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Effects of focal muscle vibration on cervical pain in Parkinson’s disease patients: a pilot study

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Abstract
Musculoskeletal pain is a common symptom of Parkinson's disease (PD) that is not adequately treated with current dopaminergic drugs. This pilot study sought to investigate the effect of focal muscle vibration (fMV) on a group of Parkinson's disease patients suffering from chronic cervical pain. In addition to conventional physiotherapy, twenty-two patients with idiopathic Parkinson's disease (Hoehn and Yahr stages II-III) received three weeks of bilateral focal muscle vibration to the trapezius muscles. The Visual Analogue Scale (VAS), the Short-form McGill, and the Present Pain Intensity scales were used to assess pain at baseline (T0), after three weeks of treatment (T1), one week after the last treatment session (T2), and three weeks after T2 (T3). Pain intensity decreased significantly from baseline to T1 across all pain scales (p < 0.0001). Furthermore, the beneficial effect of fMV on cervical pain lasted up to one month after treatment. Our findings show that fMV, in combination with conventional physiotherapy, is effective at reducing pain intensity in PD patients, with results visible even after a month of follow-up.

Introduction
Musculoskeletal pain is a highly prevalent disorder in Parkinson’s disease (PD). Compared to age matched individuals, around 40 to 85% of people with PD suffers of some form of muscle or joint pain with a negative impact on their quality of life.1-3 Epidemiological data on the prevalence of cervical pain in PD are currently insufficient however, data from the general population estimate a prevalence between 12–40%, with a trend to increase with aging.1 The true origin of cervical pain in PD is not completely understood, however multiple factors seem to be involved. Disease-specific factors include axial rigidity, dystonia, poor trunk coordination, musculoskeletal changes, and postural alterations;3 other contributing factors may include intervertebral joint and disc degeneration, irritation of the spinal nerve roots, and low mood.1
Common postural alteration observed in PD, like camptocormia and anterocollis, are associated with a series of biomechanical changes that negatively affect the cervical spine and muscles. Studies conducted on people with forward neck posture showed excessive vertebral extension, and scapular kinematic resulting in excessive load on the posterior cervical structures and neck pain. Focal muscle vibration (fMV) is a rehabilitation technique that influences sensory-motor function and pain by means of repetitive high frequency vibration. Decades of applications in different fields have provided robust evidence of efficacy and safety. As shown by multiple studies, delivery of local vibrations over muscle bellies and tendons activates large, myelinated Aβ fibers connected to muscle spindle, Golgi tendon organs and Pacinian corpuscles. The analgesic mechanism of fMV has been traditionally attributed to the spinal gate control theory according to which, stimulation of larger fibers creates a “busy line effect” that blocks the transmission of nociceptive signals from smaller type C fibers. However, the mechanism is likely more complex than this as fMV also exerts separate effects on perception, sensory-motor control, neuroendocrine and limbic system. Previous experiments on healthy subjects have shown that local vibration induces a long-lasting increase in pain threshold in response to experimental electrical stimulation, when compared to placebo. Furthermore, its effect is comparable to other analgesic techniques such as high frequency low-intensity transcutaneous electrical nerve stimulation (TENS). Despite the high prevalence and the negative impact on the quality of life, cervical pain is both underestimated and undertreated in this population. We therefore aimed to investigate the effect of fMV on a group of patients with PD suffering from cervical pain. To the best of our knowledge, no previous literature exists on this subject.

Materials and Methods

This is a prospective, interventional, pilot study. Upon acceptance and signature of informed consent, 22 patients with PD of both sexes were consecutively recruited since May to October 2022 at the Physiatry Clinic of the Gemelli IRCCS University Hospital Foundation of Rome. Eligibility of the participants was based on the following criteria: a diagnosis of PD according to the criteria of the Brain Bank of London; Hoehn and Yahr stage II-III; presence of recurring cervical pain for at least 6 months, absence of cognitive impairment (Mini Mental State Examination (MMSE) ≥ 24/30) and effective pharmacological control of the pathology. Exclusion criteria were a diagnosis of atypical Parkinsonism; poor pharmacological compensation of the disease; presence of other neurological, neuromuscular or osteo-articular pathologies; previous cervical spine surgery, and presence of shoulder pain.

Study design

Focal muscle vibration protocol

Each patient underwent fMV in association with conventional physiotherapy three times a week, for
three weeks, for a total of 9 sessions, similar to our previous study. The vibration was applied using a pneumatic vibration device (EVM Endomedica, Italy) at a frequency of 100 Hz and an amplitude of 0.2 mm. Each session consisted of three stimulation blocks of 10 minutes each, interspersed with 1 minute of rest. The stimulus was applied at the level of the upper and lower fascicles of the trapezius bilaterally, with the patient in sitting position (Figure 1).

