Background: Chronic idiopathic axonal polyneuropathy (CIAP) is a frequent neurologic disorder in elderly persons. In view of the aging population, it is important to know the long-term prognosis of CIAP.

Objectives: To determine if CIAP is influenced by the superposition of the effects of aging and to evaluate the severity of CIAP according to the disease duration.

Design: Controlled cohort study.

Setting: Outpatient clinic for neuromuscular diseases at the University Medical Center Utrecht, Utrecht, the Netherlands.

Participants and Methods: One hundred twenty-seven patients with CIAP and 108 age-matched control subjects were included. We defined CIAP on the basis of symmetrical distal sensory or sensorimotor symptoms and signs with evolution over at least 6 months, exclusion of causes by history taking, results of clinical and laboratory investigations, and electrophysiologic findings that agreed with the diagnosis of axonal polyneuropathy.

Results: No important neurologic or electrophysiologic differences were found between patients with early-onset (before the age of 65 years) and late-onset (at or after the age of 65 years) CIAP, but patients with early-onset CIAP who had a short disease duration (<10 years) experienced more disability than patients with late-onset CIAP who had a similar disease duration. Old controls (age of 65 years or older) more often had symptoms, sensory signs in the legs, absent ankle jerks, and lower mean distal amplitudes of compound muscle action potentials and sensory nerve action potentials than young controls (aged <65 years). Absence of the sural nerve sensory nerve action potentials or presence of spontaneous muscle fiber activity in the anterior tibial muscle was common in patients with CIAP (51% and 60%, respectively), but exceptional (both 2%) in controls.

Conclusions: Neither aging of the peripheral nervous system nor disease duration affects CIAP to a considerable degree, but CIAP has a greater influence on the daily life of nonretired patients with early-onset CIAP. The diagnosis of axonal polyneuropathy is probably supported best by either the absence of the sural nerve sensory nerve action potentials or the presence of spontaneous muscle fiber activity in the anterior tibial muscle.

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AFTER extensive investigations, no cause can be identified in 10% to 20% of the patients who have polyneuropathy. In most of these patients the polyneuropathy presents insidiously in the sixth decade of life with predominantly sensory or sensorimotor symptoms and a slowly progressive course. Electrophysiologic studies invariably show axonal polyneuropathy. For this clinical entity the term “chronic idiopathic axonal polyneuropathy” (CIAP) has been introduced. Others have used “cryptogenic (sensory) polyneuropathy.” Severe disability or ambulatory impairment has not been observed 5 to 10 years after disease onset.

Neurologic symptoms and signs suggestive of polyneuropathy occur more frequently with successful aging. Also, there is a decline of nerve conduction parameters. Furthermore, age-related degenerative changes have been demonstrated in pathologic studies of peripheral nerves in subjects without peripheral nervous system disease.

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The age-dependent decline could affect the clinical course of CIAP with differential consequences regarding disability and prognosis for younger and older patients. However, it is unknown whether CIAP with
PARTICIPANTS AND METHODS

PATIENTS AND CONTROLS

A total of 127 patients (87 men and 40 women) with CIAP and 108 successfully aged controls (72 men and 36 women) were included. Fifty-seven patients with CIAP also participated in a quality-of-life study.21 Patients were referred to our outpatient department for neuromuscular diseases after previous evaluation by other neurologists. The diagnosis of CIAP was made according to the following criteria14,15: (1) symmetrical distal sensory or sensorimotor symptoms and signs of the limbs, compatible with polyneuropathy; (2) insidious onset and slow or no progression of the disease over at least 6 months; (3) no identifiable cause after extensive clinical and laboratory investigations; (4) no indication of hereditary polyneuropathy; and (5) electrophysiologic findings that agreed with the diagnosis of axonal polyneuropathy.

