Brain (1996), **119**, 1751–1762

Central nervous system modifications in patients with lesion of the anterior cruciate ligament of the knee

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Summary

Patients with traumatic lesion of the anterior cruciate ligament often experience knee instability, which, recent studies suggest, is probably due to reduced knee proprioception. We studied knee proprioception and somatosensory evoked potentials (SEPs) after stimulation of the common peroneal nerve at the knee above the articular branches subserving the sensory innervation of the anterior cruciate ligament, in 19 patients with traumatic anterior cruciate ligament lesion. Ten patients showed decreased position sense of the knee, and of these, seven presented loss of cortical P27 potential while preserving lemniscal P20 and spinal N14 responses to common peroneal nerve stimulation on the side of the anterior cruciate ligament lesion. All our patients had normal SEPs to stimulation of the posterior tibial nerve at both the ankle and the knee. We suggest that in patients showing SEP abnormalities, the dysfunction of the central somatosensory conduction is located above the medial lemniscus and is limited to common peroneal nerve somatosensory pathways. Therefore, it is likely that in the seven patients showing SEP abnormalities, the loss of the knee mechanoreceptors was followed by remodelling of the CNS above the medial lemniscus. In five patients with P27 absence after common peroneal nerve stimulation, we also recorded SEPs after stimulation of the peroneal nerve at the ankle and obtained a normal cortical positive response; moreover, in our healthy subjects, cortical responses were significantly higher in amplitude after peroneal nerve than after common peroneal nerve stimulation. These findings strongly suggest that proprioceptive afferent inputs from the knee are more effective than distal afferent inputs in generating the greater part of the common peroneal nerve cortical SEPs. Since common peroneal nerve stimulation probably allows selective recording of the responses produced by the activation of the cortical representation of the knee, minor lesions with a reduction in the number of knee mechanoceptors could result in SEP changes after common peroneal nerve stimulation.

Keywords: somatosensory evoked potentials; knee; anterior cruciate ligament

Abbreviations: SEP = somatosensory evoked potential; T12 = 12th dorsal vertebra

Introduction

In the past few years it has become evident that the anterior cruciate ligament plays an important role in knee proprioception. Lesions of the anterior cruciate ligament often cause a persistent instability in the knee that may not benefit from surgical reconstruction of the injured anterior cruciate ligament. Earlier studies (*see* Skoglund, 1973) focused on the loss of dynamic protective reflexes due to anterior cruciate ligament failure (for instance, hamstring contraction and quadriceps relaxation near the extremes of the knee extension). More recently, it has been claimed that proprioceptive loss plays a direct role in determining the functional disability of the knee. Barrack *et al.* (1989) found decreased position sense in anterior cruciate ligament deficient knees, using a method that allows for a selective examination of proprioceptive sensation in the knee. Moreover, it has been demonstrated that this proprioception impairment in anterior cruciate ligament injuries also persists after surgery (Co *et al.*, 1993). Mechanoreceptors are included in the anterior cruciate ligament (Schultz *et al.*, 1984; Schutte *et al.*, 1987) and it is generally agreed that specialized mechanoreceptors, such as Ruffini endings, Golgi tendon organs and Pacinian corpuscles play an important role in signalling the knee position (*see*

Skoglund, 1973). In this light, the loss of proprioceptive inputs from the injured anterior cruciate ligament can account for the impairment of knee coordination and stabilizing reflexes as well, since they originate in the same receptors. The neuroreceptive function of the anterior cruciate ligament has been confirmed by the recording of scalp evoked potentials after direct stimulation of this ligament (Pitman *et al.*, 1992).

Alterations in peripheral inputs are known to modify somatosensory system responsiveness; previous studies on experimental animals have demonstrated that the somatotopic organisation of the parietal cortex is susceptible to change in response to damage to the peripheral nerve trunks (Merzenich *et al.*,1983; Wall *et al.*, 1986). Since several factors suggest a loss of proprioceptive inputs from the knee subsequent to anterior cruciate ligament lesions, our aim was to study the consequences on the nervous system after this proprioceptive impairment.

Somatosensory evoked potentials are a reliable and non-invasive means of studying somatosensory pathways, probably including those subserving articular structures. Although it is still debated whether cutaneous (Kakigi and Jones, 1986) or muscular afferent inputs (Burke *et al.*, 1981) contribute most to cortical SEPs after lower limb stimulation, articular fibres have been found in both motor and cutaneous fascicles of nerves (Burke *et al.*, 1988). Moreover, it has been demonstrated that cortical potentials can be obtained by mechanical stimulation of joints (Desmedt and Ozaki, 1991). Therefore, to activate fibres subserving the anterior cruciate ligament, we studied SEPs in our patients after stimulation of the common peroneal nerve in the popliteal fossa, above the site at which any articular branches would have joined the main trunk. Although common peroneal nerve stimulation in the popliteal fossa should also activate fibres subserving calf and foot, many factors discussed in the recent literature appear to indicate that afferent inputs from distal sites contribute little to the cortical response after common peroneal nerve stimulation (Cohen *et al.*, 1985; Pelosi *et al.*, 1987; Onishi *et al.*, 1991). To verify whether common peroneal nerve stimulation in our patients actually reflects the almost exclusive activation of proximal fibres, we compared SEPs from stimulation of common peroneal nerve at the knee and of peroneal nerve at the ankle in five healthy subjects and in five patients. Lastly, since scalp SEPs after common peroneal nerve stimulation may be barely detectable, due to the great intersubject variability in scalp distribution, we studied common peroneal nerve SEP scalp topography by means of a scalp 20-channel montage in nine healthy subjects and nine patients.

Proprioceptive sensation of the knee in all patients was evaluated using the method described by Barrack (1989).

