HIGH LIGHT

Dysynchiria: Watching the mirror image of the unaffected limb elicits pain on the affected side

Abstract—People with complex regional pain syndrome type 1 (CRPS1) watched a reflected image of their unaffected limb being touched and felt pain or paresthesia at the corresponding site on the affected limb. The authors suggest that allodynia and paresthesia can be mediated by the brain and that dysynchiria has implications for the understanding and management of CRPS1.

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Complex regional pain syndrome type 1 (CRPS1), characterized by nonlocalized burning pain and motor and sudomotor disturbance, occurs after benign injury or after stroke. In CRPS1, there is reduced representation of the affected limb in somatosensory cortex[1] and sensory referral to adjacent areas.[2] Similar changes are observed in amputees with phantom pain and poststroke patients, both of whom demonstrate synchiria: stimulation of one hand evokes sensation on both hands.[3] We also found one anecdote of pain evoked in the phantom limb of an amputee when he watched the mirror image of a cup being yanked from his other hand[4] (page 43). Available studies that have specifically tested this in stroke patients report that pain could not be evoked by this method,[3] but data are limited and the possibility cannot be excluded. We stimulated the unaffected limb of people with CRPS1 while they watched the reflected image, the "virtual limb," in a mirror. We hypothesized that if brain mechanisms underpin allodynia (pain evoked by normally nonpainful stimuli) and paresthesia (altered sensation) in CRPS1, then those phenomena should be evoked by watching an image of the painful hand being touched (visual input alone), in a manner similar to synchiria.

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Methods. Ten patients diagnosed with CRPS1 according to revised International Association for the Study of Pain criteria, 9 patients with neck-related arm pain of comparable intensity and paresthesia, 9 patients with non-CRPS1 localized pain of comparable intensity, and 9 asymptomatic controls participated (table).

After providing consent, patients described their symptoms. On a line drawing of the affected body part, patients "mapped" the areas they thought would be painful to touch (allodynia) and the areas they thought would have altered sensation to touch (paresthesia). Two assessments were then undertaken: 1) with patient's eyes closed, sensation was tested at numerous points on the affected limb by application of light touch (a pen lid), punctate pressure (exposed tip of a paper clip), and cold (application of ice); and 2) with a mirror placed between the patient's limbs, the affected limb was hidden from view and the patient watched the reflected image of the opposite limb, the virtual limb, receiving the sensory assessment outlined above. Patients concentrated on the virtual limb throughout. In each assessment, patients reported the quality and location of the evoked sensation. Both assessments were performed on the other patients and the asymptomatic controls.

Results and discussion. In CRPS1 patients, four distinct phenomena were present (figure, A). First, when the stimulation site on the pain-free limb corresponded to an area of normal sensation on the affected limb, patients reported a normal sensation at the stimulated site. That is a normal response and was consistently present in all the subjects tested. Second, when the stimulation site on the pain-free limb corresponded to an area of allodynia on the affected limb, CRPS1 patients reported normal sensation at the stimulated site but pain at the corresponding site on the affected limb. Several patients quickly withdrew their affected limb, and two patients chose not to finish an assessment because it was too painful. Third, when the stimulation site on the pain-free limb corresponded to an area of paresthesia on the affected limb, CRPS1 patients reported normal sensation at the stimulated site but "pins and needles" or "tingling" at the corresponding site on the affected limb. Thus, it was possible to map areas of allodynia and paresthesia on the virtual limb. We propose these latter phenomena collectively be called *dysynchiria*. Fourth, when ice was applied to the pain-free limb in an area that corresponded to an area of paresthesia on the affected limb, patients

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Table *Subject characteristics*

