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Motor deficits in patients with large-fiber sensory neuropathy

(posture/centrally programmed movement/feedback/deafferentation)

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ABSTRACT **The issue of whether brain signals in the absence of peripheral feedback are sufficient to specify accurate movement was evaluated by studying motor performance in patients with loss of somesthetic afferent input as a result of acquired large-fiber sensory neuropathy. With visual guidance, movements and postures were impaired relatively little, but when visual guidance was unavailable, the patients exhibited postural drift and gross inaccuracy of movement. Impairments were more apparent for smaller (3°) than for larger (15°) movements. Previous studies that have failed to show major motor impairments in deafferented subjects examined movements involving rather large joint displacements, and this may have been a factor in the failure of these studies to reveal severe deficits. The present results demonstrate a critical role for somesthetic feedback in regulating centrally generated levels of motor output and show that central motor programs deprived of such feedback are unable to subserve accurate motor control.**

Severe motor impairments in patients with large-fiber sensory neuropathies have been described by clinical neurologists (1–3) and are commonly observed in clinical practice, but results from a number of neuropsychological experiments have raised doubts as to the importance of sensory feedback in active movement (4–7). These "negative" studies revealed only slight motor deficits in deafferented humans, monkeys, cats, and a variety of invertebrates, and it was argued that centrally programmed brain or spinal cord activity could control movement without the need for sensory feedback (8).

We reexamined this issue in patients with somesthetic losses due to acquired large-fiber sensory neuropathy, and our results help to resolve the discrepancies between clinical and neuropsychological investigations: whereas motor impairments may seem to be slight when deafferented subjects make relatively large limb displacements, impairments become progressively more apparent as movement size is reduced. Furthermore, somesthetic losses cause profound deficits in the ability of subjects to maintain the steady-state levels of active muscular contraction necessary for postural stability.

MATERIALS AND METHODS

The patients who were studied had a peripheral neuropathy with selective involvement of large sensory fibers without clinically evident weakness. Thus, while having excellent muscular strength, the patients exhibited sensory deficits, including absence of position and vibration sense to the level of the most proximal joints; moderate decrease in pinprick, temperature, and light-touch sensation below the shoulders; and absence of deep-tendon reflexes. The loss of inputs from both cutaneous mechanoreceptors (as shown by deficits in tactile sensitivity) and from muscle receptors (as shown by loss of stretch reflexes) meant that, while being selective for sensory versus motor fibers, the neuropathy was not selective for subtypes of large myelinated fibers. Thus, the motor impairments that the patients exhibited could not be attributed to loss of inputs from one particular somesthetic submodality. Muscle biopsies revealed no abnormalities in six of the eight cases studied and mild-to-moderate denervation in the other two. Needle electromyography showed denervating potentials in four of the eight cases. Nerve conduction velocity was slightly to severely diminished, and sensory nerve potentials could not be elicited in any of the patients. Nerve biopsy showed a rather selective loss of the large myelinated fibers.

Apparatus and Procedures. Maintenance of postural stability and execution of discrete movements were tested with an apparatus in which the hand was placed between two padded metal plates that allowed flexion–extension movements of the wrist. The wrist joint was positioned above the axle of a torque motor that was coupled to the metal plates, and the amount of muscular contraction necessary for maintenance of a given wrist position depended on the opposing torque generated by this motor. The subjects were prevented from seeing their hands but could be given visual feedback via a TV screen showing a cursor representing hand position. A second cursor indicated the proper orientation for the wrist, and subjects sought to maintain alignment of these two cursors.

In the first experiment, patients began by maintaining a neutral (0°) wrist position for 5 sec. Any deviation from this position was opposed by an elastic load of 0.13 $N \cdot m \cdot deg^{-1}$. At the conclusion of the 5-sec alignment period, the target cursor jumped to a new position that required a 5° wrist flexion. Subjects flexed to this new position and held it for 22 sec, following which the target cursor jumped back to the original location. After 10 trials in which both the position and target cursors were displayed continuously, there were 10 additional trials in which the visual feedback provided by the position cursor was withdrawn after the subject had successfully repositioned the hand at 5° of wrist flexion for 2 sec. The subjects then sought to maintain the flexed wrist position for a subsequent period of 20 sec in the absence of visual guidance.