### Physiotherapy
For both groups, conventional physiotherapy was carried out, three times a week, for 3 weeks, in group sessions coordinated by an experienced physiotherapist (D.R.) and included: i) exercises for the head and trunk control; ii) strengthening and stabilization of lower limbs and antigravity muscles; iii) stretching of the posterior kinetic chain muscles; iv) exercises aimed at recovering and maintaining a correct posture; v) coordination and balance exercises; v) gait training with and without obstacles according to the ability of the patients.

### Outcome measure
Patients were evaluated at baseline (T0), after 3 weeks of treatment (T1), and at the two follow ups after one week from the last treatment session (T2), and after 3 weeks from T2 (T3). Evaluation of cervical pain intensity and quality was done using the Visual Analogue Scale (VAS), the Short Form McGill Pain Questionnaire (SF-MPQ), and the Present Pain Intensity (PPI) scale. All participants were informed about the purpose of the study and signed informed consent. The study was conducted in accordance with the declaration of Helsinki and was approved by the local ethics committee with the protocol number “N 0016285/22, 11.05.2022, ID 4935”.

### Statistical analysis
All statistical analysis was performed using the software GraphPad Prism version 9.5.1 (GraphPad Software, La Jolla, CA, USA). The results are reported as mean ± standard deviation (SD). Statistical differences between each time point were calculated by Student's t-test and two-tailed p-values were determined using Wilcoxon matched-pairs signed rank test. A P value < 0.05 was considered statistically significant (*), and p < 0.01 (**), p < 0.001 (***), and P < 0.0001 (****) as highly significant.

### Results
Twenty-two chronic patients with idiopathic PD, 13 males and 9 females, mean age 69.4 ± 9,2 were enrolled in the study. Except for one patient that missed the last follow up visit at T3, all the other patients successfully completed the experiment. Furthermore, no side effects were reported at the end of the study. The clinical and demographic characteristics of the patients are summarized in Table 1.
The comparison between baseline (T0) and T1 showed a significant reduction of pain intensity (p<0.0001) in all the pain scales used (Figure 2).

In particular, an average reduction of 2.7 (±1.35) points was observed in the VAS scale (Figure 2a) and of 1.0 (± 0.69) points in the PPI scale.

For the SF-MPQ scale: sensory, affective (Figure 2d) and total (Figure 2e) an average decrease of 5.2 (± 4.1), 2.4 (± 2.23, p<0.001) and 7.5 (± 5.44) was respectively measured.

A slight trend in the reduction of pain intensity was also observed at T2 in all the applied scales, however, these data were non-statistically significant. Finally, at T3 a stable trend was maintained compared to T2.

**Discussion**

Neck pain is a frequent complaint in patients with PD with a negative impact on their quality of life. Current dopaminergic drugs do not seem to provide relief for this condition. In this study we aimed to investigate the antalgic effect of focal vibration in combination with conventional physiotherapy on a group of 22 patients with PD and affected by chronic cervical pain.

According to our results, three weeks of fMV in combination with conventional physiotherapy was effective at reducing the intensity of cervical pain. However, a statistically significant pain reduction was only evident at T1. In the other two follow up visits, a slight positive or stable improvement of cervical pain was still present, yet the effect was not statistically significant.

Our results are encouraging and show a similar trend with other literature evidence that indicate efficacy of fMV as a mean to reduce all forms of somatic and neuropathic pain.

Although no previous studies exist on the application of fMV for cervical pain, several experiments have been conducted on other type of painful conditions. A study of Staud et al. found that vibrotactile stimulation resulted in 40% pain reduction in patients with chronic musculoskeletal pain. A study of Lundeberg et al. found that vibratory stimulation was superior to placebo at relieving musculoskeletal pain of different origin. In another experiment Lundeberg et al. found that fMV was superior to TENS at reducing epicondylitis pain, but less effective at relieving low back pain. Finally, the combination of vibratory stimulation and TENS resulted in a potentiation of the pain alleviation.