Controls were recruited from relatives or friends of patients visiting our clinic and had to be free of diseases or conditions known to be associated with polyneuropathy. They had not previously consulted a neurologist for symptoms or signs. Patients were classified into 2 groups—those with disease onset before the age of 65 years (hereafter referred to as the “early-onset CIAP group” [n=66 patients]) and those with disease onset at 65 years or older (hereafter referred to as the “late-onset CIAP group” [n=61 patients]). Disease onset was defined as the age at which the symptoms or signs were first noted by the patient to be consistently present. Controls were classified into a group of persons younger than 65 years at study enrollment (hereafter referred to as the “young controls” [n=47 subjects]), and a group of persons 65 years or older at study enrollment (hereafter referred to as the “old controls” [n=61 subjects]). The cutoff was set at the age of 65 years, because it coincided with the usual retirement age and health expectancy (ie, the average age at which a person can still be expected to be disability-free or in good self-reported health) in the Netherlands.6

To evaluate if early-onset CIAP is different from late-onset CIAP, the data at referral were compared. To study the relationship between the disease duration and the severity of CIAP, the latest clinical data of 89 patients who had a short disease duration (<10 years) were compared with the data of 38 patients who had a long disease duration (≥10 years). To determine the normal manifestations of successful aging, young controls were compared with old controls. To evaluate the differences between CIAP and successful aging, patients with late-onset CIAP were compared with old controls. Comparison of patients with early-onset CIAP with young controls was considered inappropriate, because part of the patients with early-onset CIAP had already reached the age of 65 years at the time of study enrollment. The study protocol was approved by the Medical Ethical Committee of the University Medical Center Utrecht, Utrecht, the Netherlands.

CLINICAL EVALUATION

In all patients and controls, history taking and clinical examination (muscle strength, sensory function, tendon reflexes, and the Romberg test) were performed in a standardized fashion.14,22 A detailed inquiry was made about specific motor and sensory symptoms (Table 1), medical history, medication use, and toxic substance exposure. The occurrence of polyneuropathy in family members was thoroughly queried, and affected family members underwent neurologic and electrophysiologic examination, if necessary. If this could not rule out the possibility of a hereditary neuropathy, subjects were excluded.

Table 1. Neurologic Symptoms at Study Enrollment in Patients With CIAP and Control Subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Of Early Onset (n = 66)</th>
<th>Of Late Onset (n = 61)</th>
<th>P Value</th>
<th>Young (n = 47)</th>
<th>Old (n = 61)</th>
<th>P Value</th>
<th>P Value$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, median, y</td>
<td>61.0</td>
<td>72.5</td>
<td>. . .</td>
<td>60.0</td>
<td>71.0</td>
<td>. . .</td>
<td>NS</td>
</tr>
<tr>
<td>Disease duration, median, y</td>
<td>3.0</td>
<td>2.0</td>
<td>NS</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
</tr>
<tr>
<td>Sensory symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tingling or prickling</td>
<td>44 (72)</td>
<td>37 (58)</td>
<td>≤ .04</td>
<td>3 (6)</td>
<td>12 (20)</td>
<td>≤ .04</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Pain</td>
<td>35 (57)</td>
<td>24 (38)</td>
<td>≤ .01</td>
<td>3 (6)</td>
<td>3 (5)</td>
<td>NS</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Numbness or cotton wool</td>
<td>57 (93)</td>
<td>49 (74)</td>
<td>≤ .003</td>
<td>5 (11)</td>
<td>12 (20)</td>
<td>NS</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Tightness or bandlike</td>
<td>8 (13)</td>
<td>15 (23)</td>
<td>NS</td>
<td>0</td>
<td>1 (2)</td>
<td>NS</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Burning or cold or warm</td>
<td>13 (21)</td>
<td>14 (21)</td>
<td>NS</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>NS</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Motor symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle cramps</td>
<td>41 (67)</td>
<td>28 (42)</td>
<td>≤ .004</td>
<td>10 (21)</td>
<td>17 (28)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Stiffness</td>
<td>39 (64)</td>
<td>23 (35)</td>
<td>≤ .001</td>
<td>9 (19)</td>
<td>13 (21)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Weakness</td>
<td>40 (66)</td>
<td>39 (59)</td>
<td>NS</td>
<td>1 (2)</td>
<td>9 (15)</td>
<td>≤ .02</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Muscle wasting</td>
<td>18 (30)</td>
<td>13 (20)</td>
<td>NS</td>
<td>1 (2)</td>
<td>4 (7)</td>
<td>NS</td>
<td>&lt; .03</td>
</tr>
<tr>
<td>Coordination symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clumsiness, hands</td>
<td>11 (18)</td>
<td>11 (17)</td>
<td>NS</td>
<td>0</td>
<td>0</td>
<td>NS</td>
<td>≤ .001</td>
</tr>
<tr>
<td>Unsteady gait</td>
<td>46 (75)</td>
<td>52 (79)</td>
<td>NS</td>
<td>7 (15)</td>
<td>7 (11)</td>
<td>NS</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

