Sensory Changes in the Forehead of Patients with Complex Regional Pain Syndrome

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Abstract

The aim of this study was to investigate involvement of central mechanisms in complex regional pain syndrome (CRPS). In particular, we wished to determine whether hyperalgesia extends ipsilaterally from the affected limb to the forehead. The heat-pain threshold, pressure-pain threshold, and ratings of cold and sharpness were investigated on each side of the forehead and in the affected and unaffected limbs of 38 patients with features of CRPS. In addition, touch thresholds were investigated in the limbs. The pressure-pain threshold was lower on the ipsilateral forehead than contralaterally, consistent with the presence of static mechanical hyperalgesia. Although the heat-pain threshold and ratings of sharpness and cold did not differ between the two sides of the forehead in the group as a whole, the sharpness of pinprick sensations in the affected limb was mirrored by similar sensations in the ipsilateral forehead. Conversely, diminished sensitivity to light touch in the affected limb was associated with diminished sensitivity to sharpness, cold and heat-pain in the ipsilateral forehead. These findings suggest that central nociceptive processing is disrupted in CRPS, possibly due to disturbances in the thalamus or higher cortical centres.

Key words: complex regional pain syndrome; static mechanical hyperalgesia; thalamus, central pain syndrome

Introduction

Complex regional pain syndrome (CRPS) often develops after an apparently minor injury that would normally heal quickly. Nevertheless, pain and other sensory disturbances persist and may spread to other parts of the affected limb and even to other limbs (Maleki et al., 2000). Furthermore, in about one-third of patients, the pain is accompanied by loss of light tactile sensations in the affected limb and elsewhere on that side of the body (Thimineur et al., 1998; Rommel et al., 1999; Rommel et al., 2001).

A similar syndrome sometimes develops in patients with thalamic lesions. For example, Riddoch (1938) noted that a reduction in cutaneous sensation on the side opposite to the lesion was associated with pain, sometimes involving the whole of that side of the body. Furthermore, both in the thalamic syndrome and in CRPS, a wide range of stimuli (heat, cold, gentle moving contact, firm pressure, loud or unexpected noises, anxiety and distress) can aggravate pain (Riddoch, 1938; Drummond et al., 2001; Drummond and Finch, 2004). Pain, hyperalgesia and sensory loss in the thalamic syndrome may involve multiple sites on one side of the body, including the head, trunk and limbs (Riddoch, 1938). Therefore, the aim of the present study was to determine whether hyperalgesia also extends ipsilaterally from the affected limb to the forehead in patients with CRPS.

Method

Patients

The sample consisted of 28 women and 10 men aged between 17 and 58 years (mean age 36.5 years) with sensory and autonomic features of CRPS in an arm (18 patients) or leg (20 patients). Pain had started after a fracture (10 patients), laceration, surgery or needle insertion (10 patients), or after a soft-tissue injury or sprain (18

patients), and had persisted for two to 96 months (mean duration 27.9 months). Pain was aggravated further by surgery in eight patients. Sensory features of CRPS noted during a physical examination carried out by one of the authors (PMF) included diffuse or burning pain, hyperalgesia to brisk taps, and hyperalgesia or sensory loss to pinprick stimulation (Table 1). Additional sensory disturbances were detected in most patients during the standard tests of sensation described below. Evidence of autonomic dysfunction in the affected limb included abnormal sweating, swelling, flushing, cyanosis or temperature changes as reported by the patient or noted during the physical examination. In addition, motor abnormalities (weakness, tremor or reduced range of joint movement) were recorded for all but three patients during the physical examination. Each patient met the IASP diagnostic criteria for CRPS, and the majority met the more stringent criteria proposed by Harden et al. (1999). Patients who did not meet all of Harden's diagnostic criteria were included to determine whether the extension of hyperalgesia beyond the affected limb was associated with a particular subset of CRPS disturbances.

Each patient gave their informed consent for the procedures, which were approved by the Murdoch University Human Research Ethics Committee.

