Feeling Sounds after a Thalamic Lesion

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Objective: The ventrolateral nucleus of the thalamus (VL), based on its connectivity with the cerebellum and motor cortex, has long been considered to be involved with motor functions. We show that the human VL also plays a prominent role in sensory processing.

Methods: Structural magnetic resonance imaging and diffusion tensor imaging were used to localize a small lesion restricted to the right VL in a patient with contralesional sensory processing deficits. Systematic assessments of anatomic brain organization and behavioral measurements of somatosensory and visual processing were conducted at several time points after stroke.

Results: Initially, the patient was more likely to detect events on the contralesional side when a simultaneous ipsilesional event was presented within the same, but not different, sensory modality. This perceptual phenomenon, which we refer to as unisensory antiextinction, persisted for several months before transforming into a form of synesthesia in which auditory stimuli produced tactile percepts. Tractography performed on the diffusion tensor imaging data showed altered connections from the lesioned thalamus to the cerebral cortex, suggesting a neural basis for these sensory changes.

Interpretation: These results demonstrate a role for the VL in sensory processing and suggest that reorganization of thalamocortical axonal connectivity can lead to major changes in perception.

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In [other patients] the thought, sight, or noise of a scratching, rubbing or scraping motion evoked severe tingling in the affected hand. —*M. B. Bender* (1945)

The influences of one sensory stimulus on the detection of another simultaneously occurring target stimulus can often be dramatic, with target detection either impaired or facilitated depending on the nature of the task.[1–5] This is especially true in patients with lateralized sensory and attentional deficits consequent to unilateral brain damage. For example, patients with hemispatial neglect after right temporal/parietal damage (for reviews, see Driver and Mattingley,[6] Rafal,[7,8] and Vallar[9]) frequently show extinction, that is, the inability to detect and report a contralesional event when simultaneously presented with an ipsilesional one.[10–12] Extinction can occur after either cortical or subcortical damage,[12,13] including thalamic lesions,[14] is considered to be a high-level attentional deficit rather than a low-level sensory disorder, and can affect visual, somatosensory, and auditory processing. Recently, multisensory extinction has also been demonstrated (eg, a visual event on the ipsilesional side extinguishing a contralesional tactile one[15–17]), supporting the idea that extinction occurs at a high level after initial sensory encoding.

Unilateral brain damage can also produce misperceptions of a single sensory stimulus, as in the phenomena of allesthesia and intermanual sensory referral. Allesthesia occurs when a unilateral tactile stimulus delivered to the impaired side is felt in a corresponding area on the intact side.[12] In contrast, intermanual sensory referral occurs when a tactile stimulus delivered to the intact side is felt in a corresponding area on the affected side.[12,18] In both cases, a unilateral tactile stimulus is mislocalized to the corresponding portion of the opposite side of the body, suggesting cross talk between somatotopic representations in the two hemispheres of the brain. As with extinction, allesthesia and intermanual sensory referral can each occur after either cortical or subcortical damage.[12,18]

Another related perceptual phenomenon has been referred to as antiextinction, in which detection of contralesional events is *better* when a simultaneous ipsilesional stimulus is presented.[19,20] Whereas the

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psychological and neural mechanisms underlying antiextinction remain unclear, the consistent modulation of antiextinction by task requirements suggests that top-down modulation of sensory processing plays a role.[19,20] Although antiextinction has been reported in only two patients, both patients appeared to have damage to the parietal cortex and thalamus.

In this article, we describe the results of several behavioral and neuroimaging studies conducted on a patient with unique sensory phenomena after a small and discrete lesion to the right ventrolateral nucleus of the thalamus (VL; Fig 1). In the initial poststroke experiments, we observed multisensory neglect with unisensory antiextinction in this patient. More recently, however, we measured a new brain-damage–induced phenomenon where a stimulus in one sensory modality induces sensations in another. Specifically, the patient demonstrated a striking form of sensory reorganization after thalamic damage: approximately 18 months after the initial antiextinction phenomena, the patient began to feel tactile sensations in response to sounds.

Patient and Methods

Patient

The patient was a 36-year-old, right-handed female professor who approximately 9 months before the first examination had suffered a lacunar infarct to the right VL. Subsequent to the infarct, she reported noticeable changes in her sensory and attentional abilities, consistent with hemispatial neglect. For example, she reported occasionally walking into and bumping the left sides of doorways and tended to veer rightward when driving. Neuropsychological and neurological assessments conducted approximately 1 year after stroke, however, demonstrated no measurable signs of visual neglect as her line bisection, line and shape cancellation, and double visual simultaneous stimulation performance were all normal. Somatosensory functions were abnormal on the contralesional half of her body, with decreased sensations to finger taps and pricks on her left foot, hand, arm, and face. Apart from the decreased sensations contralesionally, the patient reported no other sensory or motor disturbances. The patient reported no form of synesthesia before the infarct.