*Data are given as number (percentage) of participants unless otherwise indicated. CIAP indicates chronic idiopathic axonal polyneuropathy; NS, not significant; and ellipses, not applicable.
†The early-onset group were those patients who had the disease before the age of 65 years. The late-onset group were those patients who had the disease at the age of 65 years or older. For a more detailed explanation, see the “Patients and Controls” subsection of the “Participants and Methods” section.
‡The young controls were persons younger than 65 years at the time of enrollment in the study. The old controls were persons 65 years or older at the time of enrollment in the study. For a more detailed explanation, see the “Patients and Controls” subsection of the “Participants and Methods” section.
§Comparison of the patients with late-onset CIAP vs the old control subjects.
onset at a younger age differs from CIAP with onset at an older age. Moreover, the disease duration could obscure the influence of aging. To our knowledge, the severity of CIAP after a long disease duration (which is more likely to occur in patients with disease onset at a younger age) has not been studied before. The aims of this study were to determine if CIAP is influenced by the superposition of the effects of aging and to evaluate the severity of CIAP according to disease duration. We compared the neurologic symptoms and signs, disability status, and electrophysiologic parameters of 127 patients with CIAP with those of 108 successfully aged control subjects.

**RESULTS**

Age distributions at study enrollment of patients and controls are shown in Figure 1. The men-women ratio was 2.1 in patient and control groups.

**CLINICAL EVALUATION OF PATIENTS WITH CIAP**

Profiles of symptoms and signs are shown in Figure 2A. In all patients the polyneuropathy had started distally in the legs; at the time of referral, 60 patients had symptoms distally in the legs and hands.

All patients had distal sensory signs in the legs, and 55 had sensory signs in the hands. Weakness of distal leg muscles was noted in 80 patients, and 17 also had weakness of the hand muscles. A total of 62 patients with signs distally in the legs also had signs in the hands.

Thirty-five patients used walking aids such as a cane, adjusted shoes, ankle-foot orthoses, or a wheeled walker. One patient used a wheelchair because of a hemiparesis from cerebral infarction. The scores on the modified Rankin scale were as follows: 1, 70 patients; 2, 52 patients; and 3, 5 patients. No patients had modified Rankin scores of 4 or 5.

Patients with early-onset CIAP significantly more often had tingling or prickling, pain, numbness or a cotton-wool sensation, muscle cramps, stiffness, and weakness (Table 1), but there were no statistically significant differences in the presence of signs (Table 2).

**CLINICAL SEVERITY IN SHORT AND LONG DISEASE DURATION**

In patients with early-onset CIAP who had a short disease duration, modified Rankin scores were significantly higher than in patients with late-onset CIAP who had a short disease duration (Table 3). In patients with late-onset CIAP who had a short disease duration, sensory and motor total scores of the legs were significantly higher, and modified Rankin scores were significantly
lower than in patients with late-onset CIAP who had a long disease duration (Table 3).

CLINICAL EVALUATION OF CONTROLS

Symptoms and signs were also found in controls, and more often in old controls (Figure 2B). In 54 controls symptoms were located distally in the legs, and 26 (6 young and 20 old controls; P≤.01) had symptoms in the hands as well.

In 70 controls (25 young and 45 old controls; P=.02) sensory signs were found distally in the legs, and 17 (5 young and 12 old controls; P≤.01) also had sensory signs in the hands. Muscle strength of the arms and legs was normal in all but 2 controls (ages 73 and 74 years) who had an MRC grade 4 weakness of the long extensor muscle of the big toe or anterior tibial muscle.

The walking aids used by 2 controls (ages 79 and 80 years) were a cane and a wheeled walker. The modified Rankin scores for the control subjects were as follows: 0, 51 controls; 1, 54 controls; and 2, 3 controls. No controls had a modified Rankin score of 3 or higher.