Procedures

Sensory thresholds and supra-threshold sensations were investigated by the same examiner (PDD) on the medial and lateral aspects of the dorsum of the affected and unaffected hands or feet, and on each side of the forehead. A single score for each form of sensory stimulation was calculated for each limb by averaging values obtained at medial and lateral sites. Pain thresholds to firm pressure and heat, and the degree of coldness and sharpness evoked by standard stimuli, were tested as follows.

To investigate static mechanical hyperalgesia, force was applied to each site from the rounded tip (1 cm diameter) of a spring-loaded algometer in 250 gm increments to a maximum of 2.5 kg or until pain was reported (Drummond et al., 2001). The force was applied once at each site for a few seconds while the patient was questioned about pain; then the force was released and applied at a higher level until the pain threshold was reached. Static mechanical hyperalgesia was considered to be present if the mean pressure pain threshold was at least 0.95 kg lower in the affected limb than in the unaffected limb (Drummond et al., 2001).

To assess the heat-pain threshold, skin temperature was brought to at least 32^{o}C with a servo-controlled radiant heat lamp and maintained at that temperature for 10-15 seconds. Skin temperature then increased at 0.5^{o}C per second until the patient reported pain or to a maximum of 49^{o}C. This procedure was repeated two or three times at each site. Thermal hyperalgesia was considered to be present if the heat pain threshold was at least 2.5^{o}C lower in the affected than the unaffected limb (Drummond et al., 2001). Conversely, thermal hypoalgesia (loss of heat-pain sensitivity) was defined as a heat pain threshold that was at least 2.5^{o}C *greater* in the affected limb than the unaffected limb.

To investigate sensitivity to cold, the circular end of a cylindrical metal bar (10 cm long, 1.5 cm wide, 2^{o}C) was applied once at each site for a few seconds while the patient rated the intensity of cold on a scale ranging from “not cold at all” (rated as 0) to “extremely cold” (rated as 10). Cold allodynia was considered to be present if the cold stimulus induced abnormal sensations or pain (Drummond et al., 2001).

Patients rated the sharpness at each site of a single application of a firm nylon bristle (Filament 17 or 19, Senselab von Frey Aesthesiometer, Somedic Sales AB, Sweden) on a scale where 0 corresponded to “not sharp at all” and 10 to “extremely

sharp". Sufficient force was applied to bend the bristle for 1 second. Filament 17 was used for all sites if the patient was unable to tolerate Filament 19.

In addition, the touch threshold in the limbs was investigated with thin filaments from the Senselab von Frey Aesthesiometer set. Patients closed their eyes throughout the procedure, and identified the site of stimulation on the symptomatic or non-symptomatic limb if a sensation was detected. The sequence started with a mid-range filament, and stronger or weaker filaments were then used as required until the detection threshold was established for each site. Below threshold, the stimulus was missed on at least two of three trials (Drummond et al., 2001). Punctate allodynia was considered to be present if an abnormal sensation or pain was evoked at or below the touch threshold. Punctate hypoaesthesia (loss of touch sensation) was defined as a mean touch threshold that was three or more filament steps greater in the affected limb than in the unaffected limb (Drummond et al., 2001). The touch threshold was not investigated in the forehead because in a few preliminary studies patients were able to detect even the finest filaments on both sides of the forehead.

The touch threshold in the limbs was investigated first, followed by assessments of pressure-pain, sharpness, cold and heat-pain in the limbs and forehead. A new test began once sensations from the previous test had subsided. Approximately 30 minutes after the patient entered the temperature-controlled laboratory (maintained at 20-23^{o}C), the temperature of the dorsal aspect of the second phalanx of each finger or toe was measured to the nearest 0.1^{o}C with a Tempett infra-red skin thermometer (Somedic Sales, AB, Hörby, Sweden).