Patients and methods

Patients

We studied 19 patients (mean age 28 years±4.09) with monolateral anterior cruciate ligament deficiency. Both SEPs and clinical studies were carried out in all patients at intervals varying from 1 to 8 years after knee traumatic injury. The diagnosis was always confirmed by arthroscopy. Patients who required meniscal excision or repair were excluded. All patients had a positive pivot shift test. Sural nerve sensory conduction study, tibial and peroneal nerve motor conduction studies and concentric needle EMG examination in lower limb muscles did not show abnormalities. Blood tests were also performed to exclude the existence of other pathological conditions, such as diabetes mellitus or vitamin B_{12} deficiency. Our patients showed neither gait impairment nor pain and temperature hypaesthesia. Joint and touch sensation, tested by common clinical methods, was preserved in all patients. All patients and healthy normal controls gave their informed consent to participate in the study.

Clinical examination

In order to test the knee position sense, we used the apparatus already described in detail by Barrack *et al.* (1989). Subjects were seated and custom-made Jobst air splints were placed above and below the knee joint and inflated to a pressure of 20 mmHg to minimize cutaneous sensation interference. Leg extremities were connected by wires and pulleys to a slow speed motor. The starting position was 40°, with legs suspended passively, and a flexion movement between 30° and 40° was performed. Both sides were examined independently. Subjects pressed a button when they felt position changes of the knee. The linear movement of the wire was then calculated and converted to angular deflection. The test was repeated five times on each side and the average value was taken as the result.

Somatosensory evoked potential recording procedure

For SEP recording, patients lay on a couch in a warm and semi-darkened room. Stimuli (0.3 ms duration, 5 Hz) were delivered by skin electrodes at the popliteal fossa for common peroneal nerve and posterior tibial nerve, and at the ankle for peroneal nerve and posterior tibial nerve; stimulus intensity was adjusted slightly above the motor threshold. The filter bandpass was 30–3000 Hz (–3 dB at cut off point, 6 db per octave). Responses were averaged with a bin width of 196 μs on a total analysis time of 100 ms. Samples with excessive interference were automatically edited out of the average. Two averages of 2048 trials each were obtained and printed out by the computer on a desk-jet printer.

In all healthy subjects and in 10 patients, the recording electrodes (impedance below 5 kΩ) were placed over the spinal process of the 12th dorsal vertebra (T12) and at the scalp points Cz, Fz, P3 and P4 (10–20 system). In order to record spinal potential, which we labelled as N14 for common peroneal nerve and peroneal nerve and as N24 for posterior tibial nerve, we connected grid 1 of the amplifier to the T12

electrode and grid 2 to an electrode placed over the anterior abdomen. The rationale for this montage was discussed in detail in a previous study (Restuccia *et al.*, 1993). Briefly, it permits selective recording of the activity generated by the transverse dipolar source located in the lumbo-sacral spinal cord (Desmedt and Cheron, 1983); moreover, this technique can cancel noise from the ECG activity that is picked up by both T12 and anterior electrodes. We referred scalp electrodes to linked ears to record cortical as well as far-field potentials (Rossini *et al.*, 1981, Yamada *et al.*, 1982, Desmedt and Bourguet, 1985).

In nine patients and nine control subjects who underwent topographical analysis of cortical common peroneal nerve SEPs, disc recording electrodes (impedance below 5 KΩ) were placed at 20 locations of the 10–20 system (excluding Fpz). We referred scalp electrodes to linked ears. The analysis time was 64 ms with a bin width of 250 μs. The amplifier bandpass was 3–3000 Hz. In order to ensure baseline stabilization, SEPs were digitally filtered off-line by means of a digital filter with a bandpass of 19–1900 Hz. Brain maps at a fixed time showing the distribution of the responses over the scalp were obtained by linear interpolation from the four nearest electrodes.

Healthy subjects

Healthy normal subjects were randomly drawn members of the clinical staff of the Institute of Neurology of the Catholic University in Rome. We collected normative data for knee position by testing the 15 healthy subjects (mean age 29 years±4.07; eight males, seven females). In these subjects, we calculated the asymmetry of angular deflection between both knees; we established the normal limit of this value as the mean+3 SDs.

The SEP control data after common peroneal nerve as well as after ankle-posterior tibial nerve stimulation were collected from 20 healthy subjects (mean age 23.9±5.2; nine males, 11 females). In order to assess conduction in peripheral nerve fibres we measured the peak latency of the spinal potential; the interside (left–right) asymmetry in amplitude of this response was also considered by calculating the $(Amp_{max} - Amp_{min})/Amp_{max}$ ratio in percentage, where Amp_{max} and Amp_{min} represent, respectively, the larger and smaller amplitude values of spinal potential between the onset and the peak obtained in an individual after stimulation of the right or left lower limb. We calculated the latency of cortical P27 and P40 for common peroneal nerve and ankle-posterior tibial nerve, respectively, at Cz and at the parietal site ipsilateral to the stimulated nerve, where these potentials are recorded with the highest amplitude (Rossini *et al.*, 1981; Desmedt and Bourguet, 1985); we also considered the interpeak interval between the cortical and spinal responses to assess conduction in the central somatosensory pathways. Lastly, we evaluated the latency of the positive wave recorded at all scalp leads and immediately before the P27 or P40 cortical responses at Cz. This scalp far-field, which is assumed to be generated in the brainstem tract of the lemniscal pathways (Rossini *et al.*, 1981, Vas *et al.*, 1981; Yamada *et al.*, 1982, Desmedt and Bourguet, 1985), has been labelled as P30 for posterior tibial nerve stimulation (Yamada *et al.*, 1982; Desmedt and Bourguet, 1985). We labelled the analogous potential recorded after common peroneal nerve or peroneal nerve stimulation P20.

In nine healthy subjects we obtained brain maps of SEPs to stimulation of right and left common peroneal nerve, at a fixed time. The responses were identified on the basis of latency, polarity and scalp distribution. Amplitudes and peak latencies were measured from the average of the two runs obtained for each side. Amplitudes were measured from the response onset. In order to assess the distribution of the cortical P27, its amplitude at different scalp locations was normalized as a percentage of the amplitude at Cz. After this normalization, amplitudes were compared by means of paired *t* test with Bonferroni's correction for multiple comparisons.