Old controls significantly more often mentioned tingling or prickling and weakness (Table 1). Furthermore, old controls had significantly lower sensory total scores of the legs (Table 2), and they significantly more often had abnormal light touch and vibration sense, and absent ankle tendon reflexes (Figure 3; sensory functions were considered abnormal if the sensory scores in the arms or legs were below 7 for pinprick, light touch, or vibration sense, and below 3 for position sense).

CLINICAL COMPARISON OF PATIENTS WITH LATE-ONSET CIAP WITH OLD CONTROLS

In general, patients with late-onset CIAP significantly more often had symptoms and signs as well as significantly lower sensory and motor total scores (Table 1 and Table 2). However, old controls significantly more often had pure motor symptoms (0 patients with late-onset CIAP and 23 old controls; P<.001) or pure sensory signs (23 patients with late-onset CIAP and 46 old controls; P<.001).

In the legs of old controls pinprick (75%), light touch (82%), and vibration sense (83%) abnormalities were restricted to the feet, whereas in patients with late-onset CIAP these rates were significantly lower, that is, 38%, 47%, and 63%, respectively (P<.001 for all rates). Patients with late-onset CIAP significantly more often used walking aids (P=.01) and had significantly higher modified Rankin scores (P<.001).

STANDARDIZED ELECTROPHYSIOLOGIC STUDIES

None of the electrophysiologic parameters in patients or controls fulfilled our criteria for demyelination. Table 4 summarizes the findings of the standardized electrophysiologic studies in 96 patients with CIAP and 49 controls.
Standardized Electrophysiologic Studies of Patients With CIAP

In patients with late-onset CIAP the mean distal motor latency of the tibial nerve was significantly longer. Absence of the sural nerve sensory nerve action potential (SNAP) or the presence of spontaneous muscle fiber activity (ie, fibrillation potentials, positive sharp waves, or complex repetitive discharges) in the anterior tibial muscle were found in most patients (72%) (33 patients with early-onset CIAP and 36 patients with late-onset CIAP).

Standardized Electrophysiologic Studies of Controls

In old controls the mean distal compound muscle action potential amplitude of the tibial nerve and the mean distal SNAP amplitudes of the median nerve and sural nerve were significantly lower. The SNAP of the sural nerve was absent in 1 old control (age 84 years). In another old control (age 67 years) concentric needle electromyography of the anterior tibial muscle showed positive sharp waves at 1 insertion site.

Electrophysiologic Comparison of Patients With Late-Onset CIAP With Old Controls

In patients with late-onset CIAP the mean distal motor latencies were significantly longer, and the mean distal compound muscle action potentials, SNAP amplitudes, the mean motor nerve conduction velocities and sensory nerve conduction velocities were significantly lower. Absence of the sural nerve SNAP or the presence of spontaneous muscle fiber activity in the anterior tibial muscle were found significantly more often in patients with late-onset CIAP.

COMMENT

There were no important differences in clinical features, electrophysiologic parameters, or disease course between patients with early-onset and late-onset CIAP. Patients with early-onset CIAP who had a short disease duration had worse modified Rankin scores than patients with late-onset CIAP who had a long disease duration. Basic activities of daily living appear fairly resistant to aging, whereas complex or instrumental activities of daily living (eg, preparing meals, housekeeping, occupational skills) are less so.28 The modified Rankin score is an overall disability scale that integrates these levels of activities of daily living. The polyneuropathy probably has a more negative influence on the daily life of the nonretired patients with early-onset CIAP, although they are not more severely affected than the retired patients with late-onset CIAP. The low total scores of the legs and the worse modified Rankin scores in patients with late-onset CIAP who had a long disease duration are fallible because of the small sample size. The advanced age (at least 75 years old) of patients with late-onset CIAP who had a long disease duration is less likely to provide an explana-
tion, because the scores are equally low in patients with early-onset CIAP who had a similar disease duration. Moreover, as we have shown, age does not importantly affect CIAP, nor are the neurologic impairments or disability in successfully aged old controls of such severity that they can be expected to have a significant influence. In the successfully aged person 65 years and older, there is a decline of sensory function distally in the legs, ankle reflexes are more often absent, and electrophysiologic studies most notably show lower distal compound muscle action potentials and SNAP amplitudes.

