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# Modulation of parkinsonian tremor by radial nerve palsy

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**Article abstract**—We analyzed rest and postural hand tremors in a Parkinson's disease patient who developed and recovered from a right radial nerve palsy at the spiral groove, and found that, despite complete paralysis of all extensors below the elbow, tremor frequencies remained unchanged while tremor amplitudes actually increased. This provides compelling evidence for a central generation of parkinsonian tremor frequency that is not influenced by the effects of peripheral modulation. In addition, the increase in tremor amplitudes may be due to disinhibited flexor activity caused by normally operating spinal segmental mechanisms interacting with central tremor generators programmed to alternate between antagonist muscles. Peripheral treatment of tremors—with muscle paralysis or botulinum toxin, for example—therefore may not be effective in stopping tremor oscillations in Parkinson's disease and may even worsen tremor amplitudes if all antagonists of a tremoring joint are not treated equally.

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Although the effect of afferent modulation on parkinsonian rest or postural tremors remains incompletely understood, most believe that peripheral input has less influence in parkinsonian tremors than in other tremors.<sup>1-3</sup> This study analyzes the findings from a "natural experiment" in which a patient with classic Parkinson's disease (PD) recovered from a functionally complete radial nerve palsy at the spiral groove. During this period, tremor amplitudes were actually worse with paralyzed wrist extensors and became more similar to the unparalyzed side with recovery. Tremor frequencies, however, did not change. To our knowledge, this is the first physiologic evaluation of human parkinsonian tremors in the complete absence of motor and sensory feedback from an entire group of antagonist muscles. While other studies investigated tremor modulation with more widespread and permanent effects after dorsal rhizotomies or brain lesions, this study analyzed tremors after a peripheral injury involving a functionally select group of muscles (all extensors below the elbow), followed by complete recovery.

**Case report.** The patient is a 71-year-old right-handed man who has had PD for 8 years, starting with right-hand rest tremor and difficulty making a fist. Within 4 years after onset of disease, his symptoms had progressed to stage 2.5 in the modified Hoehn and Yahr scale,<sup>4</sup> with bilateral rest tremor of the hands, bradykinesia, gait difficulties, and restriction of his activities of daily living. Although he responded well to levodopa/carbidopa, his treatment was hampered by confusion and

forgetfulness over the next 4 years. He never suffered from dyskinesias or on-off fluctuations, and he has no features suggesting atypical parkinsonism or any additional nervous system involvement. His symptoms have always remained worse on the right side. After waking up one morning with his right arm over the edge of the bed, he noted a complete inability to extend his right wrist or fingers. On examination, there was 0/5 strength in all right wrist and finger extensors and mild loss of sensation over the dorsum of the right thumb. There were no other peripheral findings. Strength was 5/5 in right forearm flexors and all small hand muscles. Extensor strength gradually recovered over 3 months, confirming the diagnosis of right radial neurapraxia. There were no changes in the patient's parkinsonian status during the period of extensor weakness in the right arm.

**Methods.** *Nerve conductions and EMG.* Nerve conduction and EMG studies were done the morning after the radial nerve palsy (day 1), 6 weeks later, and 3 months later (day 85), when clinical recovery was complete. Motor and sensory nerve conduction studies (median, ulnar, and radial) and needle EMG were performed in the right arm. Needle recording electrodes in the extensor indicis proprius were used for radial motor conductions; surface recordings were used for all other conduction studies. Five stimulation sites were chosen to evaluate the level of the radial nerve lesion: the forearm, lateral antecubital space, spiral groove, axilla, and Erb's point. Antidromic sensory conductions of the radial nerve were performed with forearm stimulation 12 cm proximal to recording at the base of the thumb. Needle EMG examinations were done of the right triceps, brachioradialis, extensor carpi radialis, extensor digitorum communis, extensor pollicis longus, and extensor indicis proprius, and in selected median and ulnar innervated muscles.