In the five healthy subjects, who underwent stimulation of common peroneal nerve and posterior tibial nerve at the knee as well as peroneal nerve and posterior tibial nerve at the ankle, we compared spinal and cortical SEP amplitudes using Wilcoxon's test.

Results

Somatosensory evoked potential findings

Healthy subjects

Somatosensory evoked potential values to stimulation of common peroneal nerve and ankle-posterior tibial nerve in healthy subjects are shown in Table 1.

Scalp distribution of common peroneal nerve SEPs. The P20 potential was always recognizable in all scalp traces. Cortical P27 was always detectable at Cz, with its maximal amplitude, and at the central electrode ipsilateral to the stimulated side. It was also recorded, although inconstantly, at Fz, Pz, Oz, and in the temporal region ipsilateral to the stimulated side (Fig. 1). A negative potential was evident with almost the same latency in the hemisphere contralateral to the stimulation. Common peroneal nerve SEPs from one of our healthy subjects are shown in Fig. 2.

Distal versus proximal stimulation. The P27 cortical response at Cz was significantly smaller ($z = 2.446$, $P < 0.05$) after common peroneal nerve (0.47±0.23 μV) than after peroneal nerve (1.2±0.92 μV) stimulation. The N14 mean amplitude was significantly higher ($z = 2.09$, $P < 0.05$) after common peroneal nerve (0.87±0.35 μV) than after peroneal nerve (0.5±0.25 μV) stimulation. The P40 and N24 posterior tibial nerve SEPs were smaller after stimulation at the knee (0.69±0.92 μV for P40 and 0.45±0.21 μV for N24) than after stimulation at the ankle (1.19±0.97 μV for P40 and 0.97±0.47 μV for N24), but these differences did not reach statistical significance ($z = 1.682$, $P > 0.05$ for P40 and

Table 1 *Normal values of SEPs and knee proprioception*

	Mean	SD	Range	Limit of normal values (mean + 3 × SD)
Somatosensory evoked potentials				
Common peroneal nerve				
N14 latency (ms)	13.9	0.96	12.4–16.4	16.8
P20 latency (ms)	19.6	1.86	16.7–21.8	25.2
P27 latency (ms)	26.1	2.3	22.1–30.1	33
P27–N14 interval (ms)	12	2.4	9.6–15.2	19.2
N14 amplitude: interside difference (%)	27.3	12.2	1.23–48.8	63.9
Posterior tibial nerve				
N24 latency (ms)	22.4	1.9	18–27.2	28.1
P30 latency (ms)	29.8	1.8	27.1–35	35.2
P40 latency (ms)	38.6	2.08	35.5–42.3	44.8
P40–N24 interval (ms)	16.4	1.26	15.1–18.1	20.2
N24 amplitude: interside difference (%)	15	13.59	0.7–31	55.8
Knee proprioception				
Knee position sense: interside difference (°)	0.12	0.08	0–0.2	0.36

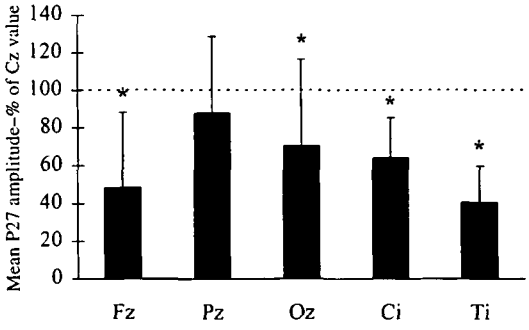

Fig. 1 Scalp distribution of the amplitude of the cortical P27 potential in nine healthy subjects. The mean P27 amplitudes at Fz, Pz, Oz and at central (Ci) and temporal (Ti) electrodes ipsilateral to stimulation are shown as percentages of the P27 amplitude at Cz (dotted line). The mean values±SDs of the P27 amplitude at these locations are: Cz (18/18 sides), 0.35±0.22; Fz (13/18 sides), 0.13±0.04; Pz (17/18 sides), 0.29±0.2; Oz (14/18 sides), 0.2±0.26; Ci (18/18 sides), 0.21±0.17; Ti (16/18 sides), 0.13±0.08. Note that the cortical P27 is always recorded only at Cz and at Ci electrodes. *Difference statistically significant.

$z = 1.784$, $P > 0.05$ for N24). Traces obtained after peroneal and tibial nerve stimulation at the knee and at the ankle in one of our healthy subjects are shown in Fig. 3.

Patients

Somatosensory evoked potential results after common peroneal nerve stimulation in patients are summarized in Table 2.

The N14 latency was always normal and no significant interside asymmetry of N14 amplitude was found in any of the 10 patients who had spinal recordings (numbers 1–10); the P20 scalp far-field potential was found with normal latency in all patients.

The P27 cortical potential was found bilaterally in 12 out of 19 patients. In these patients the N14–P27 interpeak interval was within normal limits. In the remaining seven patients (numbers 1, 2, 3, 4, 8, 13 and 14) this response was absent on the anterior cruciate ligament deficient side. Moreover, six patients (numbers 1, 2, 3, 4, 8 and 13) did not show the negative wave recorded in normal subjects in the parietal region contralateral to the stimulated nerve. In two of the nine patients (numbers 13 and 14) who had topographical analysis of cortical responses, scalp traces did not show any positive wave in the 27 ms range of latency after stimulation of the common peroneal nerve ipsilateral to the anterior cruciate ligament lesion (Fig. 4).

After posterior tibial nerve stimulation at the ankle, the N24 latency was always normal and no significant interside asymmetry in the N24 amplitude was found in any patient. The P30 scalp far-field potential and cortical P40 were found with normal latency in all patients. The N24–P40 interpeak interval was always normal.

Peroneal nerve and knee-posterior tibial nerve stimulation. In five patients with common peroneal nerve SEP abnormalities (numbers 1, 2, 3, 4 and 8), we recorded SEPs after peroneal nerve stimulation and found a clear positive cortical response on the same side as the anterior cruciate ligament lesion too (Figs 5 and 6). Somatosensory evoked potentials to posterior tibial nerve stimulation at the knee were normal in these five patients.