Similar to others,7,11,29 we evaluated each sensory modality by simple techniques. Measurement of the perception time of the vibratory stimulus from a 128-Hz tuning fork was validated earlier by De Michele et al.30 Our normal perception time values of 15 seconds at the middle finger and 10 seconds at the big toe are of similar magnitude as their mean perception times at the ankle and wrist. Hence, our normal values likely classify a larger proportion of elderly persons as having abnormal vibration sense at the feet. Others have advocated the use of the Rydel-Seiffer graduated tuning fork and contended that absent vibration sense at the feet in healthy elderly subject should be considered abnormal.31 However, individuals with absent vibration perception in at least one of the sites tested were excluded prior to the analysis. Because vibration perception at the big toe was absent in 28% of our old controls, we are less inclined to denote this as abnormal in elderly persons. Whatever sensory testing techniques used, many studies most notably show a decline of light touch and vibration sense with advancing age.7-11,30-32

![Figure 3. A. Neurologic signs of aging in young (open bars) and old control subjects (shaded bars). B. For comparison, the same signs seen in patients with early onset (gray shaded bars) and late onset of chronic idiopathic axonal polyneuropathy (CIAP) (solid bars).](image-url)
Table 4. Standardized Electrophysiologic Findings in 96 Patients With CIAP and 49 Control Subjects*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients With CIAP†</th>
<th>Control Subjects‡</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>of Early Onset (n = 50)</td>
<td>of Late Onset (n = 46)</td>
<td>Young (n = 19)</td>
</tr>
<tr>
<td>Duration of disease, y</td>
<td>62.0 ± 3.0</td>
<td>72.5 ± 3.0</td>
<td>NS</td>
</tr>
<tr>
<td>Nerve conduction studies Motor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median nerve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DML, ms</td>
<td>4.2 ± 0.7</td>
<td>4.1 ± 0.5</td>
<td>NS</td>
</tr>
<tr>
<td>Forearm CMAP, mV</td>
<td>8.0 ± 3.0</td>
<td>7.2 ± 2.8</td>
<td>NS</td>
</tr>
<tr>
<td>Forearm MCV, m/s</td>
<td>49 ± 4.4</td>
<td>50 ± 4.9</td>
<td>NS</td>
</tr>
<tr>
<td>Upper arm MCV, m/s</td>
<td>54 ± 7.5</td>
<td>52 ± 4.6</td>
<td>NS</td>
</tr>
<tr>
<td>Tibial nerve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DML, ms</td>
<td>4.9 ± 0.8</td>
<td>5.7 ± 1.6</td>
<td>≤.01</td>
</tr>
<tr>
<td>Distal CMAP, mV</td>
<td>1.8 ± 2.2</td>
<td>1.4 ± 2.1</td>
<td>NS</td>
</tr>
<tr>
<td>MCV, m/s</td>
<td>36 ± 4.5</td>
<td>37 ± 7.1</td>
<td>NS</td>
</tr>
<tr>
<td>Sensory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal SNAP, µV</td>
<td>7.3 ± 6.1</td>
<td>6.1 ± 6.3</td>
<td>NS</td>
</tr>
<tr>
<td>SCV, m/s</td>
<td>47 ± 6.2</td>
<td>48 ± 6.3</td>
<td>NS</td>
</tr>
<tr>
<td>Sural nerve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal SNAP, µV</td>
<td>2.5 ± 2.8</td>
<td>1.8 ± 2.5</td>
<td>NS</td>
</tr>
<tr>
<td>SCV, m/s</td>
<td>44 ± 6.6</td>
<td>44 ± 4.9</td>
<td>NS</td>
</tr>
<tr>
<td>Absent SNAP</td>
<td>22 (44)</td>
<td>27 (59)</td>
<td>NS</td>
</tr>
<tr>
<td>Concentric needle electromyography of anterior tibial muscle</td>
<td>Presence of spontaneous muscle fiber activity</td>
<td>27 (54)</td>
<td>31 (67)</td>
</tr>
</tbody>
</table>