Apparatus and Stimuli

For all testing sessions, an Intel-based personal computer was used for stimulus timing and presentation. For the first testing session, the computer controlled the presentation of the visual stimuli, which were light emitting diodes (LEDs) that were illuminated for 5 milliseconds, and the tactile stimuli, which were 2cm filaments that were attached on solenoids. The tactile stimuli were delivered by a computer-interfaced, custom-made relay switchboard, which controlled the solenoids. The LEDs and solenoids were mounted onto a vertical Plexiglas sheet placed approximately 57cm from the patient's eyes and directly above her outstretched hands that were resting on a table. A small filled square (0.1°) served as the fixation point in the center of the display, which was 20cm above and 15cm to the left and right of the LEDs and the right and left hands. On each trial, either a unilateral tactile (left or right), unilateral visual (left or right), bilateral tactile, bilateral visual, multisensory with tactile left/visual right, multisensory with visual left/tactile right, or no stimulus (catch trials) was delivered. Because we were interested in the magnitude of extinction that this patient exhibited, there were twice as many bilateral trials as unilateral trials in each session. The patient was tested in 6 separate sessions, with each session containing 70 trials (10 trials for each bilateral condition and the catch trials and 5 trials for each unilateral condition). Her task was to report whether something was seen or felt on either the left, the right, both, or neither sides.

The second behavioral experiment was identical to the first, except for the following changes. A 200-millisecond warning tone (500Hz) was delivered by the computer through its speaker and was used to signal the start of a trial. At 500 milliseconds after the tone, an electrical cutaneous stimulus (0.3-millisecond square wave; intensity set at 50% detection for each hand as assessed before the experiment) was delivered to the left hand alone, the right hand alone, to both hands simultaneously, or was not delivered on the catch trials. Each of these four trial types occurred with equal probability and was randomly presented throughout the experiment with the only constraint being that three consecutive trials could not be from the same condition. No visual stimuli were used in this experiment, but the patient was asked to fixate a mark on the table that was placed in between and equidistant from each hand. Eight sessions of 40 trials each were administered, for a total of 320 trials.

The third behavioral experiment used a piezoelectric stimulator that was attached to the dorsal surface of the left hand. The tactile stimulus was a 1,000-millisecond, 200Hz oscillation of the piezoelectric stimulator. The low-frequency tone was a 1,000-millisecond, 200Hz pure-frequency sine-wave auditory tone. The higher frequency tone was a 1,000-millisecond, 750Hz pure-frequency sine-wave auditory tone. A total of 45 trials for each of the 4 conditions (tactile, low tone, high tone, and no stimluus catch trials) was collected in one testing session.

Magnetic Resonance Imaging

The first diffusion tensor imaging (DTI) scans were acquired at Massachusetts General Hospital on a 3.0-Tesla Siemens Allegra head-only scanner (Siemens Medical Systems, Malvern, PA). Twenty 4mm-thick whole-brain axial slices were acquired using 6 gradient directions with a maximum b value of 700 sec/mm^2. The field of view was set at 256 $\times$ 256mm, for an in-plane resolution of 2 $\times$ 2mm. The second set of imaging data was acquired at Texas Children's Hospital using a six-channel parallel receiver array head coil on a Philips 1.5-Tesla whole-body scanner (Philips Medical Systems, Bothell, WA). The Philips 32-direction diffusion encoding scheme (high angular resolution) was used without gradient overplus. A total of 55 transverse slices were acquired using a maximum b value of 860 sec/mm^2. The field of view for this scan was 240 $\times$ 240mm, with 2.5mm slice thickness and no gap, yielding a nominal spatial resolution of 2.5 $\times$ 2.5 $\times$ 2.5mm. The third set of imaging data was acquired using a Philips 3.0-Tesla whole-body scanner at the

