Neurological Sciences (2019) 40:1465–1468
https://doi.org/10.1007/s10072-019-03821-7

BRIEF COMMUNICATION

Lack of inter-muscular coherence of axial muscles in Pisa syndrome

Emanuela Formaggio[1] · Stefano Masiero[1] · Daniele Volpe[2] · Elena Demertzis[1] · Laura Gallo[1] · Alessandra Del Felice[1]

Received: 25 October 2018 / Accepted: 4 March 2019 / Published online: 20 March 2019

Abstract

Background Pisa syndrome is a lateral deviation of the trunk described in Parkinson's disease (PD). Its etiology is still unknown; advanced muscular signal analysis techniques, such as inter-muscular coherence, could help clarifying its pathophysiology and suggest therapeutic strategies.

Methods Fourteen idiopathic PD subjects with a lateral deviation of the trunk of at least 10° were included. Electromyographic (EMG) signal was recorded from bilateral thoracic, and lumbar para-spinal and obliqui externi muscles. The synchronization between EMG right and left side signals was quantified using the magnitude-squared coherence function.

Results In our sample, coherence (range 0–1) did not exceed 0.3, which indicates a lack of intra-muscular coherence.

Conclusion This finding is suggestive of a defective muscular fine-tuning, which has been associated with bradykinesia. These data support the hypothesis of PS as a clinical sign of bradykinesia, impacting on therapeutic and rehabilitative options.

Keywords Parkinson's disease · Neurophysiology · Electromyography · Trunk lateral deviation · Inter-muscular coherence

Introduction

Pisa syndrome (PS) was first described as truncal dystonia, or "pleurothotonus," induced by antipsychotic treatment. It is a rare complication of Parkinson disease (PD), with a prevalence of 8.8% in a large sample of outpatient PD subjects, although the absence of unified diagnostic criteria hampers from pooling data on incidence and prevalence from other studies. Postural deformities have been increasingly recognized as common complications of PD in the advanced stage and have been associated with disease progression, reduction of response to L-Dopa or as a complication of surgical procedures for PD management.

The physiopathology of PS is still not fully understood. Two hypotheses have been suggested: the first sees a central cause, with basal ganglia dysfunction associated with altered sensory-motor integration and exacerbation with dopaminergic treatment; the second refers to peripheral causes with a primary alteration of the musculoskeletal system. The first hypothesis may support the increased hypertonicity of spinal muscles in PD and PS, as well as patterns of muscle activity imbalance described in PS. The second hypothesis sees myopathy and scoliosis as the primary causative factors, with muscle activity imbalance and reduced muscle strength in the affected side manifesting in the early stages of the disease.

Causal therapy does not exist; treatment of PS is based on a combination of levodopa and dopaminergic drugs. Recently, specific rehabilitative programs for PS have been suggested with favorable results [1], together with vertebral orthoses and botulinum toxin injection if a muscle hyperactivity pattern is detected at electromyography (EMG) [2].

Coherence between two signals estimates the magnitude of the linear correlation between specific frequency components in the two signals. It provides a more representative and quantitative measure of activity across muscles and signals an inter-muscular cortical control. Inter-muscular coherence could thus

✉ Alessandra Del Felice
alessandra.delfelice@unipd.it

Emanuela Formaggio
emanuela.formaggio@unipd.it

Stefano Masiero
stef.masiero@unipd.it

Daniele Volpe
dott.dvolpe@libero.it

Elena Demertzis
sunny.elena@libero.it

Laura Gallo
gallolaura4@gmail.com

[1] Department of Neuroscience, Section of Rehabilitation, University of Padova, Via Giustiniani, 3, 35128 Padova, Italy

[2] Fresco Parkinson Institute, Casa di Cura Villa Margherita, Via Costacolonna 6, 36057 Vicenza, Italy

hint to an underlying pathophysiological mechanism—i.e., increased coherence in the 4–7-Hz band [3], as demonstrated in dystonia, or a defective coherence in agonists muscles in the 15–30 Hz, which has been related to bradykinesia in PD [4].

Clear-cut evidence of etiopathogenetic mechanisms of PS is lacking. The aim of our study is to investigate activation patterns and coherence of axial muscles in a cohort of people with PS by needle EMG to identify possible dysfunctions of muscle control. This could eventually distinguish the dystonic versus bradykinetic hypothesis of PS etiopathogenesis.