A second phase of the investigation evaluated the capacity of subjects to maintain a stable wrist position while opposing a single constant load. At different times, observations were repeated with different loads that ranged from 0.64 N·m opposing flexion to 0.64 N·m opposing extension. Subjects initially adopted a position of 10° wrist flexion by aligning the position and target cursors. After an alignment period of 8 sec, the position cursor was blanked for 20 sec, and patients attempted to maintain the hand in the position it had occupied at the time the blanking occurred. Ten to 15 such cycles were performed, and the amount of postural drift was measured for each trial.

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In the third experiment, accuracy of step movements was evaluated. Patients began by repeatedly practicing wrist movements of a single size (either 3°, 6°, 9°, 12°, or 15°) by moving so as to realign the position and target cursors after the target cursor had stepped to a new position. After a series of 40 practice trials in which both cursors were displayed at all times, there was a series of 40 trials in which the position cursor was blanked as soon as the subject began the movement to realign the two cursors after the target had jumped to its new position. On trials when blanking occurred, subjects attempted to make the same movement that they had previously practiced; that is, to move to a position that would have resulted in the alignment of the two cursors. Subjects then sought to maintain alignment for a short time (2–3 sec). Movements were repeated every 3–5 sec.

RESULTS

One of the most striking motor deficits of the patients with large-fiber sensory neuropathy was an inability to maintain stability of wrist position in the absence of visual guidance (Fig. 1*A*). This loss of stability after elimination of visual feedback occurred even though the patients repeatedly had succeeded in maintaining the required position with visual guidance. Results for three patients and a control subject attempting to hold the hand steady at 10° of flexion in the absence of visual guidance are shown in Fig. 1*B*. When postural maintenance was visually guided (not illustrated), patients were able to maintain alignment relatively well, but postural stability was lost when visual guidance was withdrawn. On any one individual trial, the wrist position sometimes drifted *with* the load and sometimes *against* the load, and for some trials there was little or no drift. These three sorts of outcomes typically occurred randomly. The amount of load opposing movement did not necessarily affect the amount of drift, but instability was typically lowest when there was no load (see patients P1 and P3). Despite the marked drift on some trials (>20° at the end of the 20-sec drift period), posttest interviews revealed that patients were completely unaware of hand movements that had occurred when the visual display was blanked. Controls drifted a small amount (<0.5°) over the 20-sec period when visual guidance was unavailable.

The incremental movements of two patients and one control are illustrated in Fig. 2. When visual guidance was available, positional errors by patients ranged from 1–2° for all movement sizes. This error magnitude was approximately 3 times that of controls. Errors increased for both controls and patients when visual guidance was absent, but the increase in error was substantially greater for patients. In the absence of visual guidance, the error by patients for 3° movements was equal to or greater than the intended movement itself, whereas for the 15° movement the error was one-third to one-half of the movement size. It should be noted that movements made by patients without visual guidance were initially inaccurate (either undershoot or overshoot) and were then