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**Tremor analysis.** Rest and postural tremors were recorded from both hands on day 1 and 3 months later (day 85). On both occasions, tremor testing began about 1 hour after the patient was given his medications so that he was optimally treated at the start of the recordings. Testing then occurred over approximately 2 hours to capture tremor variability over time. Ultralight piezoresistive tri-axial miniature accelerometers ( $\pm 25$  g, 0.5 gram each) with linear sensitivities of approximately 4.5 mV/g in the physiologic range were attached over the third knuckle on the dorsum of the patient's hands at the distal end of the middle carpus bone. The axis with the highest amplitude output was selected for the final analysis. Silver/silver chloride EMG surface electrodes were used to record wrist flexors (flexor carpi radialis and ulnaris) and extensors (extensor carpi radialis and extensor digitorum indicis) bilaterally along with the accelerometry. Data were acquired and analyzed using semiautomatic interactive software developed in the Clinical Motor Physiology Laboratory in our institution.

The tremor acquisition setup allowed unhampered natural activity of both arms and hands throughout the test. Accelerometric and EMG signals were digitized at 500 Hz using a 15- $\mu$ sec 16-bit analog-to-digital system and stored in eight 4-second trials during two conditions: with the arms at rest and extended. Rest measurements were done with the patient's arms flexed 90° and held stationary at the elbow to prevent the upper arm from transmitting movement into the forearm and hand. The forearm was supported by the side of the chair with the hand freely resting over the end. In the arms' extended condition, both arms were flexed at the shoulders with the forearms, hands, and fingers held straight in a horizontal plane level with the shoulders.

Tremor amplitudes ( $\pm 0.005$  mm) were derived from double integration of wrist accelerometric data after filtering out low-frequency drift (less than 2 Hz) and averaging. A fast Fourier transform algorithm was used to generate autocorrelation spectral analyses ( $\pm 0.24$  Hz) with the y-axis power measured in squared accelerometric units ( $g^2$ ). EMGs were full-wave rectified, integrated, and processed with the accelerometric data. Statistical analysis was performed using *t* tests comparing amplitude and frequency means for each condition between day 1 and day 85.

**Results.** Nerve conductions performed within 24 hours after the onset of clinical weakness (day 1) revealed normal radial motor evoked responses in the extensor indicis proprius, stimulating from the forearm and antecubital fossa and at the spiral groove, but there were no responses from the axilla or Erb's point. Radial sensory nerve evoked responses were normal. Needle EMG revealed neither voluntary nor spontaneous motor units in any right forearm extensor muscle and showed normal voluntary motor units in the triceps. Median and ulnar nerve conduction and EMG studies were normal. At 6 weeks, right radial nerve conductions from the axilla and Erb's point revealed returning low-amplitude evoked responses. By day 85, motor evoked responses had become completely normal, documenting a neurapractic lesion in the right radial nerve distal to branch to the triceps.

Tremor analysis on day 1 revealed rest amplitudes of  $28.2 \pm 8.6$  mm (average  $\pm$  SD) on the right

