



A longitudinal study of somesthetic perceptual disorders in an individual with a unilateral thalamic lesion

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Abstract

Several aspects of tactile, thermal and pain perception were evaluated in an individual (R.S.) with a hemorrhagic lesion centered in her left lateral thalamus. Over a 4-year period, psychophysical evaluations were undertaken every 6–8 months, and five magnetic resonance (MR) studies were conducted. Early tests (1991–1992) revealed large contralateral deficits in R.S.'s perception of touch, innocuous temperature, and mechanically evoked cutaneous pain – more so for the upper versus the lower extremity. R.S. showed a similar pattern for heat pain sensitivity, but a more modest deficit than for mechanically evoked pain. She showed a deficit for cold pain sensitivity on her foot, but not for her hand. Thresholds for all types of stimuli ipsilateral to the lesion were within a normative range. Late in 1993, R.S. demonstrated improvements in sensory capacity for touch and mechanically evoked pain contralaterally, although deficits were still evident. During the same period, heat pain sensitivity improved contralaterally, and strikingly, a permanent, ipsilateral hypersensitivity to heat pain developed in her hand. Throughout the entire testing period, R.S.'s ratings of perceived unpleasantness matched the patterns of perceived pain intensity. Thus, the discriminative and the affective dimensions of her pain would change in tandem. However, perceptible innocuous thermal stimuli evoked no affective response when applied contralaterally, despite being described as pleasant when presented ipsilaterally. Throughout the testing period, R.S. reported a persistent numbness on her right hemi-body. Only during a 3-month period in 1995 did she experience spontaneous pain, which was referred to her right foot. The only change in psychophysical performance related to her right foot was a transient but intense thermal allodynia several months prior to her spontaneous pain. The MR studies over this 4-year period showed changes in the extent of edema, gliosis and/or ischemia that could be related to perceptual changes. Thus, the conspicuous observations in this thalamic lesion case were: (i) differential effects upon the various pain modalities (mechanical, heat and cold); (ii) development of thermal allodynia without mechanical allodynia, including an ipsilateral effect; (iii) a deficit in positive affective responses to temperature; and (iv) the different time courses for changes in evoked somesthetic capacity versus spontaneous paresthesias and pathological pain. © 1997 International Association for the Study of Pain. Published by Elsevier Science B.V.

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1. Introduction

Lesions involving the thalamus frequently produce alterations of somesthetic capacity, however the type and extent of perceptual abnormality can vary greatly across

individuals. The ventrobasal complex of the thalamus (VB: ventral posterior lateral (VPL) and ventral posterior medial (VPM) nuclei) has received the most attention as the 'somatosensory thalamus', with respect to both basic science and clinical studies. Yet, other regions of the thalamus receive and process somesthetic information, and are likely to be involved in perception (Albe-Fessard et al., 1985; Jones, 1985; Willis, 1985; Berkley et al., 1987). Assuming functional specialization of somatosensory processing in the thalamus, partial thalamic lesions should pro-

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duce a variety of effects, depending upon the precise regions involved and the extent of injury. There are only a few reports providing detailed, quantitative assessments of somesthetic perceptual capacity following thalamic lesions (Head and Holmes, 1911; Boivie et al., 1989; Samuelsson et al., 1994; Vestergaard et al., 1995; Bowsher, 1996). Furthermore, there are no reports describing the temporal changes in post-lesion somatosensory dysfunction. Such studies are needed in order to tease apart the neural mechanisms of various somesthetic perceptions, and to try to understand the basis for post-injury functional reorganization.

This report presents a detailed, longitudinal evaluation of an individual (R.S.) who suffered a hemorrhage from a cavernous hemangioma located within the left thalamus, and who subsequently received stereotactic radiosurgery. Various aspects of her somesthetic sensibilities were evaluated repeatedly over a 4-year period. Additionally, the magnetic resonance (MR) studies that were generated over this same time period were reviewed for possible functional-anatomical correlations. The results reveal a complex relationship among the different modalities and qualities of somatosensory perception. As such, this report stresses the need to evaluate multiple aspects of somesthetic perception in any attempt to relate CNS pathology to sensory processing.

2. Methods

2.1. Subject (case history)

At the time of the first sensory evaluation (October 1991), R.S. was a 52-year-old white female, employed as an accountant's assistant. At the age of 12, she developed an abrupt right-sided hemiplegia, from which she gradually recovered, leaving her with a mild hemiparesis and occasional numbness. This condition was stable for approximately 35 years, at which time she noticed a gradual deterioration of motor control as well as an increased frequency and intensity of numbness. An MR scan in January 1988 confirmed the earlier diagnosis of a left thalamic arteriovenous malformation, with evidence of a recent hemorrhage.

A clinical examination conducted in March 1991 showed no evidence of cognitive impairment or dysphasia, and normal visual fields. She scored 98/100 on a modified minimal state exam (Teng and Chui, 1987) administered in July 1992. Her only other medical complaints were migraine headaches, which occurred every few months for most of her adult life. She would take either aspirin or acetaminophen for these headaches.

In September 1991, R.S. received 2000 cGy in a single fraction stereotactic radiosurgery procedure. Psychophysical testing began 2 months later. R.S. reported that her symptoms were relatively stable from this point until early 1993, at which time she felt less capable of controlling her

right arm and leg, and a greater intensity of numbness over her right hemi-body. She started taking oral doses of Decadron in early May 1993 through late June 1993. She felt her symptoms starting to improve in July 1993. Early in 1994, she felt her motor control was worsening, and she voluntarily remanded her driver's license. Throughout this entire period, she maintained her part-time accountant's assistant job.

Whenever she was asked to describe the abnormal sensation on her right side, she always referred to it as 'numb'. Until February 1995, she never described her paresthesia as painful, even under direct questioning. When asked to indicate where on the body she felt this numbness, she always first indicated her right hand/arm and foot/leg. Upon further questioning, she said that her face and torso also felt numb, as if a line was drawn down the center of her body. She said that the numbness could be more intense in her extremities than her body, but that it was comparable for her upper and lower extremities. Just how 'strong a numb sensation' she felt could vary from day to day, but at least since 1990, was always present to some degree. In February 1995, she reported episodes of painful sensations in the toes of her right foot. Over the next 3 months, she continued to have intermittent painful episodes several times a week, and the pain spread to encompass more of her foot. She described the pain as tolerable, and it didn't interfere with her normal routine, but it was a distinct change from the numbness, which was otherwise still present. These painful episodes ceased by the end of May 1995.

2.2. Psychophysical procedures

A wide range of psychophysical tests were administered over a 4-year period. Typically, R.S. would come to the Skin Senses Research Laboratory at SUNY Health Sciences Center for evaluation once a week for 6–8 weeks, every 6–8 months. The vibrotactile tests were conducted at the Institute for Sensory Research at Syracuse University. Any single session lasted 2–3 h, during which time 1–3 different tests were administered. Within each 6–8-week block, most tests were administered on two different days. R.S. provided informed consent to participate in this project, and was paid \$10.00 per hour. This project was reviewed and approved by the Institutional Review Boards for the Protection of Human Subjects at SUNY Health Science Center at Syracuse and at Syracuse University.

