Dysaesthesiae induced by physiological and electrical activation of posterior column afferents after stroke

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Abstract

Six of 48 stroke patients had functionally limiting dysaesthesiae induced by repetitive light touch, joint movement, or neuromuscular electrical stimulation (NMS). Only one of these six patients had a thalamic lesion. Quantitative sensory testing showed substantial impairment of pain and temperature sensation in all six patients, whereas light touch, vibration and position sense, and graphaesthesia were normal (three patients) or relatively spared (three patients). By contrast, none of 15 stroke patients in whom NMS did not evoke dysaesthesiae had clinical evidence of dissociated sensory loss. Conscious perception of joint movement and light touch is mediated mainly by the same population of large myelinated fibres activated preferentially by low intensity electrical stimulation. It is suggested that activation of these nonnociceptive, presumably dorsal column, afferents may contribute to dysaesthesiae in some patients with sensory loss after stroke.

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Pain and dysaesthesiae have been associated with sensory loss since the description of the thalamic syndrome by Dejerine and Roussy.[1] Dysaesthesiae indistinguishable from those occurring in thalamic syndrome or thalamic pain also complicate extrathalamic stroke.[2-8] Whereas these sensory phenomena may seem to be spontaneous, they are more commonly evoked with innocuous somatic sensory stimulation,[2-4] and such "painful over-reaction to objective stimulation" is a hallmark of central pain syndromes.[2] Indeed, Kendall suggested that all central pain arises from external stimulation, and preferred to describe such phenomena as dysaesthesiae.[9]

At the level of the spinal cord, dysaesthesiae are associated with physiological[10-12] and anatomical[13-15] evidence of neospinothalamic deafferentation, with relative sparing of dorsal columns. We have suggested previously that dorsal column sparing in such patients is more than coincidental, and that dorsal column activation may contribute to the development of dysaesthesiae in patients with neospinothalamic lesions.[10-12] We have even found disinhibition of somatosensory evoked potentials in a patient with the anterior spinal artery syndrome, consistent with this hypothesis.[16] In stroke, many patients with dysaesthesiae have lesions that affect the function of the neospinothalamic tract—that is, appreciation of pin prick and temperature.[4 5 8 17] Because many of these patients also show preservation of sensory modalities attributable to the dorsal columns,[18-20] we decided to look for evidence that activation of dorsal column afferents contributes to dysaesthesiae after stroke.

Methods

We reviewed the records of 48 stroke patients referred to the Division of Restorative Neurology, Baylor College of Medicine, Houston, Texas, for neurological rehabilitation, to identify patients with dysaesthesiae related to light touch or joint movement. The extent of each patient's stroke was determined with CT or MRI.

Eighteen of these 48 patients were treated with neuromuscular electrical stimulation (NMS) in an effort to improve the fatigue resistance of paretic muscles, or to possibly modulate spasticity.[21 22] Briefly, this technique consists of electrical stimulation of weak or hypertonic muscles with trains of transcutaneous stimuli (20–50 Hz) delivered through surface electrodes overlying the muscle belly. Stimulus intensity is adjusted to produce repetitive contraction of the affected muscle without producing pain or muscle spasm. Stimulus variables are otherwise similar to those employed for transcutaneous electrical nerve stimulation (TENS).[23]

In patients identified as having dysaesthesiae, we tested sensory function with clinical and quantitative sensory testing. We tested light touch perception with Von Frey hairs, recording threshold as the lowest stimulus intensity detected in >50% of trials. We determined vibration thresholds over the clavicle, second metacarpal, first metatarsal, and anterior tibia with a vibrameter (Somedic AB) by the method of Goldberg and Lindblom.[24] We assessed thermal sensibility over cervical, thoracic, lumbar, and sacral dermatomes with a thermotest thermal stimulator (Somedic AB) according to the method of Fruhstorfer *et al.*[25]

Results

Six of 48 patients had functionally limiting dysaesthesiae induced or exacerbated by light touching or movement. None of the remaining 42 patients were affected with central pain. In three of the six patients with dysaesthesiae, these sensations were induced primarily by NMS. Table 1 summarises the clinical features of these six patients. Lesion

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Table 1   Clinical features of stroke patients with functionally limiting dysaesthesiae

Patient	Age (y)	Sex	Neurological lesion	Neurological deficit	Dysaesthesias induced by
1	54	M	Right thalamic haemorrhage	Left hemiparesis and sensory loss	Repetitive light touch Vibration
2	70	M	Left parietal infarction	Right hemiparesis and sensory loss	Electrical stimulation Repetitive light touch
3	73	M	Left brainstem infarction	Right hemiparesis and sensory loss	Electrical stimulation Joint movement
4	61	M	Left parietal haemorrhage	Right hemiparesis and sensory loss	Electrical stimulation Repetitive light touch
5	68	F	Left middle cerebral artery infarction	Right hemiparesis and sensory loss Broca's aphasia	Repetitive light touch Joint movement
6	42	F	Brainstem infarction	Left sided sensory loss Quadriparesis	Repetitive light touch Joint movement

location was variable, including brainstem and cortical regions; only one patient had a thalamic lesion. Each of these six patients had impaired thermal discrimination and pin prick sensibility (table 2). Light touch, position sense, graphaesthesia, and vibratory sensibility were normal (patients 1–3) or only variably affected (patients 4–6). By contrast, none of 15 patients in whom NMS did not induce dysaesthesiae showed clinical evidence of dissociated loss.