Clinical findings and SEP–clinical correlations

The results of clinical examination of healthy subjects and patients are shown in Tables 1 and 3, respectively.

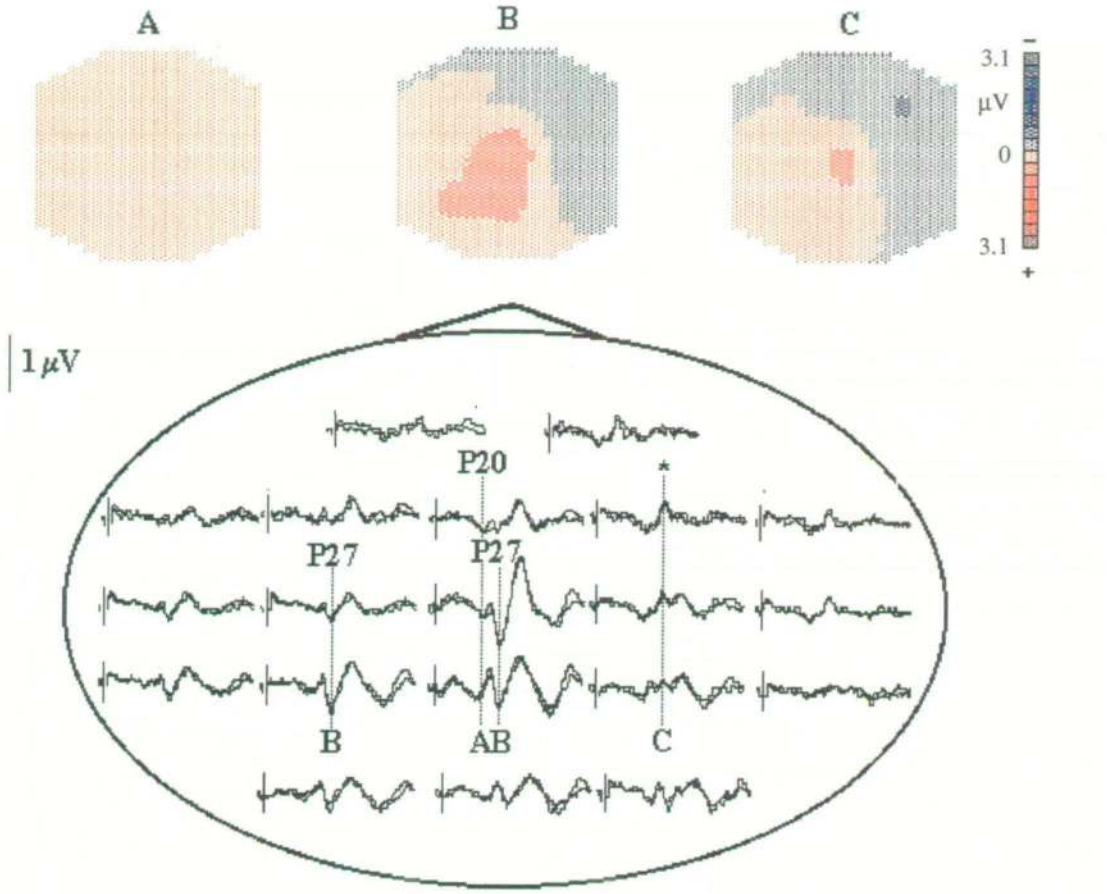

Fig. 2 Somatosensory evoked potential to left common peroneal nerve stimulation in a 27-year-old healthy subject. Traces recorded at all locations of the 10–20 system (excluding Fpz) are shown. Negativity is upward. The upper part of the figure shows three voltage maps, each calculated at a different latency; blue and red colours correspond to negative and positive potentials, respectively. The P20 far-field response is identifiable in all traces at a latency corresponding to the map A. Cortical P27 potential is present with higher amplitude at Cz, Pz and in the centro-parietal region ipsilateral to stimulation; scalp distribution of P27 responses is shown in map B. Lastly, a negative potential (asterisk) is evident at a latency corresponding to map C in the right hemisphere.

Position sense was decreased in the anterior cruciate ligament deficient knee in ten patients (numbers 1, 2, 3, 4, 8, 10, 13, 14, 16 and 17). Seven of these patients with proprioception impairment (numbers 1, 2, 3, 4, 8, 13 and 14) did not show the P27 cortical response after common peroneal nerve stimulation on the side of anterior cruciate ligament lesion. None of the patients with SEP abnormalities showed normal position sense in the anterior cruciate ligament deficient knee. Three patients (numbers 10, 16 and 17) showed normal SEPs and decreased proprioceptive sensation of the knee with anterior cruciate ligament injury. Somatosensory evoked potential abnormalities and proprioception reduction were significantly correlated in our patients (Fisher's test, $P < 0.05$).

Discussion

In our study, we found a definite pattern of SEP abnormality in patients suffering from anterior cruciate ligament lesion. First, the common peroneal nerve SEP abnormality was always seen as a loss of the cortical P27 response, with preserved spinal and subcortical potentials. Secondly, the SEP abnormality was observed only after common peroneal nerve stimulation, whereas the stimulation of the posterior tibial nerve at the knee or the ankle and of the peroneal nerve at the ankle did not reveal any abnormality.