2.2.1. Tactile sensitivity

2.2.1.1. Vibrotactile thresholds. Vibrotactile thresholds were derived using a two-alternative, forced choice tracking method (Zwislocki et al., 1958). The equipment and procedures were similar to those described by Bolanowski et al. (1988). Thresholds were estimated for stimulation of the thenar eminence at three different frequencies (1, 10 and 300 Hz), and with two different

contact areas (2.9 cm² and 0.008 cm²). This combination of frequencies and contact areas allowed for selective evaluation of each of the four mechanoreceptive channels which have been characterized in the glabrous skin of the hand (Bolanowski et al., 1988; Greenspan and Bolanowski, 1996).

2.2.1.2. Contact touch thresholds. Detection thresholds for contact touch were measured using a calibrated series of monofilaments (Stoelting Aesthesiometer kit). While less precise than the vibratory threshold test, these stimuli could be administered on several body sites. We routinely tested the dorsum of the fingers and the dorsum of the foot (the same sites used for mechanical pain testing, see below). A method of limits protocol was used, as described by Essick (1992) (his Fig. 2).

2.2.1.3. Perception of surface-parallel brushing stimuli. R.S. performed direction and velocity discrimination tasks with stimuli provided by a computer controlled brushing motor stimulator. The equipment and general protocols are described in Franzén et al. (1984) and Essick et al. (1991). For these tests, R.S. was blindfolded and wore headphones that emitted white noise. Every 10 s, a tone cue was given, followed by a brush stroke stimulus on the designated test site (either the dorsal surface of the hand or the dorsum of the foot). During directional discrimination tests, R.S. first reported if she felt anything, and if so, what direction she felt any movement: either toward or away from her fingers (or toes). During velocity discrimination tests, R.S. first reported if she felt anything, and if so, at which of three speeds of movement: slow (1.0 cm/s), medium (5.0 cm/s) or fast (20 cm/s). Prior to data collection for these sessions, R.S. sampled the stimuli while visually observing the brush's movement.

2.2.2. Mechanically evoked cutaneous pain sensitivity

A modified ascending method of limits protocol was used to estimate R.S.'s threshold for the perception of sharpness and pain produced by a small probe applying a specified force to the skin. The device and protocol are described in Greenspan and McGillis (1991). Routine testing was performed on the dorsum of digits 2 and 3, and the dorsal surface of the foot just proximal to the toes.

2.2.3. Innocuous temperature and thermal pain sensitivity

2.2.3.1. Thresholds for the perception of coolness and heat pain. A multiple staircase protocol was used to determine cool perception threshold and heat pain threshold. A circular contact thermal stimulator probe (1.2 cm diameter) was used to produce feedback-controlled temperature changes. Stimuli were applied on the thenar eminence, the dorsolateral forearm, the lateral surface of the calf, or the plantar surface of the foot. The equipment

and protocols are described in Taylor et al. (1993) and Greenspan et al. (1993).

2.2.3.2. Scaling intensity and (un)pleasantness of thermal and pain sensations. This procedure required R.S. to scale the intensity (how hot, cold, or painful) and the affective level (how pleasant or unpleasant) of her thermally evoked sensations. In one series of tests, a contact thermal stimulator was used to apply heating stimuli. Stimuli were applied to either the thenar eminence or the plantar surface of the foot. For these sessions, the adapting temperature (AT) was 35°C, and stimuli consisted of temperature increases (up to temperatures of 39–51°C) that lasted for 5 s before returning to the AT.

In another set of tests, R.S. would place her hand (or foot) in a temperature-controlled water bath. At different sessions, water bath temperatures ranged from 0°C to 20°C, and from 40°C to 47°C. R.S. would keep her hand (or foot) in the water bath for up to 3 min, or until such time that she felt it was too painful to continue. At various times while her hand (foot) was in the water bath, she was presented with the response protocol.

In both testing situations, the same response protocol was used. After receiving a temperature change with the contact stimulator or at the appropriate time during the water bath tests, R.S. was prompted to report whether she felt warm/hot, cool/cold, pain (regardless of any accompanying thermal sensation), or nothing. She was then prompted to report whether her sensation was pleasant, unpleasant, or neutral. If she reported warm/hot, cool/cold, or pain, she was presented with a visual analog scale (VAS) on a computer screen. The VAS consisted of a graduated vertical bar with numbers to the right (0 to 100 by tens), and a set of verbal descriptors to the left. The placement of verbal descriptors was based on a procedure described by Rainville et al. (1992), which was replicated in our laboratory. R.S. was instructed to verbally give a number that represented the intensity of her warm (or cool or pain) sensation at that moment. After giving that response, R.S. was presented with another numbered VAS, this time with verbal descriptors appropriate for the degree of (un)pleasantness that she was experiencing.

2.2.3.3. Localization of heat pain sensations. During one session, R.S. was instructed to localize the heat pain sensations produced by the contact stimulator. The contact thermal stimulator (maintained at 49°C) was moved around from site to site on the right forearm, while R.S. was asked to describe where on her body she perceived the resulting painful sensation. During the 5-s stimulus period, R.S. kept her eyes closed. She reported no tactile sensation associated with placing the probe on her arm. After the probe was removed, she was asked to open her eyes, describe the quality of the sensation she just experienced, and point to where she had felt it.

3. Results

The results from the various psychophysical evaluations are summarized in Table 1.

3.1. Tactile sensitivity

R.S. was very insensitive to tactile stimuli presented to her right side. This was clearly demonstrated for vibrotactile thresholds at the thenar eminence (Fig. 1), and for contact touch thresholds using monofilament probes applied to the dorsal surface of her right hand and foot (Fig. 2). Her right hand initially showed a greater deficit than her right foot. The vibrotactile thresholds for her left hand were well within the range of thresholds derived from a group of healthy female subjects similarly tested (Gescheider et al., 1994). Between mid-1993 and mid-1994, the tactile sensitivity on her right hand improved, although a deficit was still apparent. With vibratory stimuli, this improvement was only observed with the 300-Hz stimuli.

Despite R.S.'s insensitivity to punctate and vibratory stimuli, she would routinely feel ($\geq 90\%$ detection) a camel's hair brush exerting only 5 g of force stroked over her right hand or foot. However, she could not accurately report spatial or temporal features of such stimuli. In a two-alternative forced-choice task of directional discrimination, she performed at chance level on the right hand (53%

correct) and right foot (55% correct), while performing significantly above chance on the left side of the body (75% for hand and 71% for foot). She showed similar results when attempting to discriminate the velocity of the brush stroke on her hands (right = 48% correct; left = 87.5% correct).