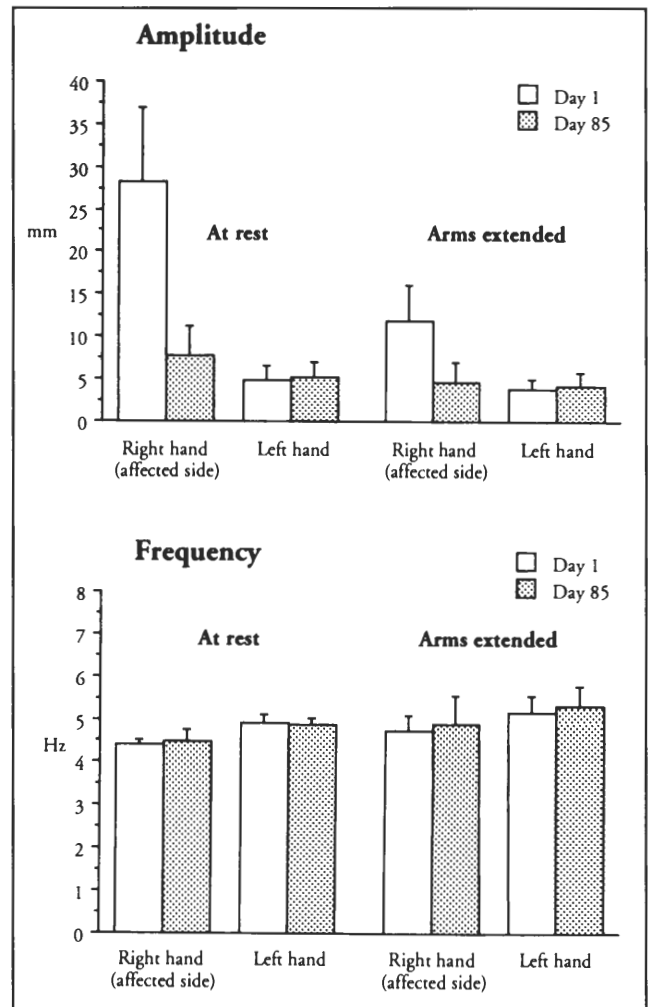


Figure 1. Bar graph representing average  $\pm$  SD amplitude and frequency data from eight trials taken over 2 hours on the first day (day 1) of the patient's right radial nerve palsy and again 3 months later (day 85). Note the significant change in amplitude in the right hand from day 1 to day 85 both at rest and with arms extended. Note also the relative absence of change in frequency over the same period. Original data in table form has been archived with the National Auxiliary Publication Service (NAPS); see Note at end of text.

and  $4.9 \pm 1.6$  mm on the left (figure 1). Left forearm EMG activity of wrist flexor and extensor muscles revealed an alternating pattern, but only flexor activity was present on the right due to the radial conduction block (figure 2). Despite the absence of extensor activity in the forearm, right-hand rest tremor amplitudes averaged almost six times greater than on the left. With the arms extended, tremor amplitudes were lower in both hands and were almost three times greater on the right than on the left.

By day 85, right wrist extensor EMG activity had emerged with an alternating firing pattern for the flexors (figure 3). Concomitant with the return of extensor activity was a significant decrease in the average rest and postural tremor amplitudes. Average rest amplitudes dropped to  $7.8 \pm 3.4$  mm,