In our patients, the P27 loss is not related to a conduction block below the medial lemniscus. Our recording technique, with scalp electrodes referred to linked ears, made it possible to analyse the P20 far-field potential, since earlier subcortical responses are picked up by scalp as well as ear electrodes and are thus cancelled (Rossini *et al.*, 1981). The P20 far-field response and the analogous P30 response after posterior tibial nerve stimulation are thought to be generated in the brainstem tract of the lemniscal pathways (Rossini *et al.*, 1981; Yamada *et al.*, 1982; Desmedt and Bourguet, 1985; Urasaki *et al.*, 1993). Thus, the finding of a normal P20 response to common

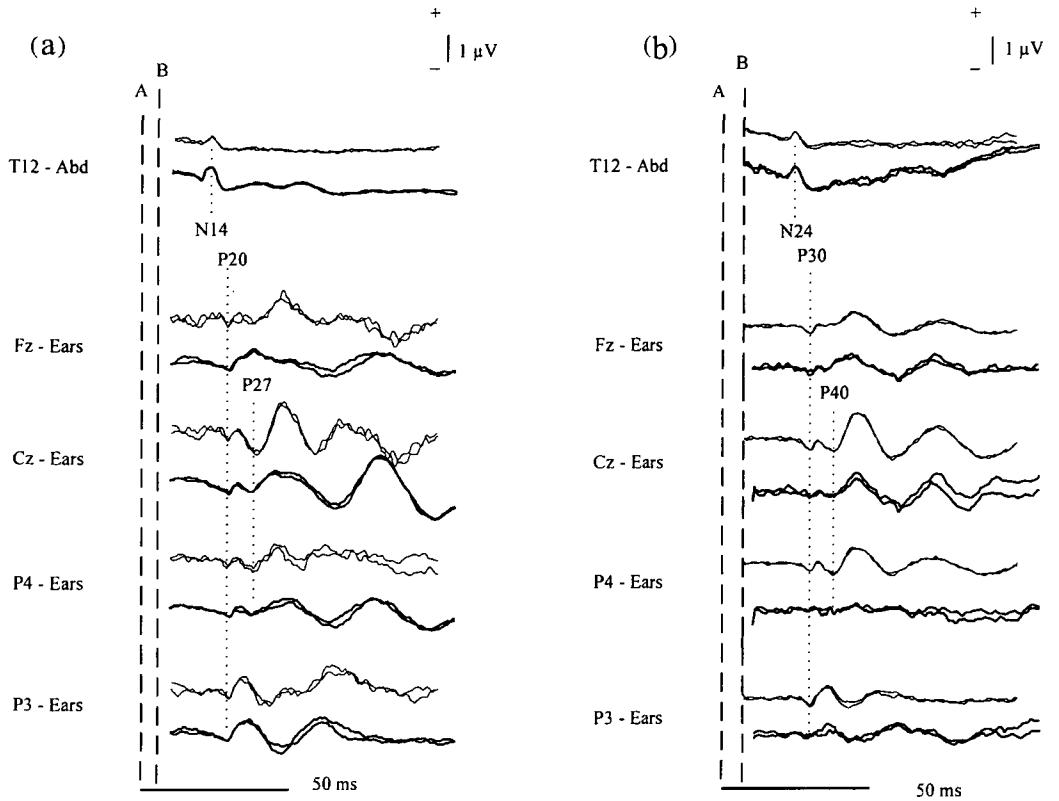

Fig. 3 Right common peroneal nerve, peroneal nerve and posterior tibial nerve SEPs in a 23-year-old healthy subject. Common peroneal nerve (thick traces) and peroneal nerve (thin traces) SEPs are shown in part **a**. Somatosensory evoked potentials to posterior tibial nerve stimulation at the ankle (thick traces) and at the knee (thin traces) are shown in part **b**. All traces were aligned at the peak latency of the spinal responses, and therefore trace onsets after proximal stimulation (*see* B) are delayed in comparison with those after distal stimulation (*see* A). T12–anterior abdomen: 12th thoracic vertebra, referred to an electrode located above the umbilicus. For scalp trace recordings, reference electrodes are placed over the ears. Negativity is upward. Spinal recordings show clear N14 and N24 responses. No difference in amplitude is evident (across proximal or distal stimulation sites) in subcortical responses labelled as P20 for common peroneal nerve and peroneal nerve recordings, and as P30 for ankle- and knee-posterior tibial nerve recordings. In part **a** the cortical P27 potential recorded by Cz and P4 electrodes is of higher amplitude after peroneal nerve than common peroneal nerve stimulation. In part **b** a clear P40 potential is evident at Cz and at P4 with higher amplitude after ankle-posterior tibial nerve- than after knee-posterior tibial nerve-stimulation.

peroneal nerve stimulation in the seven patients showing loss of the later P27 response demonstrated that the central somatosensory dysfunction involves the somatosensory system above the medial lemniscus. It has been suggested that the P27 cortical response after common peroneal nerve stimulation can barely be detected at central scalp locations, due to the great intersubject variability of its scalp distribution, which may explain its loss in some of our patients (Pelosi *et al.*, 1988). Nevertheless, in our healthy subjects we found that the cortical P27 showed its maximal mean amplitude at Cz and that it could always be recorded at Cz and in the parietal region ipsilateral to stimulation. Moreover, the two patients with SEP abnormalities, who had the 20-channel recording, showed no P27 response in Cz or in any other traces, thus confirming that the P27 loss after stimulation of the anterior cruciate ligament deficient side is a truly physiological finding.

Central somatosensory dysfunctions were revealed in our patients by abnormal common peroneal nerve SEPs only. The common peroneal nerve was stimulated above the site at which any articular branches would have joined the main trunk, but this stimulation obviously activated fibres not only from the knee articular structures, but also from more distal sites. Therefore, one may wonder why distal peroneal nerve stimulation gave normal results in our patients. This finding seems to suggest that proximal common peroneal nerve stimulation could selectively activate the common peroneal nerve fibres supplying the knee. This hypothesis cannot be supported by mere anatomical factors, since fascicles corresponding to the different branches of the common peroneal nerve are usually mixed in the proximal tract of the nerve (Sunderland, 1978). Moreover, motor threshold stimulation commonly used in our own, as well as in other laboratories, activates