4. Perception of sharpness and mechanically evoked pain

As with tactile sensitivity, R.S. demonstrated a large right-sided deficit with respect to her thresholds for perceiving mechanically evoked, cutaneous pain (Fig. 3), and sharpness (not pictured). Also akin to her tactile thresholds, this deficit was initially more pronounced on her hand than on her foot. Mechanical pain and sharpness thresholds for her left hand were very close to the median of thresholds derived from a group of healthy female subjects similarly tested (Greenspan and McGillis, 1991, 1994). The difference between her right and left hand thresholds were always more than two standard deviations from normative values (Greenspan and McGillis, 1994), implying a consistent, significant deficit on her right. When tested in late 1994, a comparable right-sided deficit was observed for the thenar eminence (Fig. 3, top, inset). R.S. showed an improvement in sensitivity on her right between the mid-

Table 1

Results from psychophysical evaluations

		Hand	Foot
<i>Touch</i>	Contact threshold	Large R deficit; partial improvement by 1994	R deficit, less so than with hand. No improvement in 1994
	Vibration	Large R deficit; partial improvement only with high frequency by 1994	Not tested
<i>Innocuous temperature</i>			
Warming	Contact probe	No warm/hot sensation on R	Large R deficit
	Water bath	No warm/hot sensation on R (except 6/94)	Large R deficit; not pleasant on R; allodynia on R, 6/94
Cooling	Contact probe	No cool/cold sensation on R	No cool/cold sensation on R
	Water bath	Little cool sensation on R; allodynia on R, 7/94	Cool on R same as L; not pleasant on R; allodynia on R, 7/94
<i>Pain</i>			
	Mechanical thresholds	Large R deficit; partial improvement late 1993	R deficit; less so than w/ hand; partial improvement late 1993
Heat	Contact probe thresholds	Small R deficit; (larger R deficit on forearm); L hyperalgesia in late 1993	No L/R difference on plantar; small R deficit on dorsum; (small R deficit on leg); L hyperalgesia in 1995
	Contact probe scaling	R deficit, except at highest temperature (no L/R difference 6/92). Over time, R and L increase sensitivity; development of L hyperalgesia	No L/R difference
	Water bath scaling	R deficit at 45–46°C. No sign of late L hyperalgesia	R deficit at 45°C, not at 46°C; L hyperalgesia 5/95
Cold	Water bath scaling	No L/R difference, except R hyperalgesia in 1994; no hyperalgesia in 1995	R deficit, except R hyperalgesia in 1994; no hyperalgesia in 1995

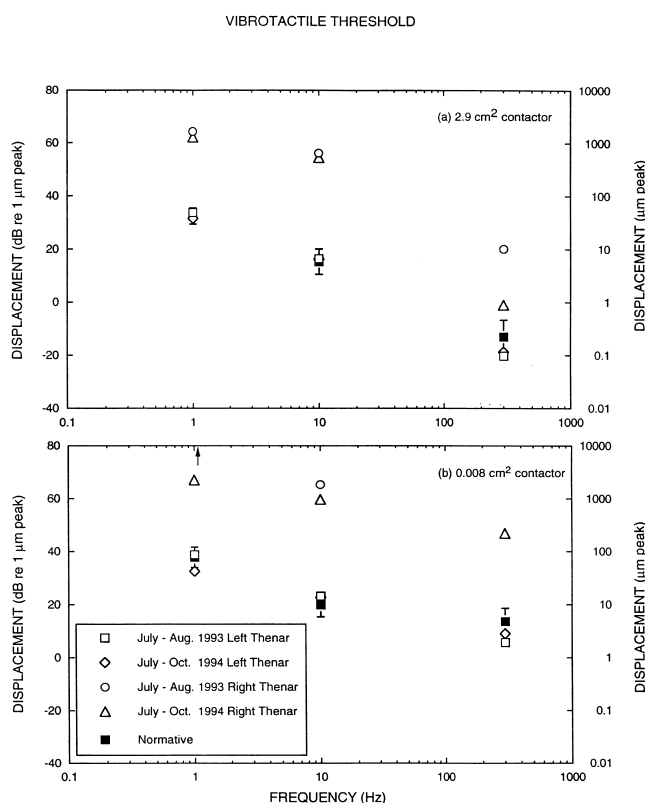


Fig. 1. Average thresholds plotted as a function of stimulus frequency for detection of 1-, 10-, and 300-Hz signals applied to the thenar eminence. Contactor size was either 2.9 cm² (top) or 0.008 cm² (bottom). The arrow above the open triangle at 1 Hz (bottom graph) denotes that the displacement required for threshold was above the ceiling value of 66 dB (2000 μm). The filled squares represent normative data: the mean of thresholds derived from an age-matched sample of 10 female subjects (Gescheider et al., 1994). Error bars signify ±1 standard deviation for the normative thresholds. Data were collected over a 3-day period in 1993 and a 2-day period in 1994.

1993 and late 1993 testing sessions; however a deficit was still evident.

5. Innocuous temperature sensitivity

In general, R.S. was very insensitive to innocuous thermal stimuli. With the contact thermal stimulator, R.S. never reported ‘cool’ or ‘cold’ (with temperatures down to 22°C), and rarely reported ‘warm’ or ‘hot’ (with temperatures between 36°C and 44°C) applied to her right hand, arm, leg, foot, or the right side of her forehead. During immersion of her right hand in a 20°C water bath, R.S. reported only slight (July 1992) or no cool sensations (July 1993; Fig. 4, top). In contrast, she consistently reported cool sensations for her right foot, at an intensity level comparable to that for her left foot. Even though R.S. felt cool sensations of the same intensity in both her feet, she described the sensation as moderately pleasant for her left

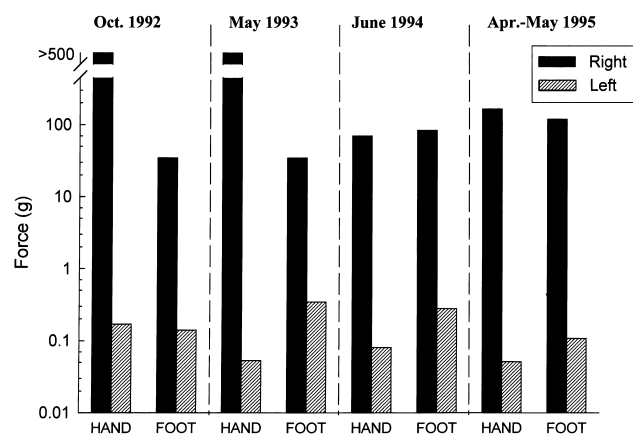


Fig. 2. Tactile thresholds derived from calibrated monofilaments (Stoelting Aesthesiometer Kit). Each value is based on a single day’s testing, consisting of two ascending and two descending staircases, except for 1995 data, which is the average of 2 days of testing.

foot, but neither pleasant nor unpleasant for her right (Fig. 4, bottom).

In July 1994, R.S. found the 20°C water to be intolerably painful for either her right hand or foot. With repeated attempts, she removed her right hand or foot within 15 s

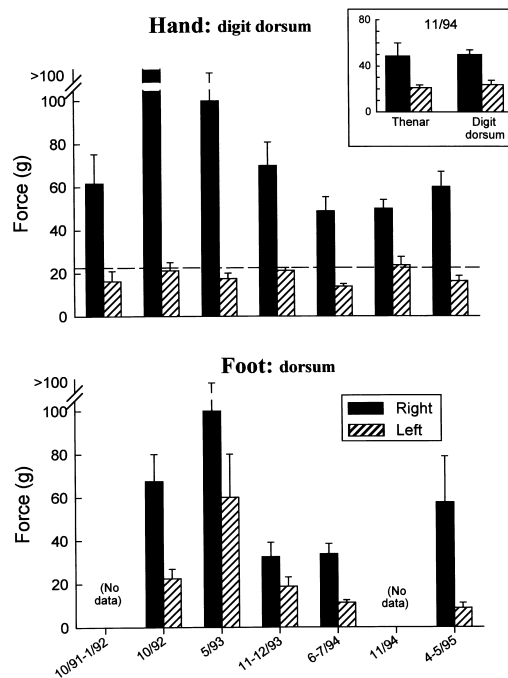


Fig. 3. Thresholds for mechanically evoked cutaneous pain on the digit dorsum (top) and the dorsal surface of the foot (bottom). Each value is a mean (plus one standard error) based on four estimates from 2 days of testing, except that May 1993 data are based on 1 day of testing. The dotted horizontal line in the upper graph represents the median pain threshold value derived from a group of 24 healthy female subjects tested on the left hand. The inset at the top right compares thresholds at two sites of the hand.