Results

Allodynia or hyperalgesia in the affected limb was detected during the laboratory tests in 31 of the 38 patients, including three patients with apparently

normal motor function (Table 1). In addition, clear signs of sensory loss (elevated touch or heat pain thresholds) were detected during the laboratory tests in the distal part of the affected extremity of seven patients (Table 1). There was no obvious separation between positive and negative sensory disturbances, which often co-existed in the affected limb.

As shown in Figure 1, the pressure-pain threshold was lower in the forehead ipsilateral to limb pain than contralaterally [$t(36)=5.74$, $p<0.001$], consistent with the presence of static mechanical hyperalgesia. The threshold was lower by 250 gm to 1,500 gm ipsilaterally in 29 patients (78.4%), was symmetrical in six patients (16.2%), and was greater ipsilaterally by up to 500 gm in two patients (5.4%). The asymmetry in the forehead pressure-pain threshold was not influenced by age, gender, site (arm versus leg) or duration of pain, and was not limited to patients with cold or punctate allodynia or with clear signs of autonomic disturbance (including thermal asymmetry) or sensory loss in the affected limb. In the group as a whole, sensitivity to cold, sharpness and heat-pain did not differ between the two sides of the forehead (Figure 1).

The association between static mechanical hyperalgesia in the ipsilateral forehead and sensory disturbances in the affected limb was investigated with Pearson's correlation coefficient. As shown in Table 2, diminished sensitivity to light touch in the affected limb was associated with static mechanical hyperalgesia in the ipsilateral forehead. Curiously, diminished sensitivity to light touch in the affected limb was also associated with *diminished* sensitivity to cold, sharpness and heat-pain in the ipsilateral forehead (Table 2). Similarly, in the affected limb itself, diminished tactile sensitivity was associated with diminished sensitivity to cold, sharpness and heat-pain but not with static mechanical hyperalgesia (Table 3).

Asymmetry of sharpness in the limbs was mirrored by a similar asymmetry of sharpness in the forehead (Figure 2). This association was stronger for the arms than the legs.

Discussion

The main finding was the presence of static mechanical hyperalgesia in the forehead of CRPS patients, ipsilateral to the affected limb. This appears to be a general characteristic of CRPS because it was unrelated to the patient's age or sex, or to the site or duration of pain. However, static mechanical hyperalgesia in the ipsilateral forehead was greatest in patients with a diminished capacity to detect light touch sensations in the affected limb.

The co-existence of hyperalgesia to brisk taps and sensory loss to pinprick stimulation was observed in many patients during the physical examination. Similarly, during the standard tests of sensation, loss of sensitivity to light touch or heat pain in the affected limb often co-existed with hyperalgesia to blunt pressure, and sometimes also with allodynia to cold and to punctate stimulation at the touch threshold. This trend resembles the pattern of sensory disturbance in patients with thalamic lesions. Riddoch (1938) noted that pressure from an algometer was more effective at evoking pain in patients with thalamic lesions than local cutaneous stimulation (e.g., with pinpricks), possibly because the algometer stimulates deep somatic pressure sensors in addition to cutaneous mechanoreceptors (Kosek et al., 1995; Graven-Nielsen et al., 2005). A similar dissociation involving persistence of deep-pressure pain and loss of cutaneous sensation was observed recently in patients with central post-stroke pain following sub-cortical and parietal or frontal lobe infarcts (Mailis and Bennett, 2002), indicating that painful cutaneous and deep-pressure sensations are processed by different central mechanisms.

Rommel et al. (1999; 2001) detected generalized sensory deficits to light touch and thermal stimulation on the side of the body ipsilateral to the affected limb in about one-third of CRPS patients, but did not investigate pressure-pain sensitivity in the forehead. In line with these observations, we found that sensitivity to sharp stimulation, cold and heat-pain was diminished in the ipsilateral forehead of patients with diminished touch sensitivity in the affected limb. Rommel and colleagues noted that hemi-sensory input from the face and limbs converges in the thalamus before arriving at the somatosensory cortex. They postulated that thalamic dysfunction in CRPS mediates loss of cutaneous sensations in the affected limb and ipsilateral face. Indeed, a decrease in thalamic activity contralateral to the painful limb appears to be an important correlate of chronic CRPS (Fukomoto et al., 1999) and other forms of neuropathic pain (Iadarola et al., 1995).