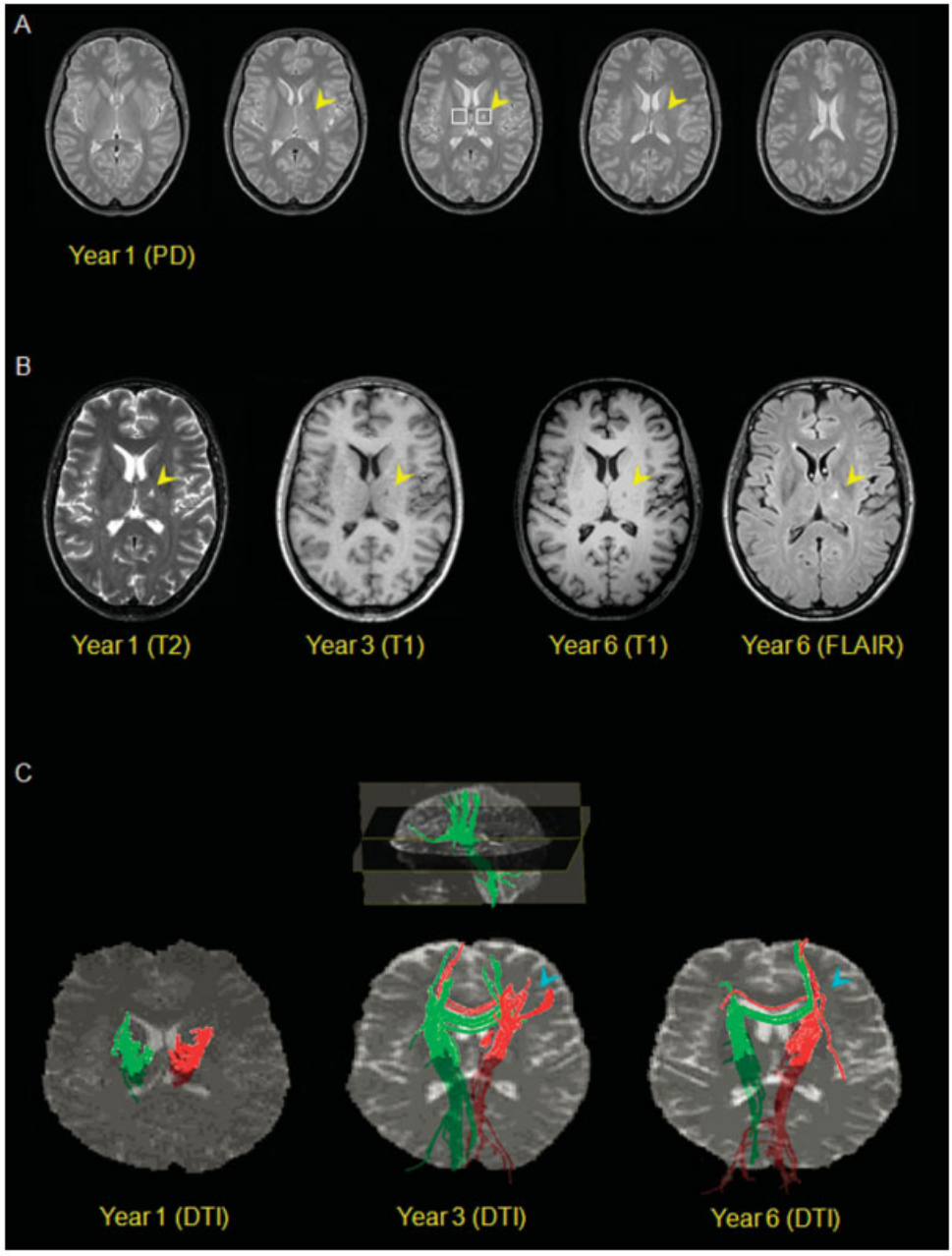

Fig 1. (A) A proton density (PD)–weighted, 3-Tesla structural magnetic resonance imaging (MRI) scan of the patient 1 year after her stroke. A ventral-to-dorsal series of axial slices through the brain are shown (right is right in all images). The lesion, located in right ventrolateral nucleus of the thalamus (VL), is visible on only three sequential 2mm-thick axial slices (yellow arrowheads). Squares *outline the seed regions of interest (ROI) used for diffusion tensor imaging (DTI) fiber tracking from the affected right and unaffected left VL. (B) Single axial slices from structural MRI scans taken at three different poststroke time intervals show no changes in the lesion size or volume* (yellow arrowheads). *T1 = T1-weighted imaging sequence; T2 = T2-weighted imaging sequence; FLAIR = flip-angle inversion recovery imaging sequence. (C) Results of the DTI tractography. Fiber bundles leaving the normal left VL ROI are shown in green, whereas fiber bundles leaving the damaged right VL ROI are shown in red. The underlying image is the b0 (null direction) DTI image. The 1-year poststroke DTI shows no asymmetry between the left and right hemispheres; fiber bundles in both hemispheres are artificially shortened because of the magnetic resonance acquisition parameters. The sagittal view (top) of the 3-year DTI data illustrates normal focal projections from unaffected VL to the motor and premotor cortex. The axial view for the 3-year DTI scan shows reduced and disjointed projections from the right VL to cortex* (cyan arrow), *relative to the left VL. The DTI data from the 6-year poststroke scan also show different projection patterns between the right and left VL. Projection patterns from the normal left VL to cortex are similar between the 3- and 6-year DTI datasets, whereas projections from lesioned right VL to cortex show differences.*