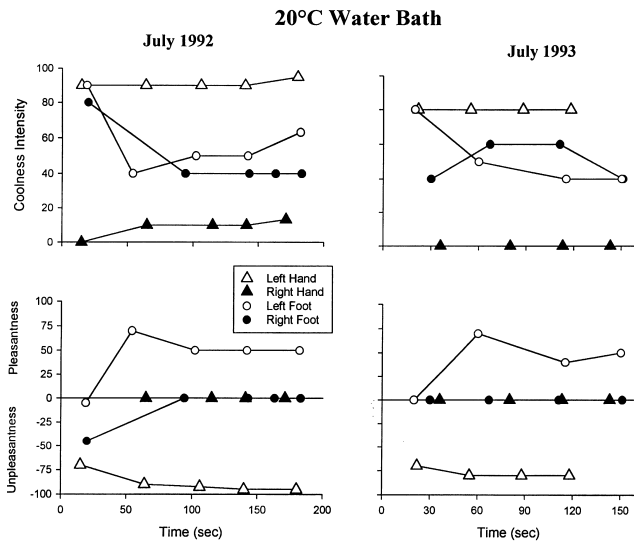


Fig. 4. Scaling of the perceived coolness (top) and (un)pleasantness (bottom) resulting from placing the subject's hand or foot in a 20°C water bath.

of immersion. She still reported this temperature to be cold but not at all painful for her left hand or foot. In June 1995, R.S. reported only a transient cool sensation in her right hand, and no sensation at all in her right foot in the 20°C water bath.

When initially tested, R.S. reported either transient or no warmth sensation when immersing her right hand or foot in a 40°C water bath in 1992 and 1993. She reported some

warmth sensation with her right foot in a 43°C water bath (Fig. 5, top left and middle). In July 1994 (at the same time as her cold allodynia described above), R.S. showed a dramatically increased sensitivity to both the 40°C and 43°C water baths with her right foot (Fig. 5, upper right). She characterized her sensory experience at this point as a burning pain, but localized only to her big toe. Elsewhere on her right foot she felt nothing. With her right hand, she still felt nothing with the warm water, except for a transient (5–10-s) uncomfortable sensation with the 43°C bath. During subsequent evaluations (October 1994 and May 1995), R.S. reported no pain with bath temperatures of 40–43°C for either her right hand or foot.

5.1. Heat pain sensitivity

R.S.'s heat pain sensitivity was measured in three different ways. Since the various protocols revealed somewhat different features, they will be considered separately.

5.1.1. Contact stimulator pain thresholds

Despite the very large deficits described with the other somatosensory submodalities, R.S. showed relatively less disturbance in heat pain thresholds. In October 1991, R.S.'s heat pain threshold for her right hand (thenar) was only 1.1°C higher than for her left hand (Fig. 6, top left). Her threshold for her right foot (plantar) was 0.5°C lower than for her left foot (Fig. 6, bottom left). Both of these values were well within the range of laterality differences derived

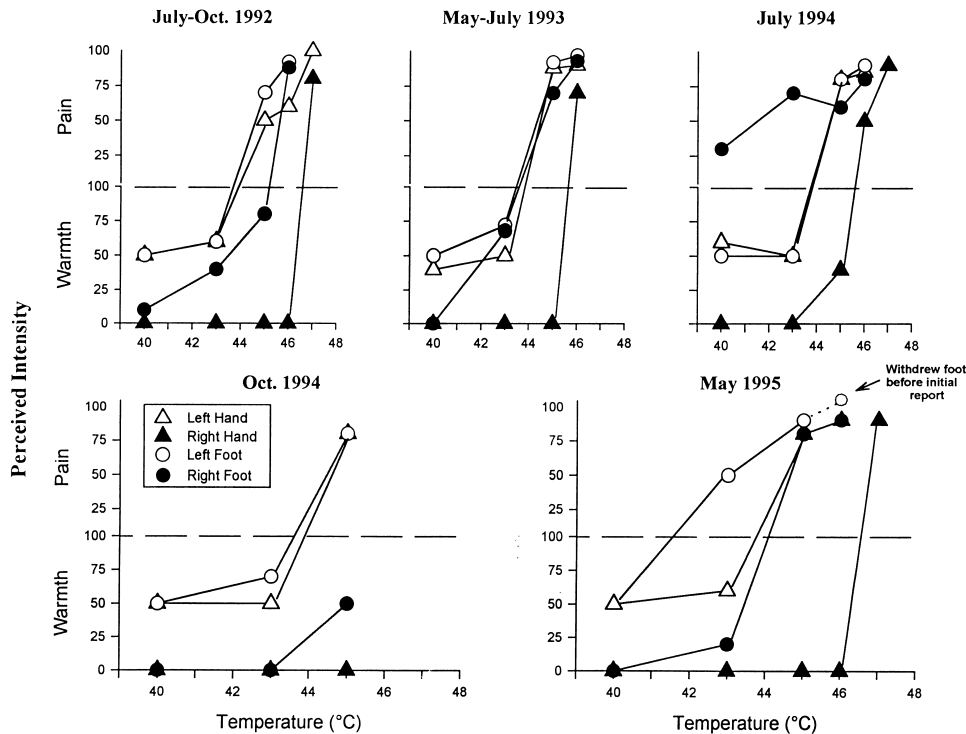


Fig. 5. Scaling of the perceived warmth or pain resulting from placing the subject's hand or foot in water baths of various temperatures. Each data point represents the perceived intensity after the hand (or foot) was immersed for 1 min.