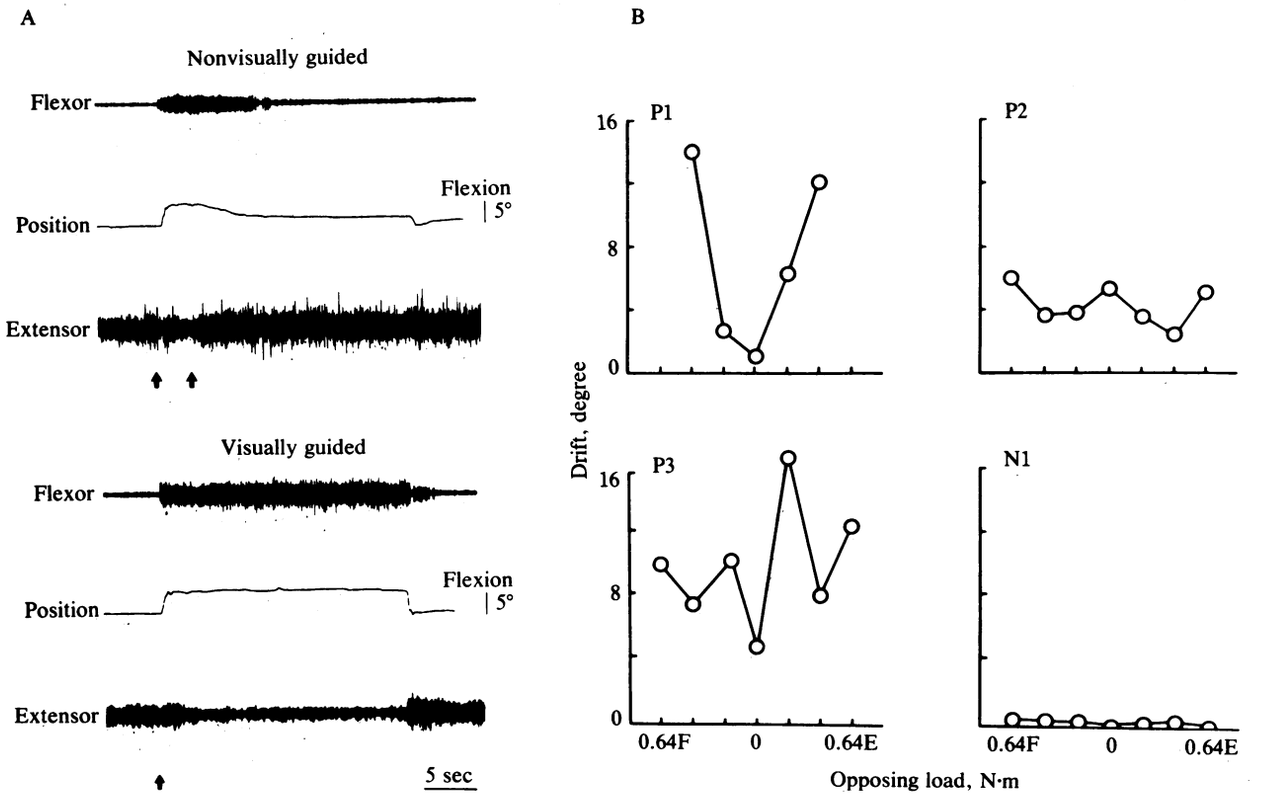

FIG. 1. Postural control with and without visual guidance. (*A*) Hand position and agonist (flexor) and antagonist (extensor) electromyogram during movements against an elastic load of 0.13 N·m·deg^{-1}. The leftmost arrow under the upper three records and the single arrow under the lower three records indicate when the target jumped to the new position. The second arrow under the upper records indicates removal of visual guidance. Visual guidance was restored 5 sec after return to the original position. In the lower three traces, note (*i*) the ability of the patient to maintain a flexed position against the elastic load and (*ii*) the reciprocal electromyogram in wrist flexor and extensor muscles. In the upper three traces, note the almost immediate deterioration of positional and muscle control when visual guidance was removed. (*B*) Postural responses of three patients and one control are shown during maintenance of 10° of flexion without visual guidance. The abscissa indicates the constant torques opposing postural maintenance (0.64F = 0.64 N·m opposing flexion; 0.64E = 0.64 N·m opposing extension). The ordinate shows the average absolute value of the postural drift for the 20-sec period without visual guidance. Patients P1 and P3 drifted the least when no load opposed movement. Only patient P1 showed load dependence on the amount of drift. The normal subject was able to maintain alignment with 0.5° of wrist rotation.