A number of observations suggest that loss of inhibitory cutaneous influences enhances the excitability of nociceptive neurons in the thalamus or higher cortical centres. For example, electrical stimulation of the ventrocaudal nucleus of the thalamus evokes paraethesiae in most people but often provokes painful sensations in patients with post-stroke pain (Davis et al., 1996), possibly because stroke-induced injury to low-threshold mechanoreceptive thalamic neurons disrupts inhibitory influences on thalamic nociceptive neurons. Cutaneous anaesthesia of the forearm enhances tactile discrimination and the perception of touch in the hand (Bjorkman et al., 2004), presumably because anaesthesia unmasks latent excitatory influences in the thalamus or higher cortical centres. A similar process may account for the rapid development of referred and phantom limb sensations, including pain, following limb amputation (Ramachandran and Hirstein, 1998; Borsook et al., 1998).

If this applies to CRPS, it might be expected that disinhibition of central nociceptive neurons would exacerbate static mechanical hyperalgesia in the affected limb, particularly in patients with diminished sensitivity to light touch. However, there was no association between static mechanical hyperalgesia and sensitivity to touch, cold or sharp stimulation in the affected limb. Moreover, there was no association between static mechanical hyperalgesia in the affected limb and the ipsilateral forehead. Instead, static mechanical hyperalgesia in the affected limb was associated with hyperalgesia to heat, suggesting the involvement of a peripheral mechanism (e.g., sensitization of polymodal nociceptive afferents due to chronic inflammation; van der Laan and Goris, 1997). This peripheral process might have masked central influences on static mechanical hyperalgesia in the affected limb.

Both magnetoencephalography and functional magnetic resonance imaging studies have shown that cortical centres involved in processing nociceptive sensations are unusually active during painful stimulation of the affected limb in CRPS patients (Juottonen et al., 2002; Maihofner et al., 2003; Maihofner et al., 2005). For example, pinprick hyperalgesia is associated with activation of centres thought to be involved in the sensory-discriminative dimension of pain (the somatosensory cortex, insula, and parietal association cortex), and the affective-motivational dimension of pain (the cingulate cortex, frontal cortex, and supplementary motor cortex). In contrast, in patients with chronic intractable pain associated with profound but inexplicable sensory loss, unperceived cutaneous stimuli are associated with *deactivations* in the primary and secondary somatosensory cortex, posterior parietal cortex and prefrontal cortex (Mailis-Gagnon et al., 2003).

Curiously, the area in the somatosensory cortex that represents the painful upper limb in CRPS shrinks and shifts toward the adjacent cortical region

representing the lip (Juottonen et al., 2002), particularly in patients with intense pain and mechanical hyperalgesia (Maihofner et al., 2003). This shrinkage suggests that nociceptive input inhibits normal sensory processing in the cortex, perhaps contributing to loss of normal tactile sensitivity. Moreover, heightened nociceptive excitability and cortical reorganization might distort the processing of sensory input in CRPS (including somatic sensations from the ipsilateral side of the body), and could result in referred sensations. When vision is obscured, stimulation of the painful limb in CRPS patients can provoke tactile or pinprick sensations in somatotopically adjacent regions of the body (McCabe et al., 2003). The referred sensations disappear when vision is allowed, implying the involvement of a cortical process that integrates vision with somatic sensations. Heightened excitability of nociceptive processing sites in the thalamus or cortex of CRPS patients could also contribute to increases in pain during psychological arousal (Drummond et al., 2001; Drummond and Finch, 2004). For example, generator potentials evoked by activity in the ascending projections of locus coeruleus neurons might facilitate neural discharge in hyper-excitable thalamic or cortical nociceptive neurons (Zhang et al., 1998).