University of Texas Health Sciences Center in Houston, equipped with a six-channel parallel receiver array head coil. The Philips 32-direction diffusion encoding scheme (high angular resolution) was used with the gradient overplus option. Sixty transverse slices were acquired using a 224 × 224mm field of view with 2mm slice thickness and a maximum b value of 800 sec/mm^2. Unfortunately, because of scanner and patient availability, it was not possible to scan the patient in the same scanner with the same pulse sequence.

All DTI data were analyzed using DTI Studio Software (https://www.mristudio.org). DTI and ADC images were created by removing all background noise pixels with intensity values lower than 30 for the Siemens scan and 10 for the Philips scans. A 7 × 7-voxel region of interest (ROI), centered on the lesion in the right VL, was then outlined on the DTI images (with reference to the high-resolution anatomic images) for all slices in which the lesion was visible, and for one slice dorsal and one slice ventral to the lesion. A control ROI of the same size was created in the left VL by mirroring the right ROI. Fiber tracts were computed from these ROIs using the fiber assignment by fractional anisotropy continuous tracking algorithm[21] implemented in DTI Studio with a fractional anisotropy threshold of 0.25 (tracts containing voxels with fractional anisotropy < 0.25 were discarded) and a turning angle threshold of 70 degrees (tracts containing angles greater than 70 degrees were discarded from the analysis). All fiber tracts meeting these criteria were superimposed on the b0 image as colored streamlines.

High-resolution structural scans were acquired at the same time points as the DTI scans (see Fig 1). Both a proton density–weighted and a T2-weighted scan were acquired 1 year after the patient's stroke. At 3 years after stroke, a T1-weighted scan was performed. At 6 years after stroke, a T1-weighted scan and a flip-angle inversion recovery scan were acquired. The T1 anatomy of the patient's brain from the 6-year time point was normalized to the International Consortium for Brain Mapping 452 T1 Atlas using AFNI software (http://afni.nimh.nih.gov) to measure the location of the lesion in standard space.[22]

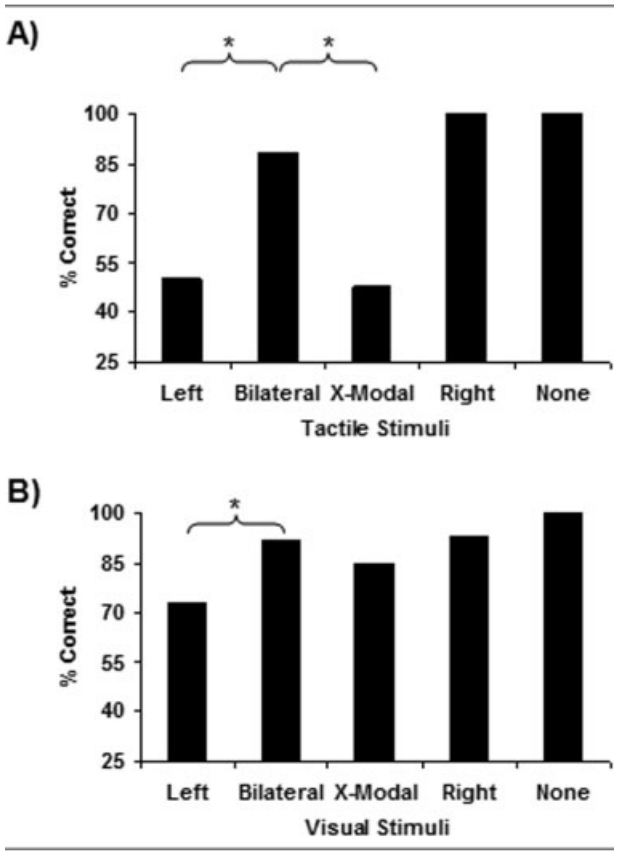

Fig 2. (A) Data demonstrating unisensory antiextinction for touch. The multisensory condition used a tactile stimulus on the left hand and a visual stimulus on the right. (B) Data demonstrating unisensory antiextinction for vision. The multisensory condition had a visual stimulus on the left hand and a tactile stimulus on the right. For both vision and touch, note the better contralesional target detection performance (ie, bilateral reports) when it was simultaneously presented with an ipsilesional target. *p < 0.05.