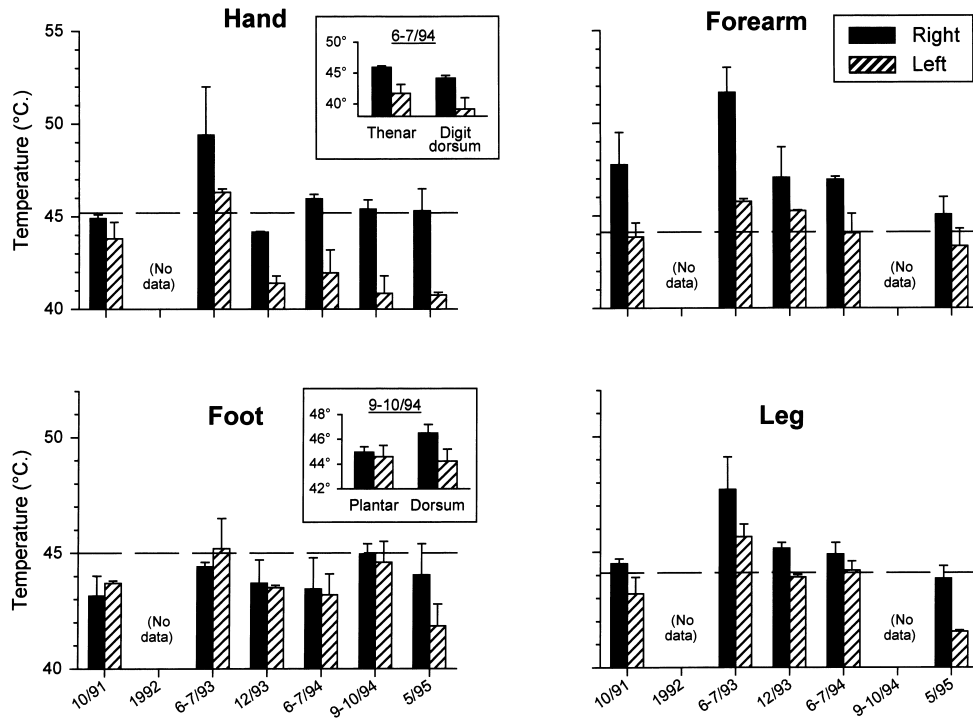


Fig. 6. Heat pain thresholds over time at four body sites. The dashed horizontal line represents the mean threshold derived from a group of 15 healthy female subjects, similarly evaluated. Inset graphs in upper and lower left allow for comparisons between two different areas of the hands and the feet. Each threshold is based on 2 days of testing.

from a group of healthy women tested in the same way (Taylor et al., 1993). The largest laterality difference was observed for her forearms (3.9°C), which was the only value that was more than two standard deviations from the normative data base (Fig. 6, top right).

Over the 4 years of testing, R.S. showed changes in her heat pain thresholds, which differed somewhat across body sites. For the right hand, arm and leg, she showed a pattern of greatest hypalgesia in mid-1993, and markedly improved (lower) thresholds by the end of 1993. Laterality differences were always more pronounced for her upper extremity than for her leg. She demonstrated no laterality difference in heat pain thresholds on the plantar surface of her feet, until 1995 (Fig. 6, lower left). At that time, the laterality difference was attributable to a change in the left foot, ipsilateral to the lesion. She consistently showed a small difference on her legs (Fig. 6, lower right), and, when tested in 1994, a comparable difference on the dorsum of her foot (Fig. 6, lower left, inset). Thresholds on her left side were stable, with two exceptions: her left hand showed a distinctly lower threshold beginning in December 1993 (Fig. 6, upper left), and her left foot and leg showed the same change in 1995. The left hand hypersensitivity was demonstrable on both the thenar eminence and the dorsal surface of digit 3 (the test site for mechanically evoked pain) (Fig. 6, upper left, inset).

5.1.2. Contact stimulator suprathreshold scaling

A statistically significant laterality difference, equiva-

lent to a 1–1.5°C deficit on the right, was initially observed for the thenar eminence. Subsequent testing demonstrated no laterality difference in July 1992, and marginally significant differences after that. In contrast, there was never a statistically significant laterality difference in pain ratings for stimulation of her feet (Fig. 7). These results, then, generally matched those seen for heat pain thresholds described above. Furthermore, the laterality difference evident in September 1994 is largely due to a left-handed hypersensitivity, which also paralleled her heat pain threshold results.

When rating both the intensity and unpleasantness of painful heat stimuli, R.S. would typically rate the unpleasantness as equal to or slightly lower than the pain intensity (Fig. 8). This trend was consistently observed throughout the testing sessions.

5.1.3. Water bath suprathreshold heat pain scaling

The earliest evaluation with 45–47°C water baths (July–October 1992) showed a clearly reduced sensitivity on the right relative to the left, more so for the hands than the feet (Fig. 5, top left). Subsequent testing indicated an increased sensitivity for pain in the right hand and especially the foot (July 1994), however sensitivity was dramatically decreased 3 months later (Fig. 5, bottom left). In 1995, R.S. demonstrated a hypersensitivity in her left foot to hot water baths (Fig. 5, bottom right), which was consistent with the lower heat pain thresholds (Fig. 6, lower left).

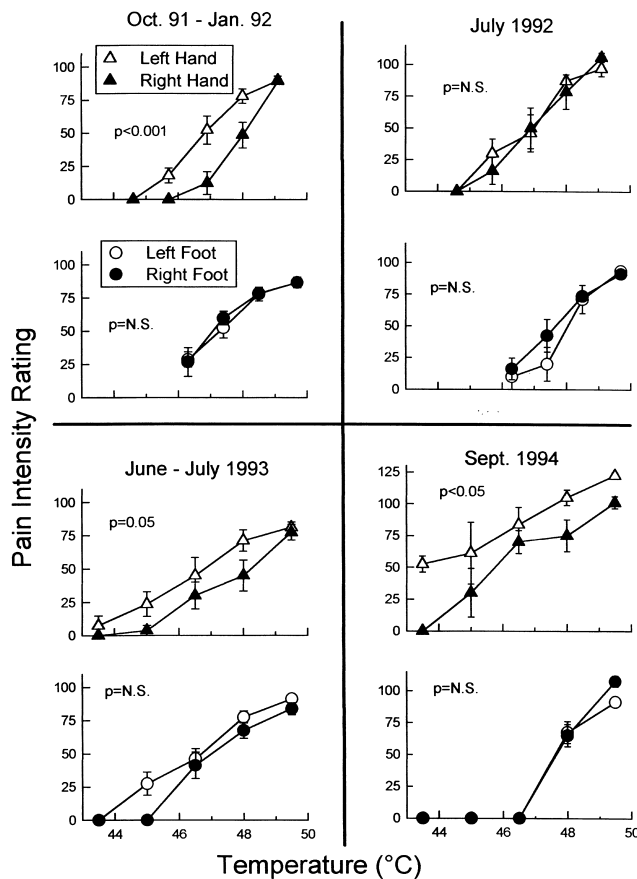


Fig. 7. Scaling of pain intensity of heat stimuli applied with the contact stimulator to the hands and feet, at different time periods. Each data point represents the mean (\pm standard error) based on eight estimates over 2 days, except the September 1994 data are based on four estimates from a single day of testing. Note the Y-axis scale change for September 1994. The *P*-values in each graph represent the statistical probability of a laterality difference, based on a series of 2-way ANOVAs that considered stimulus intensity and laterality as factors. *P* = N.S. indicates that laterality was not found to be a significant factor at a 95% confidence level.

5.2. Cold pain sensitivity

Cold pain perception was assessed by water bath immersion. Early evaluations used 0°C and 10°C baths, and measured the duration of time that R.S. would keep her hand immersed. There was no indication of a reduced sensitivity to cold pain in her right hand, and, if anything, a suggestion of hypersensitivity with the 10°C water bath (Fig. 9). In 1992 and 1993, R.S. found a 17°C water bath highly painful for her right hand, but not at all painful for her right foot (Fig. 10). As mentioned earlier, in 1994 R.S. found the 20°C water bath intolerably painful for her right hand and foot, so a 17°C water bath test was not attempted. This cold hypersensitivity was not observed in 1995, and in fact, R.S. was less sensitive to the 17°C water bath than ever before.