At the spinal level, sensitization of second-order nociceptive and wide dynamic range neurons is thought to mediate pain induced by innocuous stimulation such as light touch or gentle warmth or cooling (Gracely et al., 1992). The mechanism of central sensitization is not completely understood, but may involve disinhibition or facilitation of spinal and trigeminal nociceptive discharge by neurons that project from medullary sites (Porreca et al., 2002; Vanegas and Schaible, 2004). Central sensitization seems to be extremely plastic, spreading in a matter of hours from the head to the ipsilateral upper and lower limbs during attacks of migraine headache (Burstein et al., 2000a; 2000b). As sensory input from the head and limbs converges

in the thalamus, this implies that sensitization spreads from trigeminal nuclei to the thalamus during migraine. By analogy, sensitization to nociceptive discharge might spread up the neuraxis in CRPS, ultimately distorting sensory processing from broad regions of the body.

Sensitivity to sharp (punctate) stimulation was diminished in the affected limb and the ipsilateral forehead of some CRPS patients, consistent with thalamic or cortical dysfunction (Rommel et al., 1999; Rommel et al., 2001). However, other patients reported heightened sharp sensations in both regions. The punctate stimulus (a firm bristle) presumably excited both cutaneous and deep somatic nociceptors and mechanoreceptors. Our findings imply that a disturbance in central nociceptive processing diminished sharpness (a cutaneous sensation) in some patients but accentuated another component of sensation in others (e.g., the deep aching pain associated with static mechanical hyperalgesia). The strong association between sharp sensations in the ipsilateral forehead and sharp sensations in the affected upper limb supports the concept of a spread of excitability in central nociceptive neurons in an ipsilateral somatotopic distribution.

In conclusion, sensory disturbance in the ipsilateral forehead appears to be characteristic of CRPS, which implies that central nociceptive processing is disrupted. A finding of mechanical hyperalgesia in the ipsilateral forehead may well assist in the diagnosis of CRPS, and indeed represents a new “sign” in this puzzling condition. The specificity of this sign for CRPS requires further investigation.

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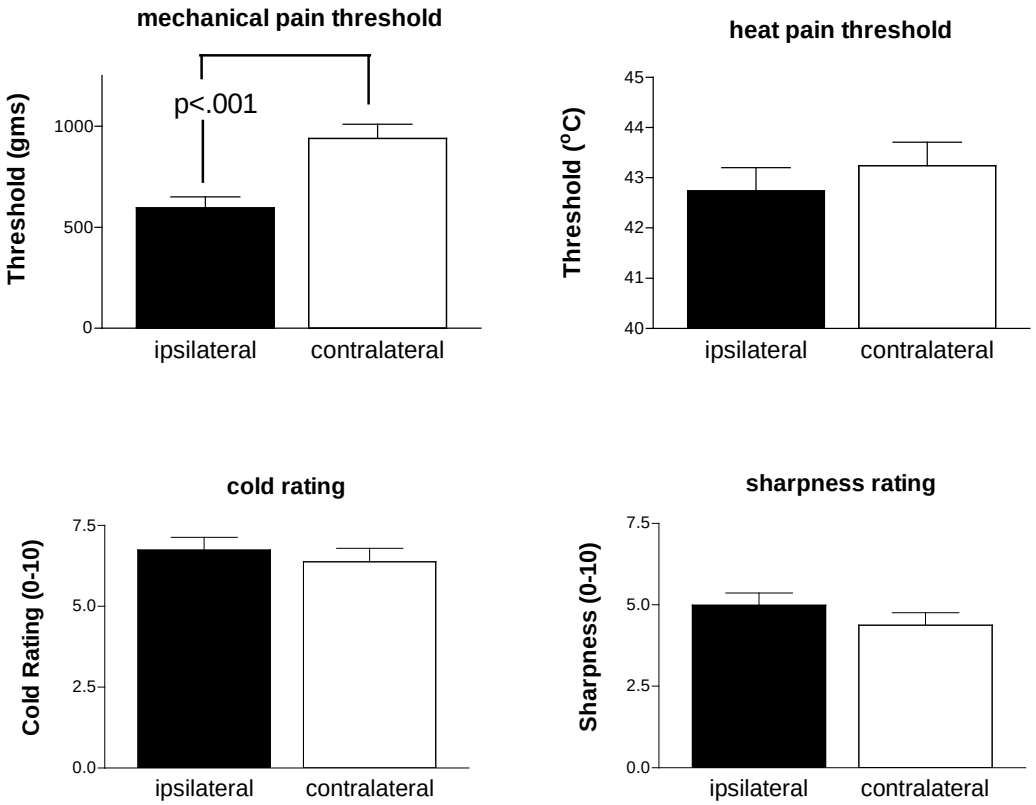
Figure legends