PATIENT 1
This 54 year old man developed left sided sensory loss and hemiparesis after a right thalamic haemorrhage. At the onset of his neurological deficit, he noted dysaesthesiae described as "intensely uncomfortable sensations, not pain." These sensory abnormalities affected the left side of his face, neck, and trunk, to the level of his waist. The sensations were also experienced throughout his left leg, but were less intense. Thermal discrimination and pin prick sensibilities were impaired throughout his left side. By contrast, the thresholds for detection of vibratory and tactile stimulation of deafferented regions were normal, but caused allodynia, interpreted as a distressing "burning-tingling sensation" spreading from the site of stimulation. Position sense and graphaesthesia were normal. Phenytoin, carbamazepine, and amitriptyline had no effect on dysaesthesiae. Electrical stimulation through electrodes implanted in the thalamus[26][27] 2·5 years after the onset of symptoms caused some improvement.

PATIENT 2
This 70 year old physician developed right hemiparesis and sensory loss after a left parietal infarction. Six months later, he noted "burning" dysaesthesiae during movement of his paretic right arm. These improved with amitriptyline and gradually subsided; amitriptyline was discontinued. Eight years

later, we evaluated him for rehabilitation. He had hemiparesis and decreased pin prick and temperature perception over his entire right side. Vibratory and position sense, light touch perception, and graphaesthesia were normal. Treatment of his spastic right arm with NMS was initially tolerated, but was stopped after several sessions due to recrudescence of his original "burning" dysaesthesiae, extending up the arm and over the anterior thoracic region. These dysaesthesiae were directly related to repetitive light touching of the arm, which now elicited reflex withdrawal. These sensations did not persist beyond the duration of light mechanical stimulation.

PATIENT 3
This 73 year old man developed a right hemiparesis and sensory disturbance after a left brainstem infarction. He noted mild right sided dysaesthesiae during the next two years, described as an unpleasant "heavy sensation" of "muscles pulling" during movement of his arm and leg. These sensory abnormalities affected his entire right arm, the lateral aspect of his right chest, and the anterior aspect of his right leg. A right foot drop persisted as his most significant problem. Thus four years after his stroke he was referred for NMS. He had impairment of pin prick and thermal sensibilities, and mild impairment of vibration. Light touch, position sense, and graphaesthesia were normal. Dorsiflexion strength seemed to be improved by NMS, but after several weeks it caused increasingly intolerable exacerbation of the patient's sensation of "heaviness" in his arm and leg. Although the patient noted that NMS helped him to walk, he could no longer tolerate the stimulation. Interestingly, movement of his right arm now worsened dysaesthesiae in his right leg, and vice versa.

PATIENT 4
This 61 year old man developed right hemiparesis and "burning" dysaesthesiae after a

Table 2   Quantitative sensory testing in stroke patients with dysaesthesias

Patient	Temperature discrimination	Thermal pain perception	Pin prick sensibility	Light touch Von Frey hairs	Vibratory sensation	Graphaesthesia	Position sense
1	1	1	1	0	0	0	0
2	1	2	1	0	0	0	0
3	2	1	1	0	1	0	0
4	2	1	1	1	1	1	1
5	2	2	2	2	2	2	1
6	2	1	2	0	0	NT	1

0 = Normal; 1 = threshold 2–5 times higher on symptomatic side; 2 = threshold > 5 times higher or perception absent on symptomatic side (modified from Boivie *et al*[5]); NT = not tested.

left parietal haemorrhage. These sensory abnormalities affected the entire right hemibody. Three years later, he was referred for NMS to treat dorsiflexion weakness. He had a spastic right hemiparesis with right sided sensory loss; temperature discrimination was severely impaired and all other sensory modalities were moderately affected. Repetitive light touching and vibration aggravated the "burning" dysaesthesiae. When used as a functional prosthesis, NMS seemed to improve his gait, but increasingly worsened his dysaesthesiae, and was discontinued at his insistence.

PATIENT 5

This 68 year old woman developed a Broca's aphasia with right hemiparesis and sensory loss after a left middle cerebral artery stroke. When evaluated two months after the stroke, she had severe impairment of all sensory modalities, but with relative sparing of position sense. In physical therapy sessions, she developed gradual intolerance to passive manipulation of the fingers or wrist of her plegic right hand. Although non-fluent, she expressed her displeasure with striking facial grimacing during passive movement or repetitive light touching of her right arm.

PATIENT 6

After chiropractic cervical manipulation, this 42 year old woman developed a spastic tetraparesis, diplopia, sensory disturbance, and a brainstem infarction. Angiography showed occlusion of the right vertebral artery. Five months after the stroke, she had involvement of the right third and fourth cranial nerves, right sided dysmetria, and a spastic tetraparesis. She had impaired pin prick sensibility throughout her left arm and leg, but light touch, vibration, and position sense were normal. She complained bitterly about "deep aching" and "burning" sensations precipitated by repetitive light touching or movement of her left arm or leg. These sensory abnormalities predominantly affected her left hand and her entire left leg. She considered volitional leg movement impossible because of these dysaesthesiae.