5.3. Pain localization

During many of the sessions evaluating painful sensations, R.S. volunteered that she sometimes felt her sensa-

tions at body sites that were clearly away from the stimulator. It was not uncommon for her to report that heat stimulation of her right thenar or forearm produced painful sensations in her fingers rather than at the site of stimulation. At other times, even within the same testing session, she would say that her sensations were well localized to the stimulus site. On some trials, R.S. reported a painful experience, but she could not localize it at all. R.S. would also mislocalize or not be able to localize the painful sensations resulting from mechanical stimuli.

During one test session (December 1993) R.S. was instructed to report where on her body she felt painful sensations resulting from a 49°C probe being placed at various sites on her right forearm. Her reports derived from 18 trials are presented in Table 2. Only a few reports corresponded to the stimulus site. At other times, sensations were either displaced, extensively localized (fingers and arm together), or not localized anywhere. In a similar experiment applying 44–46°C stimuli to her right leg (February 1994), her pain was localized to within 10 cm of the stimulus site for 18/19 stimuli, and only once did she incorrectly refer to a distal site more than 20 cm away.

5.4. Temporal extent of evoked pain

During heat pain and mechanical pain testing, R.S. was occasionally asked to describe how long her sensations per-

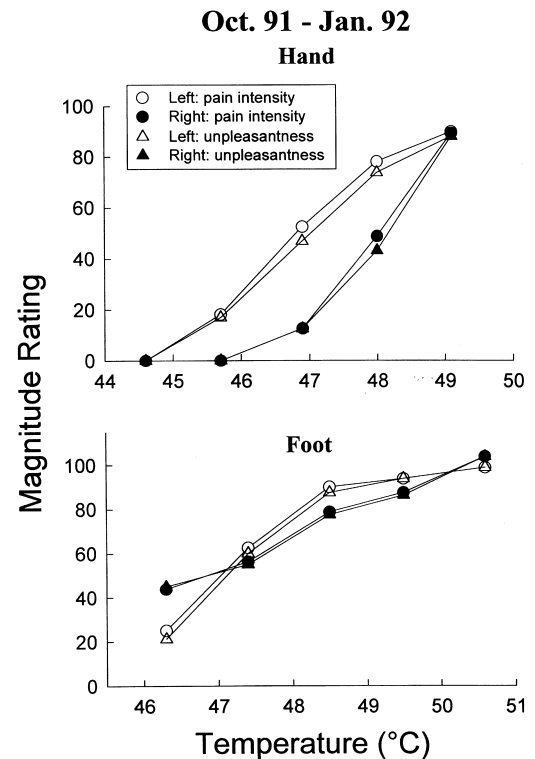


Fig. 8. Scaling of pain intensity (circles) and unpleasantness (triangles) of heat stimuli applied to the thenar eminence (top) and plantar surface of the foot (bottom). Each point represents the mean of eight estimates from 2 days of testing.

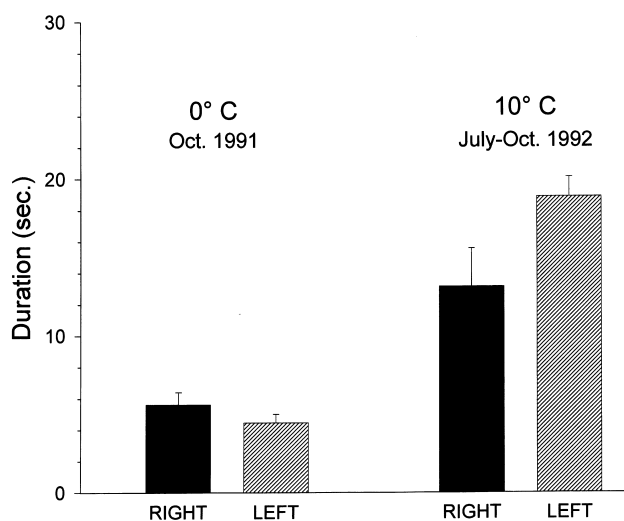


Fig. 9. Cold pain tolerance as measured by duration of voluntary hand immersion in cold water baths. Each bar represents the mean (plus one standard error) of either two (0°C) or three (10°C) measurements.

sisted. Invariably, she said that the sensations were transient, and lasted approximately the same amount of time on her right and left sides. Thus, even in those cases when stimuli were spatially mislocalized, R.S.'s pain perceptions were temporally normal.

5.5. Anatomical evaluation of MRI

An MR scan in March 1991 revealed a nodular lesion within the left thalamus, demonstrating a hypointense band of signal peripherally surrounding a nidus of slightly inhomogeneous increased signal (Fig. 11, A–C). The hypointense band, noted on both T₂-weighted and proton density-weighted images, is most likely susceptibility-artifact from hemosiderin distribution. The nidus demonstrated an increased signal on T₁-weighted images, which is compatible with blood products (predominantly extracellular methemoglobin), and indicative of a prior hemorrhage. Six months after this MR study, R.S. received 2000 cGy in a single fraction, stereotactic radiosurgery procedure.

A July 1992 MR study revealed a new halo of increased signal surrounding the left thalamic lesion. This new halo,

Table 2

Projection of pain sensations resulting from 49°C stimulus applied to the forearm (18 trials)

Perceived site of pain	Number of trials
Correctly localized within 10 cm of stimulus	3
Discretely localized more than 10 cm away from stimulus	2
Diffusely localized on arm	1
Diffusely localized on fingers and arm	4
Could not localize at all	6
Felt no sensation	2

which is compatible with post-radiation edema, ischemia and/or gliosis, extended into the left midbrain, previously uninvolved areas of the left thalamus, and the left parietal white matter (Fig. 11, D–F). Based on an MR scan performed in September 1993, there is further progression of the halo. The most significant changes compatible with edema/ischemia/gliosis involved the left thalamus and left parietal white matter (Fig. 11, G–I). Proton density-weighted MR images in February 1994 revealed partial resolution of the hyperintense halo involving the midbrain, left thalamus, and left partial white matter (Fig. 11, J–L). Another scan in July 1995 indicated no significant change from the 1994 scan.

6. Discussion

R.S. demonstrated clear deficits in evoked somesthetic perception with a wide variety of tests. The extent and time course of the various sensory abnormalities reveal a complexity of effects that suggest separate mechanisms of information processing at the level of the thalamus.

6.1. Tactile perception

R.S. had greatly elevated thresholds for detecting in-

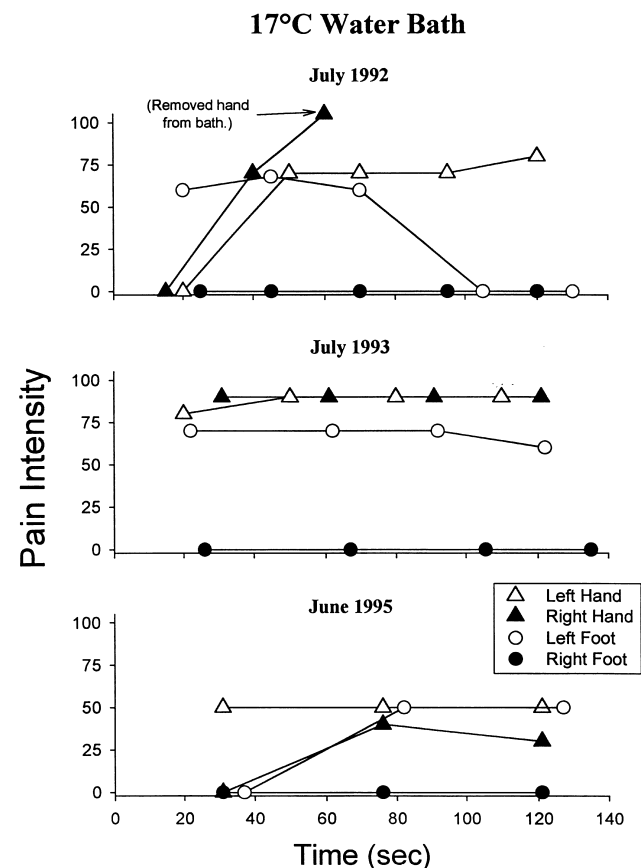


Fig. 10. Pain intensity ratings during submersion of hand or foot in a 17°C water bath.