Methods

Subjects

People with a diagnosis of idiopathic PD, according to the UK Brain Bank diagnostic criteria, referred to the Movement Disorders Rehabilitation Clinic of the University Hospital, were enrolled. The Institutional Review Board of the University Hospital approved the study (protocol number: 4398/AO/18). Participants provided written consent. Inclusion criteria were as follows: lateral spine deviation of at least 10° at goniometric measurement not present when lying supine and passively reducible; no fixed spinal deformity at spinal X-rays; no previous surgical spine treatment or exposure to any antipsychotic drug; regardless of pharmacological therapy, provided that it remained stable during the previous 6 months (Table 1).

Electromyography and signal analysis

Each subject underwent a monopolar needle electromyographic (EMG) study (Viking Synergy, Natus, USA) of thoracic and lumbar para-spinal muscles. Signal was simultaneously recorded from both hemibodies. Insertion points were identified previously to needle examination based on palpatory bony landmarks at L2 and T10 (inferior tract) and T8, T6, and T4 (superior tract). Signal was recorded in a sitting and standing position. Only those from obliquus externus muscles recordings were obtained in a standing position. In further analysis, the latter signal was included only if derived from participants with no camptocormia.

Data were analyzed in the 0–25-Hz band according to previous protocols [4], using scripts based on Matlab (MathWorks, Natick, MA). A coherence function, which provides a measure of synchronization of the two signals as a function of frequency using the spectra of the signals obtained by fast Fourier transform (FFT), was run. Output is a number ranging from 0 (no coherence) to 1 (complete coherence). Results were plotted for upper (T4–T8) and lower (T9–L2) trunk muscle groups and for obliquus externus muscles.

Results

Eighteen consecutive subjects were enrolled. Six subjects had also camptocormia, measured with compass-needle pocket goniometer, as at least 45° of thoracolumbar anteflexion; one subject at subsequent follow-ups showed the metronome phenomenon (alternating lateral trunk bending over time).

Data from four participants were discarded due to signal artifacts. Coherence (range 0–1) between the examined muscle groups remained below 0.3 in the analyzed range of frequencies (0–25 Hz) (Fig. 1).

Table 1 Participants' demographics

Participants	Sex	Age	Disease duration (years)	L-Dopa dose at visit (daily mg)	Lateral deviation (degree)	Most affect side
P1	F	84	4	400	10	R
P2	M	76	14	600	11	R
P3	F	66	7	300	13	R
P4	M	76	16	600	18	L
P5	M	74	2	300	11	R
P6	F	72	4	600	16	L
P7	F	67	2	500	11	L
P8	F	67	3	600	16	L
P9	M	82	9	350	22	R
P10	F	82	16	400	11	L
P11	F	62	1	300	10	R
P12	M	79	1	600	14	L
P13	M	69	3	350	12	R
P14	M	70	4	400	20	R

R right, *L* left

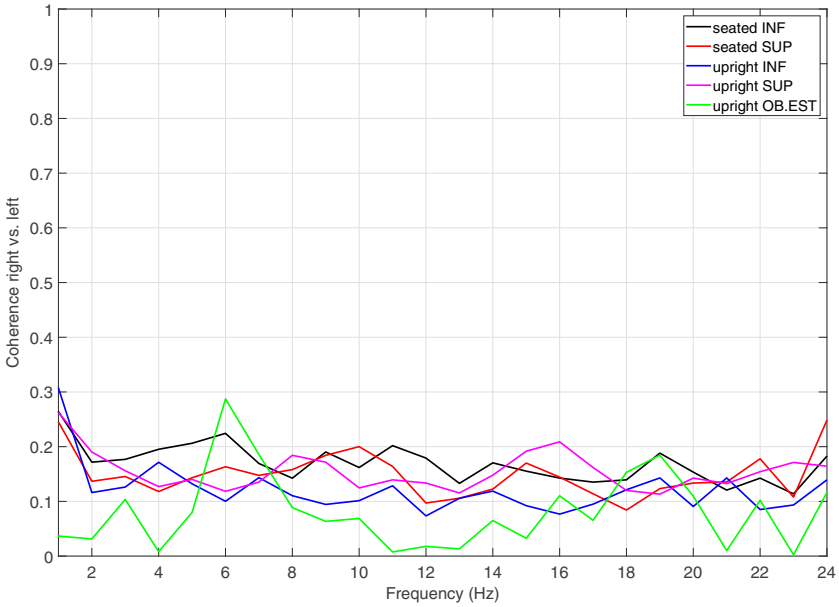

Fig. 1 Grand average EMG coherence between left and right side for inferior and superior para-spinal muscles during seated and standing position and obliquus muscle during standing. Coherence takes values of one in the case of a perfect linear inter-dependence between the two signals and values close to zero in absence of any interaction