Discussion

We noted that somatic stimulation induced dysaesthesiae in six of 48 patients after stroke. We analysed sensory function in these patients to clarify this phenomenon. With quantitative sensory testing, we found substantial impairment of pin prick and temperature sensibilities in all patients, virtually a consistent finding in patients with dysaesthesiae after stroke.[48] Sensibilities attributable to dorsal column function[18-20] were, however relatively preserved in our patients. This finding is similar to the experience of other investigators,[48] including findings of "thalamic pain" in patients with normal somatosensory evoked potentials.[17] Non-noxious, somatic stimulation may also produce or exacerbate dysaesthesiae in patients with traumatic spinal cord injury,[10] anterior spinal artery syndrome,[11] and

anterolateral cordotomy.[28] These patients all have impairment of neospinothalamic pathways, with relative preservation of the dorsal columns.

Our patients had dysaesthesiae induced by repetitive light touch, vibration, and joint movement. Under normal circumstances, such mechanoreceptive stimuli probably activate low threshold, myelinated, dorsal column afferents.[18-20] Similarly, NMS,[22] which caused dysaesthesiae in three of our patients, probably produces preferential activation of large diameter, non-nociceptive afferents,[29 30] innervating both skin and muscle. As our patients experienced dysaesthesiae with low intensity tactile and electrical stimulation, our findings suggest either an abnormal CNS response to physiological stimulation of large myelinated afferents, or sensitisation of primary nociceptors.[31] Clearly, nociceptive sensitisation[32] seems an untenable explanation for our findings, in the absence of concomitant peripheral injury. Some findings, however,[31 33-36] indicate that physiological activation of low threshold, large myelinated fibres may induce dysaesthesiae associated with peripheral nerve injury.

In patients with injury to the CNS, dysaesthesiae induced by activation of large myelinated afferents may be related to dissociated sensory loss. Although our study was not prospective, we found that NMS was well tolerated by stroke patients without evidence of dissociated sensory loss on clinical examination. Transcutaneous electrical nerve stimulation (TENS) increased pain intensity in one third of patients with poststroke pain.[37] Most of these patients had impaired temperature appreciation but relative sparing of epicritic sensibilities.[45] Stimulus variables used for TENS are similar to those we used for NMS, and TENS activates large myelinated afferents.[23] Treatment by TENS was also reported as being "intolerably painful" in a group of patients with "thalamic syndrome".[38] Further, dysaesthesiae have been evoked or exacerbated by direct electrical stimulation of the dorsal columns in patients with dissociated sensory loss due to spinal cord lesions,[10 11 39] and during local anaesthesia.[40] These findings are consistent with our hypothesis that activation of dorsal column afferents may cause dysaesthesiae in patients with lesions of neospinothalamic pathways.

Admittedly, our findings do not prove a causal role for the dorsal columns. Indeed, there is evidence of considerable redundancy in the transmission of sensory information associated with mechanoreceptive sensibilities, such as vibration and position sense.[41 42] (See Greenberg *et al*[43] and Davidoff[44] for reviews.) On the other hand, clinical studies have traditionally associated disorders of light touch, joint position, and vibration with abnormal somatosensory evoked potentials (SEPs).[45] There is convincing experimental evidence that the dorsal columns are the primary neural substrate for SEPs in primates.[46] In humans, Berić and colleagues found that preservation of thresholds for light touch and vibration correlated with preservation of SEPs in 110 patients with spinal cord injury studied

with quantitative sensory testing.[19] Even if the sensory information associated with discriminative sensibilities is not conveyed solely by the dorsal columns, the importance of our clinical findings is that pervasive, unpleasant sensations may accompany activation of nonnociceptive afferents in patients with central sensory abnormalities. The mechanisms for this misinterpretation of physiological sensory input are unknown. These phenomena, however, suggest the possibility[12 16] that neospinothalamic and associated pathways may normally have inhibitory influences on sensory input conveyed via non-nociceptive pathways.

In conclusion, we emphasise that our findings do not necessarily apply to all unpleasant sensations that may be experienced after stroke. To suggest otherwise would be implausible. For one thing, they seem to be directly opposite to those anticipated by the gate control theory of pain.[47] Indeed, some patients with poststroke pain do obtain relief with non-noxious counterstimulation.[37] Yet these apparent conflicts with our findings are only relevant if we suppose that all unpleasant sensations experienced after stroke reflect the same pathophysiological mechanism. Many of our patients observed that their dysaesthesiae were distinct from pains that they had experienced previously, and most of our patients did not experience any dysaesthesiae in the absence of somatic stimulation. Therefore, we suggest that our patients did not experience pain, but rather dysaesthesiae—abnormal physiological responses to non-noxious activation of somatic afferents. Thus our findings do not necessarily conflict with the gate control theory. Future prospective studies are required to further assess these issues, and to ascertain the incidence of dysaesthesiae after stroke.

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