Table 2 *Somatosensory findings after common peroneal nerve stimulation*

Patient	Side	N14 latency (ms)	P20 latency (ms)	P27 latency (ms)	P27–N14 interval (ms)	N14 amplitude: interside difference (%)
1	R	12.8	18.4	25.6	12.8	40
	L*	12.8	18.8	Absent	–	
2	R*	15.5	19.8	Absent	–	15
	L	15.1	19.8	27.5	12.4	
3	R*	12.7	16.8	Absent	–	14
	L	12.6	16.7	24	11.4	
4	R	13.2	18.4	25.2	12	41
	L*	13.6	18	Absent	–	
5	R	14.7	20.4	28.9	14.2	10
	L*	14.6	20	28.4	13.8	
6	R	14	21	29	15	50
	L*	13.6	20.4	28	14.4	
7	R*	15.4	21.2	28.8	13.4	0
	L	15.6	21.6	29.2	13.6	
8	R*	14.8	19.6	Absent	–	40
	L	14	20	27.6	13.6	
9	R*	13.6	17.2	24.8	11.2	28
	L	13.2	16.8	24	10.8	
10	R*	13	19.8	27.6	14.6	28
	L	12.8	19	26.4	13.6	
11	R*	–	20.3	26.8	–	–
	L	–	20.3	27.5	–	
12	R*	–	21.5	26.3	–	–
	L	–	21.5	26.3	–	
13	R*	–	20	Absent	–	–
	L	–	19.5	27.8	–	–
14	R	–	22.5	27.3	–	–
	L*	–	22.5	Absent	–	
15	R*	–	18.5	24.5	–	–
	L	–	18.8	25	–	–
16	R	–	21.3	30.3	–	–
	L*	–	22	30.5	–	
17	R	–	21	25.5	–	–
	L*	–	22	26.5	–	
18	R	–	19.5	25.3	–	–
	L*	–	19.3	25	–	
19	R	–	19	23.8	–	–
	L*	–	18.9	24.8	–	

R = right; L = left. *Side of anterior cruciate ligament.

the largest fibres regardless of their functional significance. However, a number of factors indicate that afferent inputs from calf and foot contribute little to the cortical response after common peroneal nerve stimulation at the popliteal fossa. For example, cortical responses obtained by common peroneal nerve stimulation do not reduce their amplitude after the anaesthetic block of the nerve just distal to the stimulation (Onishi *et al.*, 1991). Moreover, in our own, as in other series (Cohen *et al.*, 1985; Pelosi *et al.*, 1987), the proximal common peroneal nerve stimulation at the knee in healthy subjects evokes cortical responses significantly lower in amplitude than the distal stimulation of the peroneal nerve at the ankle. We also obtained similar results for the posterior tibial nerve, although the difference between the P40 amplitudes evoked by distal and proximal stimulation did not reach statistical significance. These findings suggest that afferent inputs from the knee contribute most to cortical SEPs after common peroneal nerve stimulation. Interference between muscle and cutaneous afferent inputs at the central level (Burke *et al.*, 1982; Burke and Gandevia, 1988) has been claimed to explain why distal afferent inputs contribute little to the cortical common peroneal nerve SEPs (Pelosi *et al.*, 1987).

Clinical–neurophysiological correlations

In this study, we found a significant correlation between mild sensory deficit, limited to the knee proprioception, and common peroneal nerve SEP abnormalities. No SEP abnormalities were found in patients without proprioception impairment. This finding suggests that patients who are