Subject: sex/ age, y/ dominant hand	Anatomic location of symptoms, injury	Diagnosis	Sensory findings	Motor findings	Autonomic findings	Pain/ duration, mo
M/36/R	L hand, minor impact	CRPS1	HA, AD, PT	PoM, Trem, RoM	Color, sweating, temp.	7/2
M/30/R	R foot, ankle sprain	CRPS1	HA, AD, PT	PoM, RoM	Color, sweating, temp.	5/1
M/58/R	R hand, sprain	CRPS1	HA, AD, PT	PoM, Trem, RoM	Color, sweating, temp.	7/2
F*/56/R	L knee, minor impact	CRPS1	HA, AD, PT	PoM, Trem, RoM	Color, sweating, temp.	6/32
F*/50/R	L elbow, minor impact	CRPS1	HA, AD, PT	PoM, Trem, RoM	Color, sweating, temp.	5/16
F/51/L	L hand, unknown	CRPS1	HA, AD, PT	PoM, RoM	Color, sweating	6/7
M*/34/R	L hand, colles†	CRPS1	HA, AD, PT	PoM, RoM	Color, sweating	4/4
F*/36/R	R hand, colles†	CRPS1	HA, AD, PT	PoM, Trem, RoM	Color, sweating	5/7
F*/45/L	L wrist, CTR surgery	CRPS1	HA, AD, PT	PoM, Trem, RoM	Color	7/6
F*/52/R	R hand, sprain	CRPS1	HA, AD, PT	PoM, Trem, RoM	Sweating	5/9
M/56/R	R hand/arm, MVA	WAD	HA, PT	PoM, RoM		6/7
F/46/R	R hand, unknown	WAD	HA, PT	PoM, RoM		3/48
M/51/R	R hand/arm, unknown	Neck and arm pain	HA, PT	PoM, RoM	Sweating	6/12
F/36/R	L hand/arm, MVA	WAD	PT	RoM		4/8
F/46/R	L hand, unknown	Neck and arm pain	HA	PoM	Sweating	5/13
F/51/L	R hand/arm, MVA	WAD	PT	PoM		4/11
M/57/R	R elbow, MVA	WAD		PoM, RoM		3/8
M/36/R	L elbow/arm, MVA	WAD	PT	PoM, RoM		5/6
M/22/R	R hand, football injury	Neck and arm pain		PoM		6/9
F/57/R	R hand, –	OA		PoM		5/60
M/42/R	L elbow, occupational	Lateral epicondylalgia	HA, AD	PoM		3/7
F/32/R	L knee, arthroscopy	Postsurgical pain	HA, AD	PoM, RoM		5/1
F/39/R	R ankle, sprain	Ankle pain	HA	PoM, RoM		5/11
F/22/R	R ankle, sprain	Ankle instability		PoM, RoM		5/6
M/58/L	R hand, crush injury	Metacarpal†	HA, AD	PoM		7/18
M/49/R	R elbow, tennis	Lateral epicondylalgia		PoM		5/12
M/36/R	L foot, sprain	Ankle pain		PoM, RoM		4/4
F/33/L	R foot, fibula†	Ankle pain	HA	PoM, RoM		4/8

* Participated in experiment 2. Nine control subjects (6 women, mean age = 42 years) also participated.
† Noncomplicated fracture.

Pain = mean intensity of pain on visual analog scale over past week; R = right; L = left; CRPS1 = complex regional pain syndrome type 1; HA = hyperalgesia; AD = allodynia; PT = paresthesia; PoM = pain on movement; Trem = tremor on movement; RoM = range of movement; color = color changes; sweating = sweating changes; temp. = temperature changes; CTR = carpal tunnel release; MVA = motor vehicle accident; WAD = whiplash-associated disorder; OA = osteoarthritis.

reported perceiving a cold stimulus on both limbs: thus, synchiria to cold. Dysynchiria and synchiria were not present in the other patients or controls, or when patients with CRPS1 could not see the virtual limb being stimulated, which suggests the effect is not due to enhanced synaptic efficacy in bilateral projections of peripheral neurons.

Dysynchiria is consistent with conventional belief that sensory input from a painful limb is neither sufficient nor necessary for pain. It is also known that allodynia involves profound changes in the properties of central neurons.[5] However, dysynchiria provides the first evidence that allodynia and paresthesia can be mediated with clearly defined sensory boundaries, by the brain and in the absence of peripheral input from the area. Perhaps the brain holds an implicit perceptual representation that can be activated by contralateral somatic input, via central neurons with bilateral inputs, and visual input, which together indicate that the body part in question is being stimulated. That would be consistent with work in amputees with rheumatoid arthritis in whom perceived stiffness