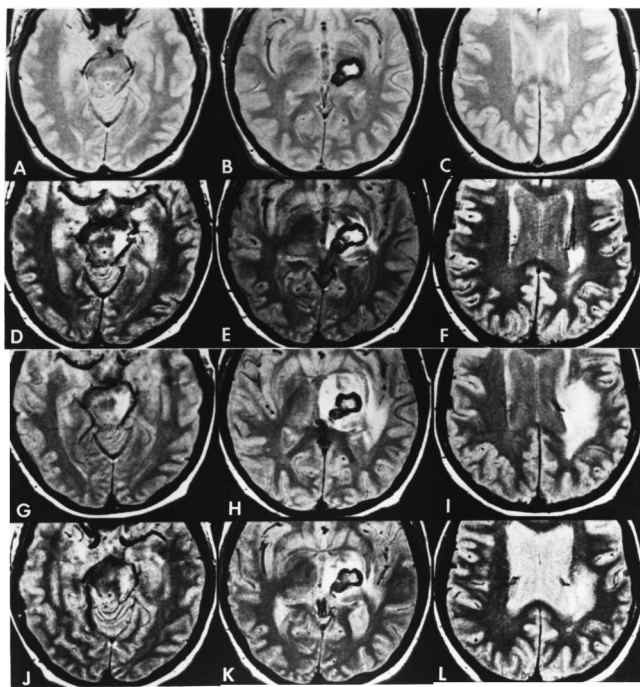


Fig. 11. Axial proton density weighted MR images. The size and configuration of the left thalamic hemorrhage is stable over time. Note changes in surrounding edema/ischemia/gliosis. A–C: March 1991. Hemorrhagic lesion in left thalamus, with little surrounding edema/ischemia/gliosis. D–F: July 1992. Progression of edema/ischemia/gliosis inferiorly to left midbrain, previously uninvolved areas of the left thalamus, and left parietal white matter. G–I: September 1993. Stable findings in midbrain; additional increase of edema/ischemia/gliosis in left thalamus, and left parietal white matter. J–L: February 1994. Partial resolution of edema/ischemia/gliosis in midbrain, left thalamus, and left parietal white matter.

nocuous mechanical stimuli. The significant laterality differences in threshold curves across all vibratory frequencies indicates a diminution in tactile perception across all mechanoreceptive channels (Bolanowski et al., 1988). R.S. showed a selective improvement in threshold with high frequency vibration in 1994 (Fig. 1), suggesting an improvement in sensory transmission only from PC mechanoreceptors. This observation lends support to the idea that information from PC mechanoreceptors is processed separately from other cutaneous mechanoreceptor input at the thalamic level (Dykes et al., 1981; Kaas et al., 1984; Herron and Dykes, 1986). R.S. also showed lowered contact touch thresholds during this same period (Fig. 2), but only for her hand. Since monofilament stimulation excites all types of cutaneous mechanoreceptors, including PCs (Johansson et al., 1980; LaMotte and Whitehouse, 1986), one would expect better performance on contact touch detection with improvement in any of the mechanoreceptive channels.

Despite the high tactile thresholds on the right side, R.S. could routinely detect light brushing along her skin. This may be due to the fact that surface parallel brushing is a particularly good stimulus for activating cutaneous mechanoreceptors (Greenspan, 1992; Edin et al., 1995; Essick and Edin, 1995). Or, it may be that the spatio-temporal pattern of successively activated mechanoreceptors is more effective

than single site stimulation in transmitting signals through the compromised thalamus. Even though R.S. could routinely detect a brushing stimulus on her hand or foot, she could not extract directional or velocity information from such a stimulus.

6.2. Mechanical pain versus heat pain perception

In some respects, mechanical and heat pain thresholds showed similar patterns. For both, deficits were greater for the upper body than the lower body, at least initially. Also, thresholds on the right side were highest in mid-1993, and clearly improved by late 1993 or early 1994. These trends were also observed for tactile thresholds (see above), and thus, could be considered global features of R.S.'s somesthetic disturbance.

However, in other respects, there were distinct differences between mechanically evoked and heat evoked pain. First, the degree of deficit in pain threshold, expressed as the number of standard deviations (SDs) beyond the normative laterality differences, was consistently larger for mechanically evoked pain (always greater than 2 SDs) than for heat pain (usually less than 2 SDs). This difference was apparent for both the hand and the foot. Secondly, there was a dramatic thermal allodynia observed in June–July 1993, but never evidence of a mechanical allodynia. Thirdly, there was a dramatic decrease in heat pain threshold for the left hand after mid-1993 (Fig. 6), and a corresponding increase in pain intensity scaling for contact heat stimuli applied to that hand (Fig. 7, September 1994). This ipsilateral change in heat pain sensitivity was observed on both palmar and dorsal surfaces (Fig. 6, upper left), but was not seen for mechanical pain sensitivity tested on the same skin sites (Fig. 3, top, inset).

Very few reports have evaluated both mechanical and thermal pain perception for people with central lesions. Boivie et al. (1989) performed extensive sensory testing upon nine people with lesions involving the thalamus. All nine demonstrated elevated thermal pain thresholds on body sites contralateral to their lesion, but 8/9 were hyperalgesic to pin prick, and only one was hypoalgesic. While this is not the same pattern as described in the present report, it demonstrates the ability of thalamic lesions to dissociate effects upon thermal pain versus mechanical pain perception. A recent study describing the sensory capacities of central post-stroke pain (CPSP) patients reported that 80% were hypoalgesic to pin prick, but only one-quarter had 'clearly elevated' heat pain thresholds (Vestergaard et al., 1995).

Although many nociresponsive thalamic neurons are reported to be excited by both noxious heat and noxious mechanical stimuli, a sizable fraction only respond to noxious mechanical stimuli. One systematic study of such neurons in the VPLc of monkey thalamus described approximately 20% (13/67) of the mechanically nociresponsive neurons to be unresponsive to noxious heat stimuli up to

50°C (Kenshalo et al., 1980). A subsequent study from the same laboratory revealed that of a sample of 39 neurons responsive to noxious mechanical stimuli, only nine also responded to temperatures up to 49°C (Chung et al., 1986). More recently, an investigation of single-unit recordings in the human ventral caudal thalamus (analogous to the monkey VPLc) reported that 64% (7/11) of the mechanically nociresponsive neurons were unresponsive to heat stimuli up to 51°C (Lenz et al., 1994). Thus, a significant fraction of nociresponsive neurons in the main somatosensory nucleus of the thalamus are only responsive to mechanical stimuli, and their injury would presumably have a selective effect upon mechanically evoked versus thermally evoked pain. This relationship suggests that the core region of ventral caudal thalamus has particular importance for both mechanically evoked touch and pain perception, and less critical importance for thermally evoked sensations. An alternative interpretation is that the mechanically nociresponsive neurons may be more susceptible to injury, at least in this case.