Figure 1. Mechanical pain threshold, heat-pain threshold, sensitivity to cold and sensitivity to sharpness on each side of the forehead, ipsilateral (black bars) and contralateral (clear bars) to limb pain. Error bars represent standard errors.

Figure 2. Difference in sharpness ratings between the affected and unaffected limbs, plotted in relation to the difference in sharpness ratings between the ipsilateral and contralateral sides of forehead. Some patients reported diminished sharpness both in the affected limb and the ipsilateral forehead (lower left-hand quadrant of the figure), whereas others reported *heightened* sensations in both regions (upper right-hand quadrant of the figure). The association between asymmetry of sharpness in the limbs and asymmetry of sharpness in the forehead was stronger for the arms (open circles) than the legs (filled circles).

Forehead Sensitivity



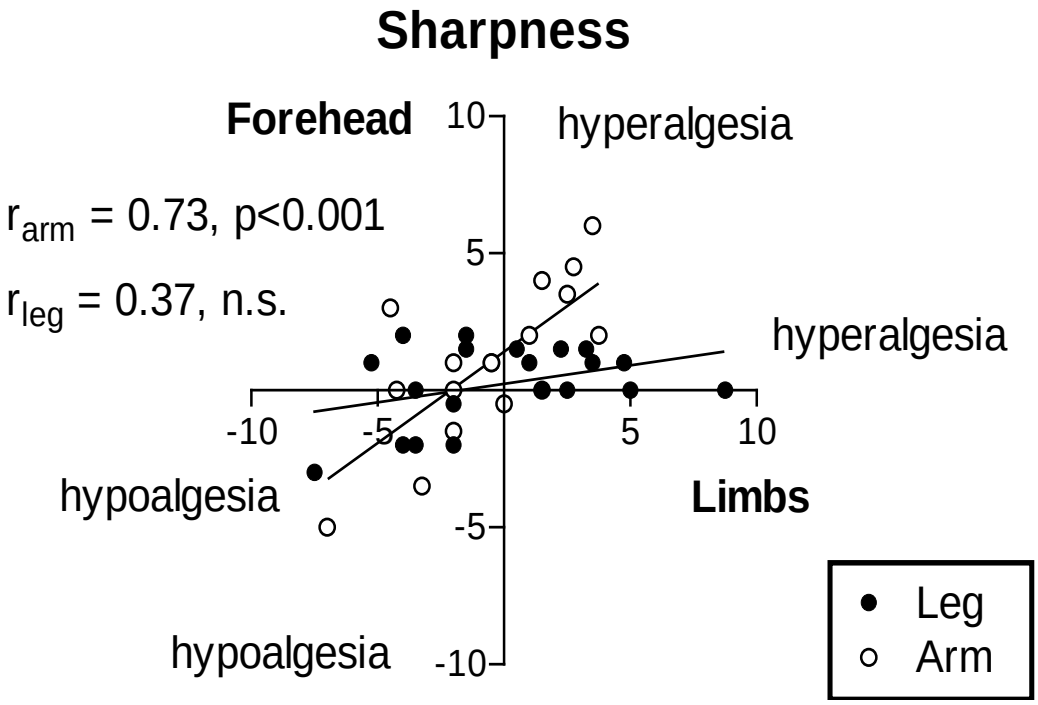

Sharpness
Forehead
r_{arm} = 0.73, p<0.001
r_{leg} = 0.37, n.s.
hyperalgesia
hyperalgesia
hypoalgesia
hypoalgesia
Limbs
10
5
-5
-10
-10
-5
5
10
Leg
Arm