Results

One Year after Stroke

In the first experiment, conducted approximately 1 year after the patient's stroke, we found multisensory neglect[6,7,9] for vision and touch in this patient. In contrast with extinction, which usually accompanies neglect,[8] we measured the much rarer behavioral phenomenon of antiextinction, in which an ipsilesional stimulus aids detection of a contralesional stimulus, within both the visual and somatosensory modalities (Fig 2). When an identical ipsilesional stimulus was presented together with a contralesional one, detection was systematically increased for the contralesional stimulus (92% for tactile stimuli and 88% for visual stimuli; $p < 0.05$ for both). However, when a unilateral contralesional stimulus was presented, the patient detected only 50% of the mechanical tactile stimuli and 73% of the visual stimuli that were delivered (see Fig 2). These contralesional detection rates were significantly worse than detection of the identical sensory stimuli delivered unilaterally to the ipsilesional side (100% and 93% detection for the ipsilesional tactile and visual stimuli, respectively; $p < 0.05$ for both). These results illustrate the multisensory nature of her neglect for a unilateral stimulus presented on the contralesional side of space or her body. This demonstrates that the impaired detection with unilateral stimuli cannot be attributed to a primary sensory loss (eg, hemianesthesia or hemianopsia) because she was able to detect these same stimuli when an identical stimulus was presented on the ipsilesional side.

Antiextinction was not observed for multisensory stimuli. When a contralesional tactile stimulus was presented together with an ipsilesional visual stimulus, detection rates for the contralesional tactile stimulus were the same as for the unisensory contralesional tactile condition ($p > 0.20$; see Fig 2). When a contralesional

visual stimulus was paired with an ipsilesional tactile stimulus, detection rates for the visual stimuli were slightly greater in this multisensory condition (85%) than for the unisensory contralesional visual condition (73%) ($p = 0.058$). None of these results can be attributed to response biases because the patient was 100% correct on the catch trials, reporting that she did not feel or see anything when no stimulus was presented. These findings were replicated in an experiment conducted 3.5 months later using electrical-cutaneous rather than mechanical stimulation (see Supplementary information).

To examine the neural substrates of these behavioral effects, we conducted structural magnetic resonance imaging (MRI) and DTI[23,24] 1.3 years after stroke (ie, 2.5 months after the first behavioral experiment). The neuroimaging data showed an extremely small lesion confined to the right thalamus. The lesion was clearly visible as reduced signal intensity on a T1 image and increased signal intensity on a T2 image, because of cell death and resulting replacement of neuronal tissue with interstitial and cerebrospinal fluid. As shown in Figure 1, and based on a thorough review by a consulting neurologist of the original clinical MRI scans, the lesion was in the VL. Tractography was performed on the DTI data to measure changes in white matter pathways passing through the lesioned and contralesional thalamus. Although the lesion is clearly visible in the structural images, there was no asymmetry in the DTI tracts between the lesioned and nonlesioned side at this time point (see Fig 1C, left).

Three Years after Stroke

Approximately 3 years after the patient's stroke, and 2 years after the previous experiments, we completed several additional behavioral and neuroimaging studies. A similar behavioral experiment as the previous one was conducted to assess any changes in sensory perception that may have resulted from any neural reorganization and recovery. At this stage, the patient had a strong tendency to report feeling tactile sensations on the hands from a centrally located 500Hz, 200-millisecond warning tone provided before each trial (Table 1). On some trials, the patient reported this synesthetic phenomenon of feeling tactile sensations on both of her hands after a sound. The proportion of these bilateral illusory sensations was highly significant during the sound only/no tactile stimulation trials ($p < 0.001$), as well as in each of the sound with unilateral tactile stimulation conditions ($p < 0.001$ each for bilateral reports after unilateral right and unilateral left hand stimulation). On other trials when no tactile stimulation and only auditory stimulation was provided, the patient reported feeling a sensation only on the contralesional left hand after the sound ($p < 0.01$), but not on the ipsilesional right hand ($p > 0.10$). This difference between the hands was statistically significant ($p < 0.05$). We first found evidence for this auditory-tactile synesthesia in a testing session performed 1.5 years after stroke (see Supplementary information), which is when the patient also recalls first feeling sensations in response to certain sounds (eg, the voice of a particular radio announcer).