6.3. Heat pain versus cold pain

Sensitivity to painfully cold stimuli did not parallel heat pain sensitivity. Initially, R.S. was equally sensitive to painfully cold stimuli applied to either hand, and less sensitive to painfully cold stimuli applied to her right versus left foot, the opposite somatic pattern of heat pain sensitivity. In 1994, R.S. demonstrated a prominent cold hypersensitivity for her right hand and foot. At the same time, she demonstrated a heat hypersensitivity for her right foot in 40–43°C water baths, but not for her right hand.

Other evaluations of CPSP patients have shown that heat pain and cold pain perception can be differentially affected by a lesion of the spino-thalamo-cortical system (Vestergaard et al., 1995). Thus, one must consider that thalamic processing relevant to heat pain and cold pain perception is separable at the level of the thalamus.

6.4. Affective responses to stimuli

When experiencing painful thermal stimuli, R.S. would routinely rate the unpleasantness to be slightly less than the intensity of the pain. Such a response pattern has been commonly described for neurologically intact subjects performing these tasks (Price et al., 1983, 1987; Rainville et al., 1992). In this respect, R.S. showed affective evaluations appropriate for her reported intensity of pain. She also showed appropriate emotive reactions to the intensely painful stimuli during the test session, such as verbal exclamations and facial grimaces. Thus, both of the measured pain dimensions, perceived intensity and unpleasantness, were altered in tandem whenever perception was abnormal. This result suggests that lateral thalamic regions process nociceptive information relevant to both sensory-discriminative and affective dimensions of pain.

An unexpected alteration in affective processing was found with respect to innocuous thermal stimuli. Even though R.S. perceived a 20°C water bath to be moderately cool with either her left or right foot, she only considered it pleasant with her left foot, and described it as neither pleasant nor unpleasant with her right foot (Fig. 4). These results suggest the intriguing possibility of a selective perturbation of positive affective processing of somesthetic input resulting from this lesion.

6.5. Paresthesia, central pain, and sensory deficits

Even though deficits in pain and/or thermal perception frequently accompany CPSP (Boivie et al., 1989; Tasker et al., 1991), central lesions can produce such sensory deficits without the appearance of pathological pain (Agnew et al., 1983; Andersen et al., 1995; Bogousslavsky et al., 1988; Samuelsson et al., 1994). Thus, while disruption of the thermal and/or pain sensory systems may be necessary for pathological pain to develop, it is not sufficient. There was no striking correlation between the spontaneous paresthesias or pains that R.S. experienced, and the sensory deficits measured psychophysically. Throughout the testing sessions, R.S. described a hemi-body numbness on her right side. Beginning in February 1995, R.S. reported intermittent pain sensations in the toes of her right foot. Over the next few months, these pains spread to encompass a good portion of her foot, before disappearing in May 1995. There was no dramatic change in somatosensory test performance associated with the development of R.S.'s pain during this period. The only related phenomenon was R.S.'s intense heat allodynia in her right foot 8 months earlier. She also experienced a cold allodynia at that time, but it was present in both her hand and foot, and she never reported any spontaneous pain in her hand. The relationship between thermal allodynia and central pain development is suggestive in this case, but clearly requires further evaluation.

6.6. Thalamic neuropathology and lesion effects

R.S. sustained at least one hemorrhagic incident prior to the start of the sensory testing. There was no indication of additional bleeding in subsequent MR studies throughout this period. Instead, subsequent changes are consistent with post-radiation effects: white matter damage with non-specific changes to myelination, vacuolation, edema, and gliosis. These pathologies result at least in part from small vessel damage, especially within the deep portions of the brain (Kirkwood, 1990). Apparent collateral areas of damage occurred within the left midbrain, previously uninvolved regions of the left thalamus, with extension into the white matter of the left parietal lobe. This collateral damage could represent edema, gliosis and/or ischemic changes, which cannot be differentiated on the basis of the MR studies available.

With reference to an atlas of human thalamic anatomy

(Dewulf, 1971), the hemangioma and surrounding hemosiderin occupy a major portion of the left VB complex, encompassing most if not all of the VPL and ventral posterior inferior (VPI) nuclei, major receiving nuclei of nociceptive input from the spinal cord (Bowsher, 1957; Berkley, 1980; Jones, 1985; Gingold et al., 1991). The hemangioma encroaches somewhat medially, but clearly spares portions of the medial thalamus. It has long been suggested that the VB area of the thalamus is important, if not essential, for the 'sensory-discriminative' aspects of touch and pain, that is, the ability to discriminate the intensive, spatial and temporal aspects of a stimulus (Melzack and Casey, 1968; Albe-Fessard et al., 1985; Willis, 1985). In the present case, the various discriminative dimensions of heat pain were affected to different extents. Specifically, spatial localization was grossly distorted, intensity scaling was offset near the threshold range, but otherwise appropriate, while the temporal perception of heat pain was unaffected. An investigation of the somesthetic response properties of medial thalamic neurons in the awake monkey may be relevant here. Bushnell and Duncan (1989) demonstrated that some of the medial thalamic neurons could encode noxious heat intensity to the same extent as lateral thalamic neurons, however these medial thalamic neurons have very large (non-discriminating) receptive fields on the body. These observations suggest that portions of the medial thalamus receiving nociceptive input have the ability to preserve stimulus intensity information, but not necessarily spatial (somatotopic) information. If so, one would expect that a laterally located lesion would have the differential effects upon intensive and spatial aspects of pain perception that were observed in the present study.

The particular pattern of heat pain hypalgesia, only at the lower end of the range (Figs. 5, and 7), was similar to the pattern produced by an individual with a corpus callosum lesion (Stein et al., 1989). This 'split-brain' case was tested in a manner so that the subject would report perceptions resulting only from information relayed via ipsilateral spinal cord and brain stem pathways. Thus, the heat pain scaling pattern revealed by R.S. could be based on sensory input solely mediated by ipsilateral pathways.

Due to the ambiguous boundaries of edema, gliosis and ischemia, it is not possible to precisely demarcate the extent of pathological versus normal tissue of the thalamus and surrounding areas in this case. The more posterior regions of the thalamus that are known to receive spinothalamic input (Bowsher, 1957; Berkley, 1980; Jones, 1985; Gingold et al., 1991; Craig et al., 1994) were within the hyperintense halo surrounding the hemangioma. At least some of the sensory changes paralleled MR-observable changes in the hyperintense halo, and thus may be related to changes in neural tissue function within the halo region. Specifically, the maximum extent of the halo (and presumably its greatest influence on thalamic processing) was observed in the September 1993 MR study, while the highest thresholds contralaterally for all tests were recorded in the spring (touch

and mechanical pain) or summer (heat pain) of 1993. The next MR study (February 1994) showed a significant resolution of this halo, and R.S. demonstrated improved (lower) thresholds in the same tests during late 1993 and early 1994. It is perhaps significant that the thermal allodynia and spontaneous pain only developed after the resolution of the cerebral edema, and after partial sensory recovery.

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