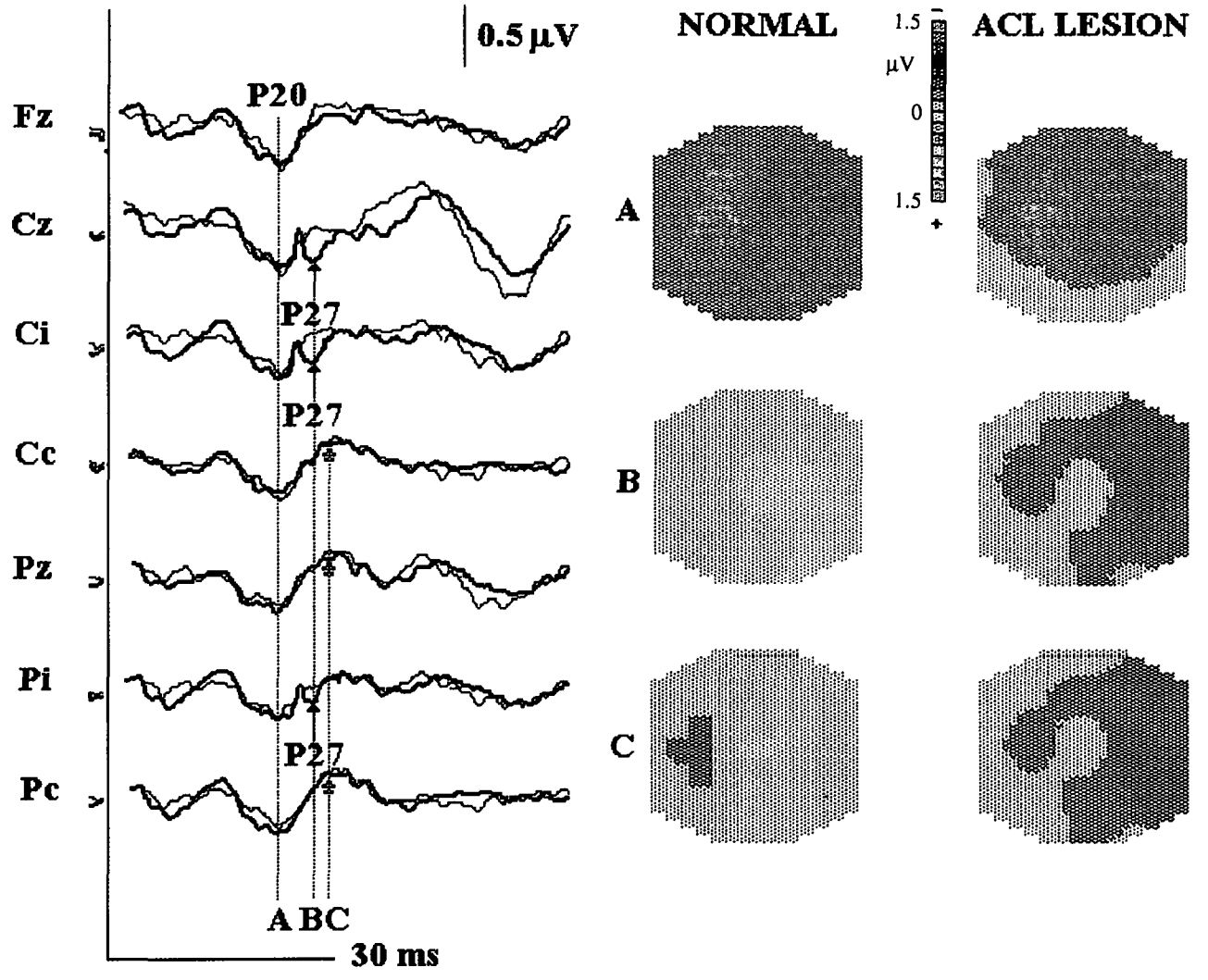

Fig. 4 Common peroneal nerve SEPs in Patient 14 with left anterior cruciate ligament lesion. The left part of the figure shows traces recorded by Fz, Cz and Pz electrodes, by central electrodes ipsilateral (Ci) and contralateral (Cc) to stimulation and by parietal electrodes ipsilateral (Pi) and contralateral (Pc) to stimulation. Thin and thick traces correspond to left and right common peroneal nerve SEPs, respectively. Negativity is upward. On the right, the voltage maps were calculated at three different latencies corresponding to the three vertical dotted lines A, B and C after right (NORMAL) and left (ACL LESION) (ACL = anterior cruciate ligament) common peroneal nerve stimulation. Lemniscal P20 potential is identifiable with the same latency in all traces of both sides, corresponding to maps A. Conversely, a clear P27 response is recorded by Cz, Ci and Pi electrodes only, and then only to right common peroneal nerve stimulation; in maps calculated at the corresponding latency (B), a positivity is evident only on the right side, while no positive response is present on the side with anterior cruciate ligament damage. Lastly, a negative potential (asterisks) is recorded after both right and left common peroneal nerve stimulation in the hemisphere contralateral to the stimulated side (maps C).

able to compensate for the loss of anterior cruciate ligament inputs (possibly through inputs from other knee and muscular proprioceptors), develop neither impairment of the knee position sense nor central somatosensory abnormalities. Lastly, three patients with abnormal sensation had normal SEPs. By considering the variable innervation of the knee, a possible explanation for the discrepancy between clinical and SEP findings in these last three patients may be advanced if we admit that, in these cases, inputs from the receptors responsible for the knee position sense travel in nerve trunks other than the common peroneal nerve. Indeed, it is known that posterior tibial and obturator nerves can also provide sensory fibres to the knee (Kennedy *et al.*, 1982).

Central somatosensory dysfunctions and deficit of peripheral proprioceptive inputs

Previous neurophysiological studies have demonstrated CNS changes in severe peripheral deafferentation. Somatosensory evoked potential studies in amputees have shown that

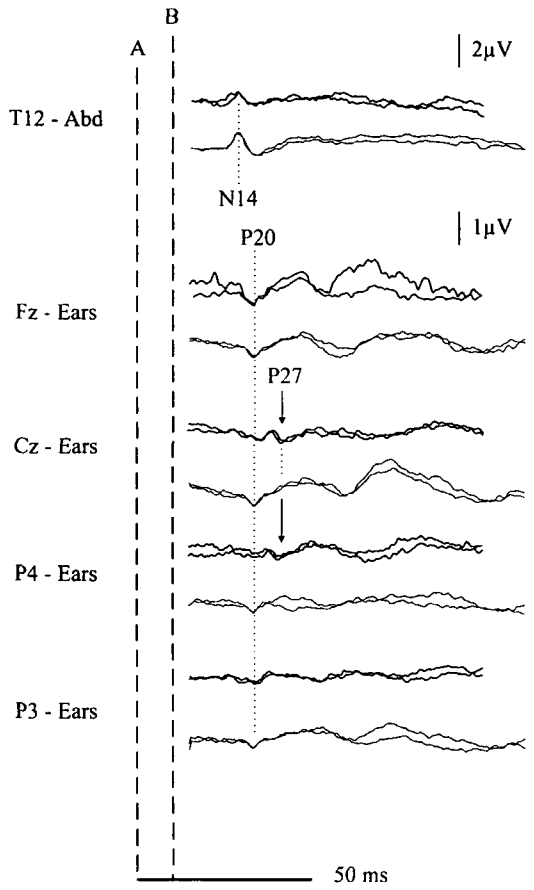

Fig. 5 Right common peroneal nerve (thin traces) and peroneal nerve (thick traces) SEPs in Patient 2 with a right anterior cruciate ligament lesion. The presentation is otherwise as in Fig. 3*a*. Negativity is upward. Spinal recordings show clear N14 responses. All scalp traces show a normal subcortical P20 response without it showing an obvious difference in amplitude after common peroneal nerve and peroneal nerve stimulation. While a normal P27 response is shown in Cz after right parietal peroneal nerve stimulation, no positive potential is identifiable at around 27 ms latency in responses following common peroneal nerve stimulation.

