganglia motor control circuits [54]. Our results support the existence of a reduction in the speed of elocution and articulation [52], and were opposed to those reporting the opposite effect [55, 56]. The high speed in fluency speech is attributable to a compensatory mechanism in which the PD patient inadvertently shows a faster utterance under certain circumstances. Several studies that analyzed the movements of lips and jaw during speech in PD provide an explanation for this phenomenon. Caliguiri (1989) [57] reported in PD patients normal lip movements at standard rates of elocution (between 3 and 5 syllables per second), but these movements were reduced at higher rates (between 5 and 7 syllables per second) when patients talked faster. This might explain that patients have a tendency to speak more slowly to control inaccurate articulations, and hence prevent deterioration of the speed of elocution.

4.3. Relationship Between Sensorimotor Gating and Voice Deficits in PD Subjects

We found sensorimotor gating deficits and speech disorders occurring together in PD patients. This does not mean that the speech disorders were necessarily a consequence of the sensorimotor gating deficit that exhibited PD patients. However, our statistical correlation analysis showed that PD patients may have sensorimotor gating deficits alongside speech disorders, showing a statistical relationship between some of the variables analyzed in the PPI/PPF test and the voice analysis. Therefore, evaluating both sensorimotor gating paradigms and voice parameters in the same PD patient might help to establish a better diagnosis.

An estimated 70%-90% of PD patients develop speech or voice disorders [58] specifically hypokinetic dysarthria, characterized by monopitch, mono-loudness, under articulation, and hoarseness voice [59]. Our results were consistent with these studies showing significant differences between controls and PD subjects. As reflected in previous language studies in PD [7, 8, 51], we found that there were disruptions in temporal aspects of the speech sample like a breakage in the prosody, poorly controlled phonation time and fewer pauses and voice breaks. The correlation analysis with PPI values confirms that the prosodic aspects of speech characteristic of PD patients are statistical related to the inhibitory motor problems of these patients. However, the acoustic aspects of speech showed no statistical relationship with the data obtained in the PPI.

An increased in startle inhibition correlated with voice breaks, percentage of periods without voice emission and emission ratio of syllables per time lowest phonation. The pathways that follow the vocalization process consist primarily of three components laryngeal activity, respiratory movements and supra-laryngeal. The most important is the extrapyramidal pathway that connects the motor cortex - putamen - substantia nigra - parvocellular reticular formation - phonatory motoneurons [60]. The loss of motor control in PD that holds the function of the vocal folds could explain the fluctuations of voice frequency. The position of the reticular formation and ventral parabrachial regions suggests

that this area plays a crucial role in vocal motor coordination. Among the hierarchically control of vocal behavior pathways, there are two types of phonatory motoneurons input. One input for motor coordination, which comes from the motor cortex and basal ganglia via the pyramidal and extrapyramidal pathways. The other input is for the learned vocal patterns [61], that relates to a gaiting function since it becomes from structures that represent different levels of gaiting control such as the periaqueductal grey and cingulated cortex.

The damage of neuronal pathways due to neuronal loss in PD might explain the alterations in startle modulation and speech. There is a correlation between these two neurophysiologic measures that might be a functional approach to show disturbance in sensory filtering. Variations in sensory filtering discriminate PD, and the combination with a set of parameters that define speech disorders in PD could be use as biomarkers for PD.

CONCLUSION

PD patients exhibited a deficit in the process of sensorimotor integration and speech impairments. The correlation between the PPI and PPF with an alteration of the voice in PD subjects contributes toward understanding the mechanisms underlying the neurophysiological alterations in both processes. Overall, easy and non-invasive tests such as PPI, PPF together with voice analysis may be useful to identify early stages of PD.

LIST OF ABBREVIATIONS

ASR	=	Acoustic Startle Reflex
dmin	=	Minimum value of analysis
F0	=	Fundamental Frequency
GDS	=	Geriatric Depression Scale
ISIS	=	Interstimulus intervals
ITIs	=	Intertrial intervals
MMSE	=	Minimental State Examination
PD	=	Parkinson's disease
PPI	=	Prepulse inhibition
PPF	=	Prepulse facilitation
SEM	=	Standard Error of the Mean
SN	=	Substantia nigra
NHR	=	The noise-to harmonics ratio

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Ethical Committee for Clinical Research in the area of Salamanca.

HUMAN AND ANIMAL RIGHTS

No animal were used in this research. The study was approved by the Ethical Committee for Clinical Research in the area of Salamanca, following the Declaration of in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Written informed consent was obtained from all participants.

CONFLICT OF INTEREST

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; or expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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