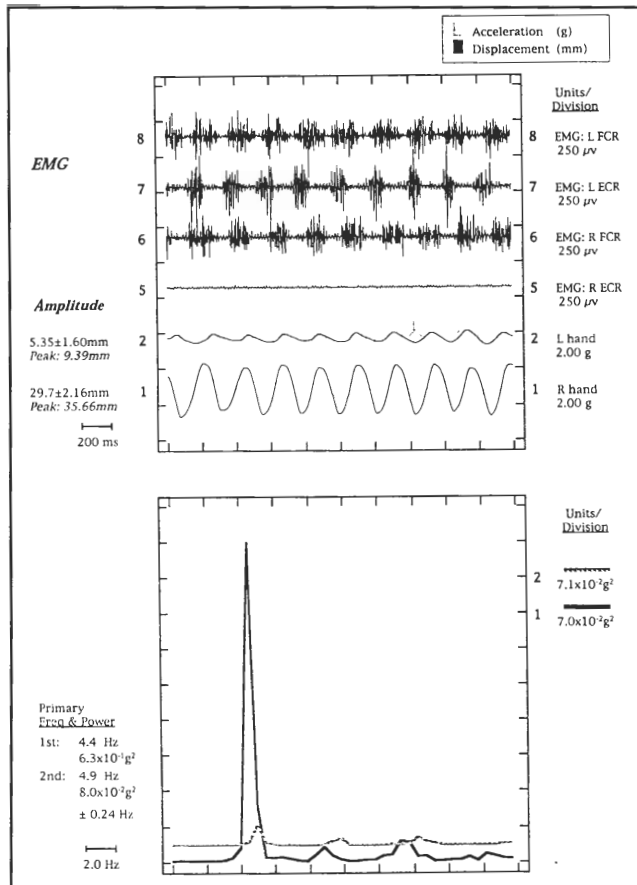


Figure 2. Sample traces on day 1 from patient with right radial nerve palsy. Tremor profile (top) shows a 2-second sample with six channels of data. Channels 1 to 2 = accelerometry and amplitudes; channels 5 to 8 = surface EMG of right (R) and left (L) extensor carpi radialis (ECR) and flexor carpi radialis (FCR). Frequency spectra (bottom) show Fourier transforms of channels 1 and 2. Labels at the left show primary and secondary frequency peaks with their corresponding powers.

and amplitudes with the arms extended dropped to  $3.9 \pm 1.7$  mm ( $df = 14$ ,  $p < 0.00001$  in both conditions). Compared with the left side, right-hand tremor amplitude ratios decreased to 1.5 at rest and 1.1 with arms extended.

Tremor frequencies, however, did not change significantly in the right hand at rest (4.4 versus 4.5 Hz,  $p = 0.59$ ) or with posture (4.7 versus 4.9 Hz,  $p = 0.48$ ) from day 1 to day 85. Left-hand frequencies and amplitudes showed no significant changes from day 1 to day 85 at rest or with posture ( $p > 0.33$  for frequency and amplitude in all cases) (figure 1).

**Discussion.** Using quantitative methods of assessment, we analyzed rest and postural hand tremors in a patient with PD that persisted in the absence of forearm extensor activity due to a radial nerve compression palsy on the right side. Remarkably, tremor frequencies were unaffected whereas tremor amplitudes actually worsened during the period of greatest muscle paralysis. With resolution of the conduction block and return of extensor func-

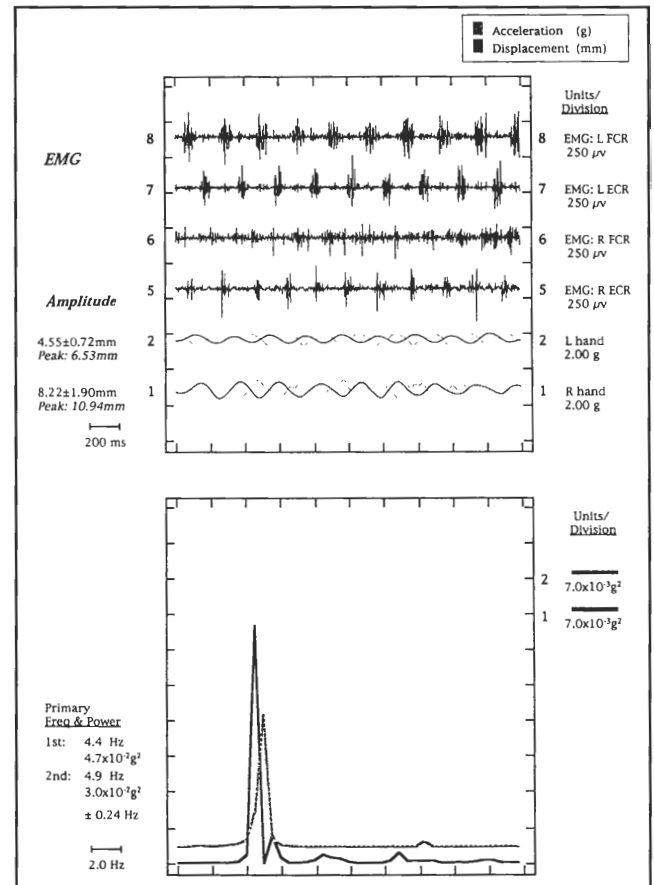


Figure 3. Sample results after recovery 85 days later. Same format as in figure 2. Note the normal-appearing EMG from the right extensor carpi radialis (R ECR) bursting alternately with the right flexor carpi radialis (R FCR), and decreased amplitude of the right-hand tremor compared with figure 2. Note also that the peak frequency in each hand has not changed.

tion, there was a concomitant decrease in the relative amplitude of both right-hand tremors, and an alternating antagonist EMG pattern characteristic of parkinsonian tremor<sup>1,5</sup> emerged in the right forearm with the return of clinical function. These findings show that tremor frequency in PD can remain unchanged even with complete loss of a functionally distinct group of muscles. Tremor amplitude, however, is significantly affected by unbalanced antagonist activity.