Regarding the mechanism of action of fMV, in the last few decades, several experiments have shed light over the neurophysiological bases of its quite complex effect that involves many systems of the human body. For many years the analgesic effect of vibration has been associated to the “gate control theory” introduced by Melzak in 1965. Nowadays new evidence has shown that analgesia mainly occurs as result of the restoration of a correct consonance between sensory inputs and motor output at cortical level and by variations in the release of chemical peptides and hormones. Previous studies on brain excitability - performed under Positron Emission Tomography (PET) and functional
Magnetic Resonance Imaging (fMRI) - have demonstrated changes in the motor cortex of patients undergoing fMV.\textsuperscript{5,16} Furthermore, other experiments under transcranial magnetic stimulation (TMS) have shown a facilitation of the muscular electrical response and a modulation of intracortical inhibition.\textsuperscript{5,16} Regarding the effect on the neuroendocrine system, experiments performed on animal models showed that the application of a 100 Hz local vibration was associated with an increase in the plasmatic and cerebrospinal fluid levels of oxytocin.\textsuperscript{11} Previous studies have shown that this hormone decreases pain sensitivity by improving mood.\textsuperscript{17} Other animal experiments have shown that vibration at frequencies between 80-250 Hz induces a release of adenosine, a purine nucleoside responsible for the regulation of multiple cellular and tissue functions including nociception.\textsuperscript{11} This proving that focal vibration can act outside the gating mechanism. Technical parameters seem also to be determinant in the overall effect of fMV. Previous experiments on healthy subjects revealed that high frequency vibration induces a long-lasting increase in pain threshold in response to noxious stimuli however, pain reduction was only evident when vibration was applied: i) at high frequency (around 100 Hz) and ii) on the same area of the noxious stimulus or neighboring regions.\textsuperscript{8,12} This supports the hypothesis that Pacinian corpuscles, which are particularly sensitive to high frequency vibration, may play an important role in the analgesic effect induced by vibration and, secondly, that nociceptive signal transmission inhibition occurs at segmental level.\textsuperscript{8,12} Regarding the long lasting reduction of pain perception, studies suggest that it could be ascribable to spinal mechanisms involving the substantia gelatinosa cells, which might be influenced by chemicals and peptides, released by the stimulated afferent fibers;\textsuperscript{8} others indicate a central modulation mechanism involving the somatosensory cortex;\textsuperscript{12} finally, it cannot be excluded that part of the pain reducing effect may be attributed to a wash-out mechanism, due to increased local blood circulation in the painful area.\textsuperscript{14} Stimulation time is also considered an important variable. A study of Lundeberg et al.\textsuperscript{14} suggests that the maximal duration of pain relief is achieved when stimulation is applied for a period of about 25-45 min.\textsuperscript{14}

The protocol used for this study is in line with the most updated literature evidence. Specifically, fMV was applied at frequency of 100 Hz, on the painful region for a total of 30 min interspersed with 1 min break to avoid any habituation phenomenon. The reduction of pain was maintained up to one month from the last treatment session.

Limitations

The are several limitations that should be noted in this study. First, the small sample and the lack of a control group limit our understanding of the characteristics of neck pain in PD as well as on the role of fMV in the treatment of cervical pain in this population. Second, in our sample, beside separately analyzing the sensory and affective subscales of the SF-MPQ, we did not specifically investigate for the presence and the severity of depression, which is a factor that previous studies have shown having a clear correlation with pain. Third, a sort of vicious cycle seems to interconnect impaired
proprioception, postural alteration and neck pain in PD: in this study we did not explore whether patients with higher degree of postural impairment experienced more pain.

Conclusions
Cervical pain is a common and bothersome disturbance in PD. fMV is a safe and versatile physical mean that can simultaneously target different disturbances such as pain, proprioception and muscle hypertonus. Regarding cervical pain, our results demonstrate that fMV in combination with conventional physiotherapy is effective at reducing the pain intensity in this population, with results visible even at 1 month of follow up. There is a fine line that connects impaired proprioception, postural alteration, and neck pain in PD. Further studies should explore and weight the effect of focal vibration in relation with each of these variables.

References


Figure 1. Schematic representation of the study protocol.

Figure 2. Patients’ pain assessment. T0 to T3 scores were determined by: (a) Visual Analogue Scale (VAS), (b) Present. Pain Intensity (PPI) and Short Form McGill scale: (c) sensory, (d) affective and (e) total score. *** p<0.001, **** p<0.0001
Table 1. Baseline characteristics of the patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>PD (N = 22)</th>
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<tbody>
<tr>
<td></td>
<td>Mean (min, max), SD</td>
</tr>
<tr>
<td>Sex (male; female)</td>
<td>13 M; 9 F</td>
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<tr>
<td>Age (years)</td>
<td>69.4 ± 9.2 (52, 84)</td>
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<tr>
<td>BMI (kg/m2)</td>
<td>25.9 ± 3.8 (20.6, 35.9)</td>
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<tr>
<td>Disease duration (months)</td>
<td>58.2 ± 29.0 (16, 112)</td>
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<tr>
<td>UPDRS score</td>
<td>22.0 ± 8.9 (9, 42)</td>
</tr>
<tr>
<td>MMSE score</td>
<td>28.2 ± 1.7 (24, 30)</td>
</tr>
<tr>
<td>LEDD (mg)</td>
<td>591.7 ± 159.3 (300, 850)</td>
</tr>
</tbody>
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BMI, Body Mass Index; H & Y, Hoehn e Yahr; UPDRS, Unified Parkinson's Disease Rating Scale; LEDD, Levodopa equivalent daily dose