Table 1

Sensory and autonomic disturbances in CRPS patients

		History and ***Physical Examination***					Laboratory Tests of Sensation					T Δ
	Limb	Autonomic Disturbances			Sensory Disturbances		Allodynia or Hyperalgesia			Sensory Loss		(^{o}C)
1. F, 37	LLE	***edema***	***vascular***	***sweats***	***hyperalgesia***	***loss***	cold	punctate		pressure		-.20
2. F, 37	LLE	***edema***	***vascular***	***sweats***	***hyperalgesia***	***loss***	cold					1.70
3. F, 35	RUE	***edema***	***vascular***	sweats	***hyperalgesia***	***loss***	cold	punctate		pressure		.70
4. M, 51	LUE	***edema***	***vascular***	***sweats***	***hyperalgesia***	***loss***						-.50
5. F, 33	LUE	edema	vascular	***sweats***	***hyperalgesia***	***loss***	cold			pressure	touch	heat -2.10
6. F, 43	LUE	***edema***	***vascular***	sweats	***hyperalgesia***	***loss***	cold	punctate		pressure	touch	heat .20
7. F, 48	RLE	edema	***vascular***	sweats	***hyperalgesia***	***loss***	cold	punctate		pressure	touch	-7.00
8. F, 20	RUE	edema	***vascular***	sweats	***hyperalgesia***	***loss***	cold		heat	pressure		-1.10
9. F, 54	LLE	***edema***	***vascular***	sweats	***hyperalgesia***		cold	punctate	heat	pressure		-.70
10. F, 33	RUE	edema	***vascular***	***sweats***	***hyperalgesia***			punctate	heat	pressure		.30
11. F, 21	LLE	edema	***vascular***	***sweats***	***hyperalgesia***		cold	punctate				-.80
12. F, 42	LLE	edema	***vascular***		***hyperalgesia***	***loss***			heat	pressure		-2.70
13. F, 51	RLE	edema	***vascular***		***hyperalgesia***	***loss***				pressure		2.90
14. F, 54	LLE	***edema***	vascular		***hyperalgesia***	***loss***		punctate				-.10
15. M, 22	LLE	edema	***vascular***		***hyperalgesia***	***loss***						-.20
16. F, 37	RLE	***edema***	***vascular***		***hyperalgesia***	***loss***			heat	pressure	touch	-1.20
17. F, 17	LLE	edema	***vascular***		***hyperalgesia***	***loss***	cold	punctate		pressure		-2.50
18. F, 35	RLE	edema	***vascular***		***hyperalgesia***	***loss***	cold	punctate		pressure	touch	-.50
19. F, 31	LUE	***edema***	***vascular***		***hyperalgesia***	***loss***	cold	punctate	heat	pressure		-.40
20. M, 27	LUE	***edema***	***vascular***		***hyperalgesia***	***loss***		punctate		pressure		-2.40
21. F, 41	LLE	edema	***vascular***		***hyperalgesia***	***loss***		punctate				-.90
22. F, 31	RUE	edema	vascular		***hyperalgesia***	***loss***		punctate		pressure		-.10
23. M, 20	RLE	edema	***vascular***		***hyperalgesia***		cold	punctate	heat	pressure		-1.80
24. M, 43	RLE	edema	***vascular***		***hyperalgesia***					pressure		heat -.70
25. F, 50	LUE	edema	***vascular***		***hyperalgesia***							heat -1.30