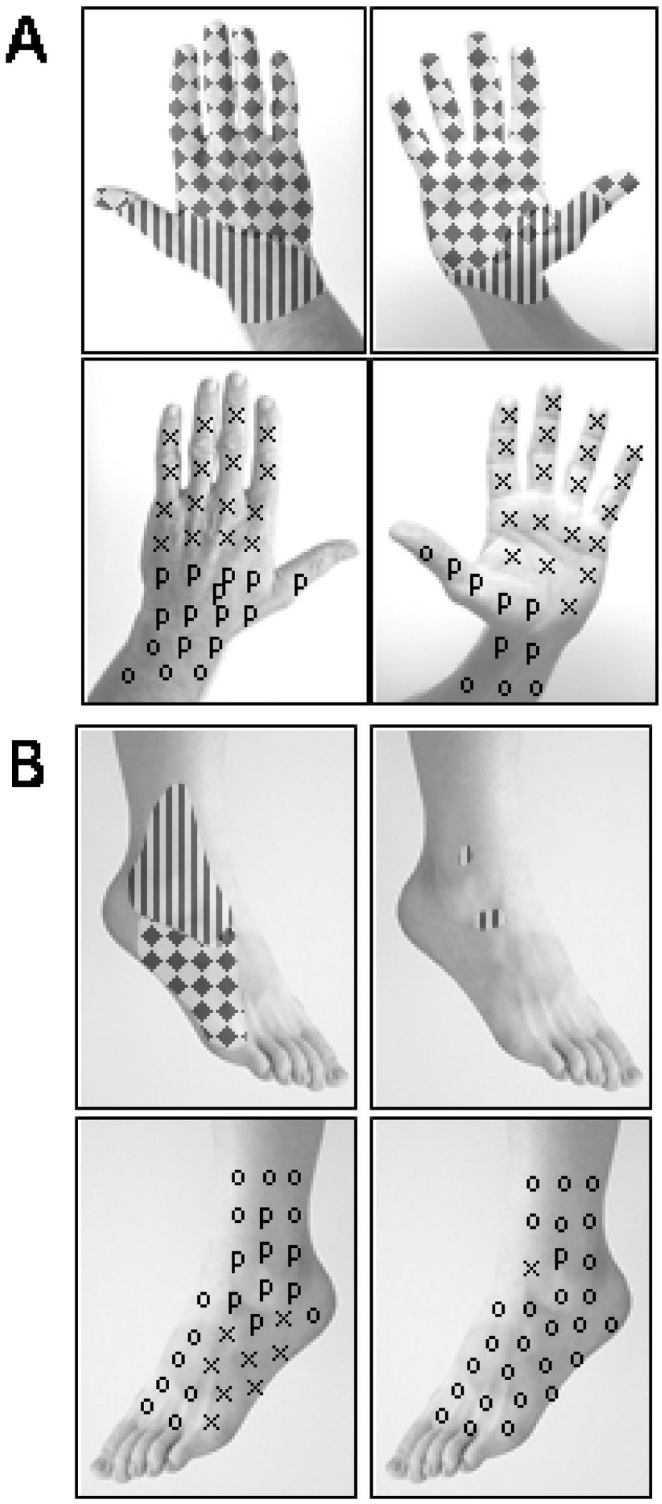

Figure. Dysynchiria in two subjects. Areas of paresthesia (checks) and allodynia (vertical lines) determined by sensory testing of the affected limb and response to light touch and punctate pressure on the unaffected limb while watching the "virtual limb" in a mirror. Areas on unaffected limb that evoked dysynchiria (x = odd sensation, p = pain), and a normal response (o = no sensation on the affected limb) on the affected limb are shown. Panel B shows the response to "training the brain." Note reduction in area of allodynia and paresthesia and parallel reduction in dysynchiria.

of phantom joints closely matched that of intact joints.[6] The experience of joint stiffness is not dependent on ongoing peripheral input and may be held in some brain perceptual representation.

If allodynia and paresthesia can be produced by the brain in the absence of corroboratory sensory input, then they should be amenable to treatment aimed at "training the brain." Such treatments (e.g., graded motor imagery) have been successful in several groups characterized by cortical reorganization, including CRPS1.[7] Therefore, after such treatment, we reassessed five patients (see table 1) who had CRPS1 of one hand. When treatment reduced the area of allodynia and paresthesia, those reductions were paralleled by a reduction in the area in which dysynchiria was observed (figure, B). Because the order in which limbs were assessed was varied between testing occasions and between patients, we conclude that changes are unlikely to reflect conscious processes or "somatosensory memory."

This work has clinical implications for CRPS1 and potentially for other conditions characterized by brain changes. The observation of dysynchiria suggests that allodynia and paresthesia can be mediated by the brain, which is in contrast to conventional notions that allodynia and paresthesia must reflect state-dependent changes, or breakdown, in peripheral or second-order spinal neurons. That said, the mechanisms by which this might occur are unclear. Possible mechanisms include bilateral projections to sensory cortices, or activation of the "mirror neuron system."[8] Alternatively, it seems feasible that the same sensitivity changes that are known to occur at, for example, the dorsal horn, also occur in the brain. In that situation, perhaps activity of bimodal visual–somatosensory cells[9] is sufficient to activate pain systems. Further research should elucidate these mechanisms. Finally, the effect of "training the brain" both on the affected limb and on dysynchiria and synchiria suggest that the brain could be a viable target for treatment in other groups characterized by reorganization, pain, and paresthesia, e.g., spinal cord injury and stroke.

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