Discussion

Physiological movements in healthy subjects are performed with a synchronization of firing of agonist muscles, which oscillate in the 15–30-Hz band during weak tonic contractions and in the 30–60-Hz band during intense tonic contractions [5] in upper limbs. Para-spinal muscles do not physiologically need the same fine-tuning as small hand muscles do; they show nonetheless a significant inter-muscular coherence between bilateral homologous muscle units below 2 Hz [6].

A lack of inter-muscular coherence in the 15–30-Hz frequency band during voluntary tonic contractions (recording from wrist extensor muscles and first dorsal interosseous muscle) has been described in people with PD [4]. Pharmacological therapy and, to a greater extent, high-frequency subthalamic nucleus stimulation restore inter-muscular coherence and reduce bradykinesia in upper extremities, suggesting that the motor state is determined by the inability of the cortico-muscular system to engage in high-frequency synchronized oscillations.

Our data provide evidence of a lack of synchronization during tonic postural contraction in para-spinal muscles in the 0–25-Hz band in people with PS. This finding suggests that bradykinesia could be one of the contributing factors to lateral trunk flexion. It supports a previous report arguing that marked asymmetry of PD, which is the clinical correlate of the lack of inter-muscular coherence among bilateral muscle groups, is associated with an increased risk of developing PS based on a higher prevalence of Pisa syndrome in people with a marked asymmetry score [3]. Inter-muscular coherence undergoes age-related modifications, although there is lack of consensus on the direction of these changes, which range to increased and stronger synchronization within a larger frequency band compared to that in young adults [7], to a substantial constant inter-muscular coherence across age spans [8], to a decrease in corticospinal activity during static ankle contraction [9]. In fact, the latter finding reports analysis of a limited frequency range (15–35 Hz), excluding slower bands (0–5 Hz, 8–12 Hz), which usually show increased coherence in the elderly during postural tasks. These inconclusive findings and the very low coherence values we detected make us confident of the existence of a pathological neurophysiological process underlying muscle activation in PD and suggest a bradykinesia-related origin of the clinical picture.

Electromyographic data on para-spinal muscle activity in PS are inconclusive, with reports suggesting a continuous tonic increased activity [10] opposed to an alternate lateralized hyperactivity, either towards or away from the flexion side. A lateralized activity could be responsible for a lack of coherence; nonetheless, EMG data suggestive for this lateralization were obtained having the subjects performing an active voluntary lateral trunk bending and cannot be compared with a tonic postural activity, as in our dataset.

From an electrophysiological perspective, dystonia presents with a distinguishing muscle oscillatory pattern, with a coherence increase in muscle activity in the 4–7-Hz band [3]. Although this pattern is more evident in limbs rather than truncal muscles and in genetically determined dystonia, its absence in our cohort is suggestive of a different etiopathology. Our data reinforce the hypothesis of PS as a postural disorder due to bradykinesia of axial muscles.

The main limitation is the lack of a control group. A comparison with controls is mandatory in future research to generalize the results. In fact, we are quite confident the very low coherence values we detected reflect an underlying neurophysiological phenomenon.

Our subjects were treated with botulinum toxin injections in the hyperactive paravertebral muscles [1]. This hampered calculation of inter-session muscle variance, since the blocking effect on the neuromuscular plate and the long-term structural modifications induced on muscle by botulinum toxin prevent a comparison of muscle activity between sessions. Similarly, no intra-session variance could be calculated. Paravertebral muscle activity is a tonic low-intensity contraction of postural muscles elicited by trunk upright position and voluntary contraction of these muscles is demanding even in highly compliant subjects. Due to the clinical setting and use of EMG data, we did not design the protocol to incorporate repeated standing and sitting trials, which could have been used for this purpose providing a block protocol necessary for this type of computation.

This finding sheds light on possible mechanisms involved in postural abnormalities in PD. Detailed EMG studies of para-spinal muscles in PS may guide mechanistic therapies, such as specific physical therapy programs or focal treatments with botulinum toxin to rebalance muscle activity.

Compliance with ethical standards The Institutional Review Board of the University Hospital approved the study (protocol number: 4398/AO/18). Participants provided written consent.

Conflict of interest The authors declare that they have no conflict of interest.

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