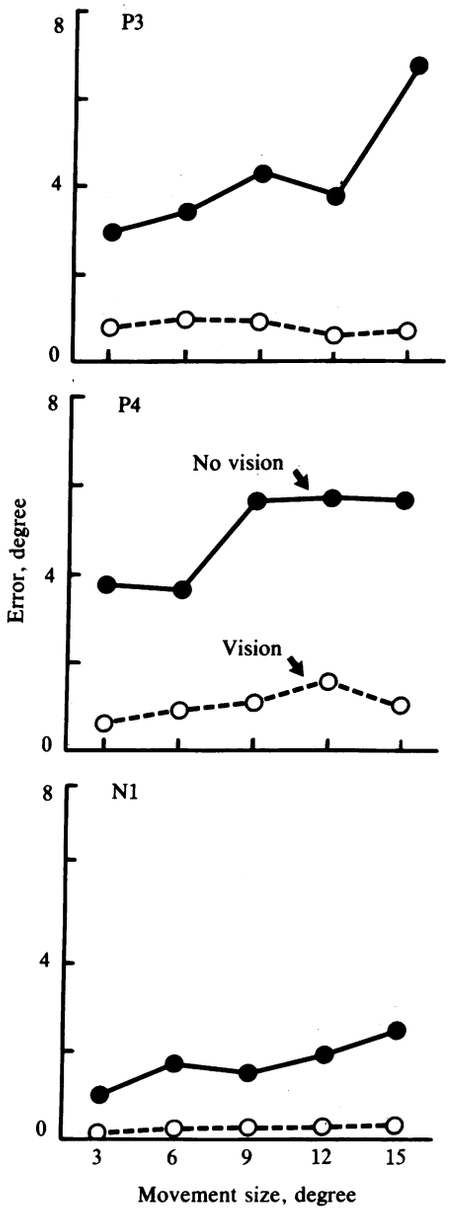

FIG. 2. Incremental movements with and without visual guidance. Movements of five sizes are shown for two patients (P3 and P4) and one normal control (N1). Subjects moved with (○) or without (●) visual guidance. Movement size (abscissa) is plotted against the average absolute value of movement error (ordinate).

never corrected. In contrast, the initial movement phase by normals was sometimes inaccurate, but movements were commonly corrected.

DISCUSSION

These results demonstrate the importance of somesthetic sensory inputs both for postural stability and for active voluntary displacements. Whereas deficits of posture and movement were most obvious in the absence of visual feedback, certain deficits were also apparent, even *with* visual feedback. Thus, even when visual guidance was available and patients attempted to maintain a given wrist position, there was often a low-frequency (<2 Hz) instability that was corrected when the patients saw they had drifted away from the target. Of course, upon removal of visual guidance, such corrections were impossible, and patients often began to drift immediately, failing to perceive that postural drift had occurred and, therefore, being unable to reposition the limb. The failure of patients to maintain a constant posture indicates that the brain mechanisms responsible for controlling steady-state excitation to the flexor and extensor motoneurons are unable to function in the absence of somesthetic feedback. It was as if the central brain structures regulating motoneuron output failed to "remember" the excitation level to motoneurons occurring prior to elimination of visual guidance and, as a consequence, motor commands began drifting as soon as visual guidance was eliminated. The inability of patients to maintain constant motor output was typically observed almost immediately after visual guidance was removed (Fig. 1*A*, top trace). The rapid deterioration of the motor command suggests that even short-term stability of motor output requires continuous updating, by sensory afferents, of the consequences of intended motor output. In this regard, Fukushima *et al.* (9) have shown that sustained voluntary activation of motor unit discharge is dependent on the integrity of the γ-motoneuron signals that regulate the sensitivity of the muscle spindles that in turn provide a major part of the proprioceptive inputs during movement.

There are a number of interesting parallels between the deficits due to somesthetic loss in deafferented humans, other vertebrates, and invertebrates. For example, the flight of deafferented grasshoppers and locusts exhibits a gradual decline in wing beat frequency after initiation of flight and, as a consequence, there is a gradual decline in lift (10, 11). Deafferentation of cockroaches causes the neurons controlling locomotion to have abnormalities in discharge patterns such that the stepping frequency and running speed decreases substantially (12). The exquisitely rhythmic swimming pattern of intact leeches becomes arhythmic after deafferentation (13). In vertebrates, deafferentation of the spinal cord changes the patterns of muscle activity during locomotion (14, 15).

In addition to deficits in postural maintenance, patients exhibited impairments in accuracy of discrete movements such that both the initial and end-point positioning phases of the movements were often grossly inaccurate. These data contrast with previous experimental demonstrations of relatively slight impairments after deafferentation when performance of large joint rotations was studied (4–6). The fact that muscle afferents and reflex muscle responses often have their greatest sensitivity to small input signals (16–20) suggests that the role of inputs from muscle receptors may be more apparent for small than for large, relatively coarse movements. Indeed, it has already been shown that accuracy of small movements and precise control of motor unit discharge are impaired by perturbing kinesthetic inputs. Small joint rotations are especially impaired by mechanical perturbations in both intact and deafferented humans (21–23). Although previous reports have not demonstrated deficits in execution of large movements as a result of perturbations leading to unpredictable kinesthetic inputs, the view that performance of larger movements is unaffected by the loss of somesthetic inputs was not supported by the present results. Our observations showing marked deficits in the 15° movements performed by patients indicate that even movements of this magnitude are impaired by somesthetic loss, though impairments were certainly more apparent as movement size was reduced to 3°. In conclusion, our data and those of Rothwell *et al.* (24) clearly demonstrate the significance of somesthetic input for accurate motor control and help to clarify what has been a discrepancy between the ideas emerging from neuropsychological experiments in deafferented monkeys and humans on the one hand and clinical observations of patients on the other.

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