Early clinical studies<sup>6,7</sup> on reflex and peripheral modulations of parkinsonian tremor found that dorsal rhizotomy had little effect in patients with PD. Work with experimentally induced tremors in monkeys subjected to limb deafferentation also found that peripheral changes did not alter tremor frequency.<sup>8,9</sup> Ohye et al,<sup>8</sup> however, found that tremor amplitude became larger and more variable after deafferentation. Our findings in this case study directly parallel these observations.

More recent physiologic investigations<sup>2,3</sup> in PD patients have shown that mechanical limb perturbation does not alter tremor frequency, although it may have some effect on phase resetting. Addi-

tional work by Britton et al,<sup>10</sup> however, has shown that if the relative magnitude of the perturbation with respect to the tremor amplitude is taken into consideration, mechanical phase resetting does not distinguish PD from essential tremor. Although these experiments manipulated tremor with perturbations rather than by paralysis, their findings support our results in providing strong evidence for a lack of peripheral modulation effect in parkinsonian tremors. In another study, Rondot et al<sup>11</sup> also found that rest tremors are resilient to peripheral modification in an experiment similar to our patient's natural experiment; they noted that weakening specific muscles with local anesthesia attenuated action tremors without a reliable effect on rest tremor.

The increased tremor amplitudes with paralysis of wrist extensors in our patient may have been due to normal spinal segmental inhibitory mechanisms superimposed on the functional paralysis of wrist extensors.<sup>12</sup> Supraspinal tremor generators that activate both wrist flexors and extensors<sup>5</sup> may have resulted in unopposed and disinhibited flexor activity, resulting in tremors of larger amplitude. Increased flexor activity may have been reinforced further by the lack of extensor Ia afferent input due to the radial nerve injury. Anatomic and physiologic studies<sup>13,14</sup> have demonstrated that all large myelinated fibers (greater than 6  $\mu\text{m}$  in diameter) are functionally blocked in compressive nerve injuries. Consequently, the radial neurapractic injury in our patient would have abolished Ia spindle input and further affected normal reciprocal inhibitory balance.<sup>12</sup> The sinusoidal appearance of tremors, sufficiently driven only by flexors, was presumably due to passive mechanical recoil between muscle bursts.

These findings illustrate how muscle paralysis and absent Ia activity from a functionally select group of muscles in a patient with PD differentially affect tremor frequency and amplitude. Indirectly, these results provide evidence for a strong central tremor frequency generator in PD that is independent of extreme peripheral changes. A therapeutic message from these findings could be that efforts to treat parkinsonian tremors peripherally, such as with botulinum toxin injections, would not be very effective in altering tremor oscillations. While botulinum toxin results only in muscle weakness and not Ia afferent block, the decreased spindle and other afferent activity from weakened muscles may result in relatively less inhibitory drive on antago-

nist muscles. If such methods were used, sets of antagonist muscles might need to be injected because treating only half the antagonists could potentially make the tremors worse.

**Note.** Readers can obtain 1 page of supplementary material from the National Auxiliary Publications Service, c/o Microfiche Publications, P.O. Box 3513, Grand Central Station, New York, NY 10163-3513. Request document no. 05109. Remit with your order (not under separate cover), in US funds only, \$7.75 for photocopies or \$4.00 for microfiche. Outside the United States and Canada, add postage of \$4.50 for the first 20 pages and \$1.00 for each 10 pages of material thereafter, or \$1.75 for the first microfiche and \$.50 for each fiche thereafter. *There is a \$15.00 invoicing charge on all orders filled before payment.*

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