*Data are given as the median for age and duration of disease; all other data are given as mean (SD) for distal motor latency (DML), compound muscle action potentials (CMAP), motor nerve conduction velocity (MCV), sensory nerve action potentials (SNAP), sensory nerve conduction velocity (SCV). CIAP indicates chronic idiopathic axonal polyneuropathy; ellipses, not applicable; and NS, not significant.
†The early-onset group indicates those patients who had the disease before the age of 65 years. The late-onset group were those patients who had the disease at 65 years or older. For a more detailed explanation see the “Patients and Controls” subsection of the “Participants and Methods” section.
‡The young controls were persons younger than 65 years at the time of enrollment in the study. The old controls were persons 65 years or older at the time of enrollment in the study. For a more detailed explanation see the “Patients and Controls” subsection of the “Participants and Methods” section.
§Comparison of the patients with late-onset CIAP vs the old control subjects.
||Data are given as the number (percentage) of the participants.

Paradoxically, old controls mentioned weakness more often than could be confirmed by neurologic examination. Weakness on standard neurologic examination is unusual in successful aging, but a decline of muscle strength can be demonstrated by more sensitive quantitative techniques (ie, isometric or isokinetic strength testing). 33

The biceps, triceps, and knee joints are usually retained after the age of 65 years.5-11,34 Some investigators have asserted that the ankle reflex should also usually be present after the age of 65 years,13,36 but others have found it to be absent as frequently as in our study.7-11,34,37 The effort made to obtain the ankle jerk (eg, reinforcement methods) and the selection and age distribution of controls may contribute to observed response rates. Because the ankle jerk may often be absent in persons older than 65 years, it is not a good indicator for the presence of polyneuropathy in elderly people.

The lower mean distal SNAP amplitudes and compound muscle action potentials in old controls compared with young controls are compatible with normal aging.8,11,13,15,19 We did not find a change with age in distal motor latencies or nerve conduction velocities unlike others,11,16,18,19 which may be because of the inclusion of younger subjects in those studies, and our rigorous temperature control.

Because absence of the sural nerve SNAP or presence of spontaneous muscle fiber activity were exceptional in controls but common in patients with CIAP, either one of these phenomena probably best supports the diagnosis of axonal polyneuropathy in a clinically suspect individual. Instead of using standard electrode placement, we palpated the sural nerve at the ankle and placed the recording electrode over the nerve, which may have contributed to our findings on the preservation of the sural nerve responses. Also, our findings are reinforced by other studies that have shown that sural nerve SNAP is absent in only small proportions (0%-9%) of the control subjects, even after the age of 60 years.14-16,19,38-44 Studies on the normal electromyography of the intrinsic foot muscles of controls have shown conflicting results regarding the presence of spontaneous muscle fiber activity.55,56 Therefore, we performed electromyography in the anterior tibial muscle, although we are unaware of normal electromyography studies of this muscle.

The superposition of aging in the peripheral nervous system does not importantly affect CIAP. Even after more than 10 years of having the disease, severe disabil-
ity (modified Rankin score >3) does not occur. Axonal polyneuropathy can probably be confirmed best on the basis of the absence of the sural nerve SNAP or the presence of spontaneous muscle fiber activity in the anterior tibial muscle. In successfully aged subjects older than 65 years, mild pure sensory or pure motor symptoms, slight and pure sensory signs confined to the feet (including absent vibration sense at the big toe), or absent ankle reflexes can be considered as normal aging manifestations. Our findings are valuable when informing patients with CIAP about the prognosis. In view of the aging population, our findings stress the importance of clinical criteria by which symptoms or signs may be attributed to normal aging or conversely to polyneuropathy.

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Author contributions: Study concept and design (Drs Vrancken and Notermans); acquisition of data (Drs Vrancken, Franssen, Teunissen, and Notermans); analysis and interpretation of data (Drs Vrancken, Franssen, and Wokke); drafting of the manuscript (Dr Vrancken); critical revision of the manuscript for important intellectual content (Drs Franssen, Wokke, Teunissen, and Notermans); statistical expertise (Drs Vrancken and Franssen); study supervision (Drs Franssen, Wokke, and Notermans).

Corresponding author: Alexander F. J. E. Vrancken, MD, University Medical Center Utrecht, PO Box 85500, 3508 GA Utrecht, the Netherlands (e-mail: a.f.j.e.vrancken@neuro.azu.nl).

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