		History and ***Physical Examination***					Laboratory Tests of Sensation					T Δ
	Limb	Autonomic Disturbances			Sensory Disturbances		Allodynia or Hyperalgesia				Sensory Loss	(^{o}C)
26. M, 34	RUE	***edema***	vascular		***hyperalgesia***							.50
27. F, 58	RUE	***edema***	***vascular***	***dry***	***hyperalgesia***							.20
28. M, 43	RUE	***edema***	***vascular***	sweats		***loss***						-.20
29. M, 23	RLE	edema	***vascular***	sweats		***loss***				pressure		-.60
30. F, 20	RLE	edema	***vascular***	sweats		***loss***				pressure		1.40
31. M, 22	LLE	edema	***vascular***		***hyperalgesia***		cold	punctate	heat	pressure		-.10
32. F, 41	LUE	edema		***sweats***	***hyperalgesia***		cold	punctate	heat	pressure		-.20
33. F, 43	RUE	***edema***		sweats	***hyperalgesia***	***loss***				pressure		.10
34. F, 43	LLE	***edema***		sweats	***hyperalgesia***	***loss***	cold	punctate		pressure		-.40
35. F, 30	RUE	edema			***hyperalgesia***		cold	punctate				-.10
36. M, 24	LUE		vascular	sweats	***hyperalgesia***							-.10
37. F, 44	RLE		vascular	***sweats***	***hyperalgesia***		cold	punctate				-.40
38. F, 49	RUE		***vascular***			***loss***		punctate				-1.00

Limb LUE: left upper extremity; RUE: right upper extremity; LLE: left lower extremity; RLE: right lower extremity.
Autonomic disturbances included swelling, signs of vascular disturbance (flushing, cyanosis or thermal asymmetry), and abnormal sweating.
Sensory disturbances noted during the physical examination included hyperalgesia to pinprick or brisk taps, or loss of pinprick sensation.
Signs of autonomic and sensory disturbance noted during the physical examination are italicized in bold.
During the laboratory tests, stimulation with a 2^{o}C metal bar sometimes induced cold allodynia, and stimulation with light von Frey hairs sometimes induced punctate allodynia at the touch threshold. The heat pain threshold was low in the distal extremity of the affected limb of some patients (heat hyperalgesia) and abnormally high in others. In addition, the touch threshold was abnormally high in the distal extremity of a few patients.
T Δ: temperature asymmetry between the distal extremity of the affected and unaffected limbs. Negative values indicate that the affected limb was cooler than the unaffected limb.
Motor disturbances (tremor, weakness or limited range of movement) were noted during the physical examination in all but three patients (numbers 12, 21 and 30).
The pressure pain threshold was symmetrical in the forehead of six patients (numbers 1, 20, 22, 26, 35 and 37), was higher on the ipsilateral than contralateral forehead in two patients (numbers 18 and 33), was not measured in one patient (number 38), and was lower by at least 250 gm on the ipsilateral forehead in the other 29 patients.

Table 2

Association (Pearson's correlation coefficient) between sensory disturbances in the affected limb and asymmetry of sensations in the forehead

Ipsilateral side	Sensations in the Affected Limb (compared with the unaffected limb)				
of the forehead	diminished touch	heightened cold	punctate hyperalgesia	heat hyperalgesia	pressure hyperalgesia
heightened cold sensation	-.45**	.20	.14	.05	.11
punctate hyperalgesia	-.40*	.29	.49**	.17	-.01
heat hyperalgesia	-.40*	.05	.13	.33	.22
pressure hyperalgesia	.38*	-.13	.07	.11	.19

Correlation coefficient statistically significant (* $p<0.05$; ** $p<0.01$)

Table 3

Association (Pearson's correlation coefficient) among different sensory disturbances in the affected limb

	Sensations in the Affected Limb (compared with the unaffected limb)			
	diminished touch	heightened cold	punctate hyperalgesia	heat hyperalgesia
heightened cold	-.48**			
punctate hyperalgesia	-.47**	.56***		
heat hyperalgesia	-.40*	.40*	.49**	
pressure hyperalgesia	.02	.20	.21	.54***

Correlation statistically significant (* $p<0.05$; ** $p<0.01$; *** $p<0.001$)