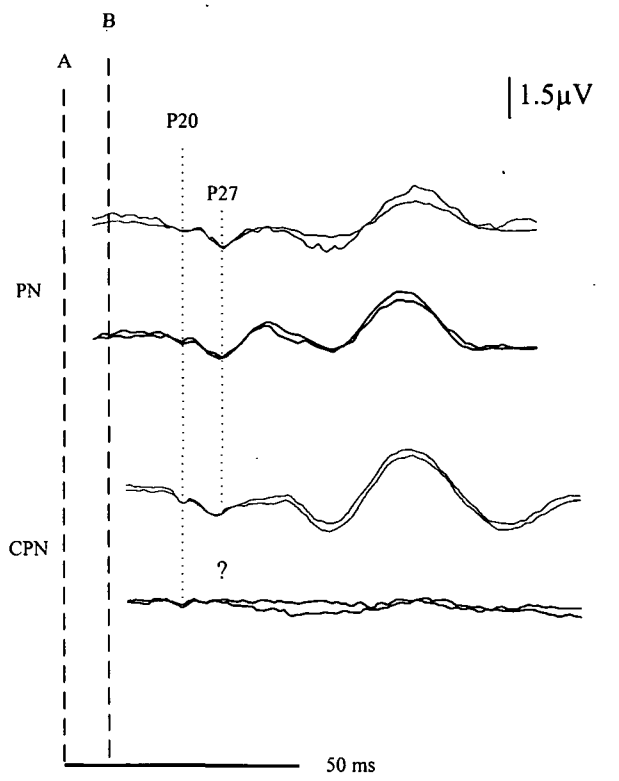

Fig. 6 Somatosensory evoked potentials to stimulation of common peroneal nerve (CPN) and peroneal nerve (PN) on both sides in Patient 3 with a right anterior cruciate ligament lesion. The figure shows Cz recordings. Thin and thick traces correspond to left and right SEPs, respectively. All traces were aligned at the peak of the P20 response, and therefore trace onsets after proximal stimulation (B) are delayed in comparison with those after distal stimulation (A). A normal latency P27 is shown after left common peroneal nerve and peroneal nerve stimulation. While no cortical potentials are identifiable to right common peroneal nerve stimulation, a clear P27 is recorded after right peroneal nerve stimulation.

cortical responses to stimulation of the nerve trunk above the stump can be reduced in amplitude or absent (McComas *et al.*, 1978; Sica *et al.*, 1984; Sica *et al.*, 1988). On the other hand, cortical representation of muscles ipsilateral to the stump has been found to be enlarged in amputees (Cohen *et al.*, 1991). Electrophysiological findings in experimental animals have suggested three different kinds of neural modification follow the loss of peripheral inputs. (i) The cortical region representing a damaged nerve is progressively occupied by new inputs from the nearest areas (Merzenich *et al.*, 1983; Merzenich *et al.*, 1984). (ii) The corresponding cortical cells undergo modifications in their physiological properties, such as increased latency and threshold of responses (Brandenberg and Mann, 1989). (iii) The topographic spinal map representing a damaged nerve undergoes some modifications due to the expansion of adjacent areas (Devor and Wall, 1981).

Our patients showing P27 absence with still preserved P20 probably underwent a CNS reorganization above the medial lemniscus, thus suggesting that CNS changes can also be found following minor lesions of proprioceptive afferent inputs. On the basis of the above-mentioned studies, the absence of P27 in our patients may be explained by (i) modifications in the response properties of the cortical or thalamo-cortical neurons; (ii) progressive occupation of the common peroneal nerve cortical representation by afferent inputs of the nearest areas; and (iii) a spinal mechanism, such as reorganization of the spinal maps in response to decreased sensory inputs from the common peroneal nerve. However, this last explanation does not correlate with the finding of a normal spinal N14 response in all our patients. The N14, like the N24 for posterior tibial nerve, is a postsynaptic potential generated by dorsal horn neurons, which are activated by collateral branches of dorsal column fibres (Desmedt and Cheron, 1983). A decrease in the number of these neurons, as might be expected after a reduction in the common

Table 3 *Clinical findings*

Patients	Knee proprioception: interside difference (°)
1	**0.6**
2	**0.63**
3	**0.8**
4	**0.75**
5	0
6	0
7	0.12
8	**0.85**
9	0.2
10	**0.54**
11	0.11
12	0.25
13	**0.55**
14	**0.46**
15	0.22
16	**0.6**
17	**0.4**
18	0.2
19	0

Bold = patients whose knee position sense was abnormal.

peroneal nerve spinal representation, would reduce the amplitude of the spinal potential. However, we did not find a significant reduction in the N14 amplitude on the side of the anterior cruciate ligament deficient knee in any of our patients.

Conclusions

The results of the present study suggest that the central somatosensory pathways are functionally modified in humans by lesions to peripheral mechanoreceptors. It is interesting that, in our patients, the lesion responsible for clinical and electrophysiological abnormalities was limited to the anterior cruciate ligament and did not directly involve a nerve trunk, while evident CNS changes in humans have thus far been found in severe peripheral deafferentation, such as limb amputations (Sica *et al.*, 1984; Sica *et al.*, 1988; Cohen *et al.*, 1991). Nevertheless, since it is likely that afferent inputs from the knee contribute most to cortical SEPs after proximal common peroneal nerve stimulation, the loss of proprioceptive inputs from the knee may explain the deficit of knee position sense as well as the common peroneal nerve SEP abnormality in our patients. Since knee proprioception is important in both gait and standing, it is possible that the cortex is involved in a complex spatial integration of the articular proprioceptive inputs. The possibility of CNS modifications after anterior cruciate ligament lesions was also suggested in a recent experimental study (O'Connor *et al.*, 1993). The assumption that the cortex integrates proprioceptive inputs from the knee and undergoes functional changes in response to minor peripheral damage implies several consequences in the prognostic evaluation of these lesions. For example, it has been suggested that anterior cruciate ligament lesions associated with proprioception impairment are less likely to mend (Walla *et al.*, 1985; Beard *et al.*, 1993).

Lastly, the results from this study confirm that the question concerning the type of fibres responsible for cortical SEPs after lower limb stimulation can not be unequivocally answered. Joint inputs are projected to the somatosensory cortex via lemniscal pathways (Mountcastle and Powell, 1959; Jones, 1983; Kaas, 1983; Mountcastle, 1984). Desmedt and Ozaki (1991) described a cortical P34 potential evoked by natural stimulation of the finger joints and suggested a dipolar source in postcentral area 2 as the generator of this response. To our knowledge, no similar studies have been performed for the lower limb joints. It is still a matter of debate whether cutaneous (Kakigi and Jones, 1986) or muscular afferent inputs (Burke *et al.*, 1981) contribute most to lower limb SEPs, but articular fibres have been found in both motor and cutaneous nerve fascicles (Burke *et al.*, 1988). Our data, from patients and healthy subjects, show that the fibres responsible for knee proprioception seem to be very important in generating the majority of the common peroneal nerve cortical SEPs.

Acknowledgement

We wish to thank Mr Fabrizio Rinaldi for his technical assistance.

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Recieved February 20, 1996. Revised May 2, 1996.
Accepted May 13, 1996