Table 1. **Percentage of Responses from an Experiment Illustrating the Development of Illusory Sensations of Touch from a Warning Tone**

Response	Stimulus			
	Left	Both	Right	None
"Left"	35	41.25	5	11.25[a]
"Both"	28.75[a]	33.75	32.5[a]	21.25[a]
"Right"	2.5	2.5	16.25	2.5
"None"	33.75	22.5	46.25	65

[a]Illusory responses at $p < 0.05$.

Two months after this behavioral experiment illustrating a brain-damage induced synesthesia, another set of structural MRI and high-resolution DTI scans were acquired (see Fig 1B). The lesion location, shape, and volume were indistinguishable from the scans performed 1 year after stroke and were still confined to the right VL, despite her major changes in sensory processing. To determine whether brain plasticity might account for the patient's behavioral changes, we performed tractography on this newly acquired set of DTI data (see Fig 1C, middle). Unlike the previous DTI data, there were clear asymmetries between the left and right hemispheres. In the unaffected left hemisphere, the DTI tracking from the thalamic ROI showed robust, direct, and focal projections to the motor/premotor cortex.[25–27] These fiber bundles provide further evidence that this patient's lesion was restricted to the VL. In contrast, fiber bundles from the lesioned right VL were disorganized and diffuse, and statistically smaller in number compared with the normal VL ($p < 0.001$). These disorganized and statistically fewer fiber bundles may be the neural basis for the sound-induced feelings of touch in this patient.

Six Years after Stroke

Approximately 6 years after stroke, an additional set of behavioral and imaging data was collected to further investigate the auditory-tactile synesthesia experienced by this patient. Before the main behavioral experiment and to obtain a qualitative sense of which sounds produced tactile percepts, we recorded the patient's self-reported percepts to 110 different natural and artificial sounds across three separate testing sessions that were separated by 35 and 15 days. A total of 23 sounds were repeated in at least 2 of the 3 testing sessions to allow

for an informal measure of consistency, which is a hallmark of synesthesia.[28–31] Note that we cannot definitively rule out any consistencies in performance as being due to memory retrieval rather than actual synesthesia because of the lack of a memory-matched control group. However, the large list of stimulus materials, the length of time between the tests, and the exceptionally high consistency performance makes a memory retrieval explanation unlikely. Of the 110 sounds that were presented to the patient, 73% of them evoked a somatosensory percept in the patient (see Table 2 for representative examples). All of the felt sensations in response to the sounds were basic rather than complex (eg, shapes) in nature and included tingling sensations, "hair-raising" ones, and "pressure." Importantly, the majority (91%) of the repeated sounds produced consistent percepts, or lack thereof, across the different testing sessions. Specifically, the patient consistently reported subjectively that some sounds were more intense than others, and that different sounds produced sensations on different parts of the left upper half of her body (eg, she felt one sound around her left ear, another on her upper arm and face, and others on the back of her hand and forearm), although the consistency in somatotopy was not as robust as the consistency in subjective intensity. These touch-inducing sounds included pure-frequency tones, which she felt primarily on her left hand and forearm (as the previous experiment demonstrated).

To investigate this auditory-tactile synesthesia more directly, we performed a behavioral experiment in which on any given trial, no stimulus was presented, a low (200Hz) or high (750Hz) sine-wave tone was presented, or a vibrotactile stimulus was presented to the patient's left (contralesional) hand. The patient reported the presence or absence of any sensation on her left hand after each trial. On a large and statistically significant proportion of the trials, the patient reported feeling tactile sensations in response to the pure frequency tones ($p < 0.001$ for both tones), with no difference between the low and high tones used in this experiment (Fig 3).

Neuroimaging data were again collected. The structural images showed no change in the location, extent, or shape of the lesion (see Fig 1B). To further confirm that the lesion remained confined to the VL, we normalized the high-resolution MRI scan into standard coordinates and the center of the lesion was located (14mm R, −12mm P, 13mm S). Comparisons of the lesion location to standard brain atlases and the on-line Talairach demon[32] showed that the entirety of the lesion was confined to the right VL (Fig 4). As in the 3-year poststroke data, tractography performed on the DTI data showed a significant asymmetry, with apparently normal connectivity from the unaffected left VL to cortex, but disorganized and diffuse bundles from the affected right VL to cortex. The right VL projections 6 years after stroke appeared even less organized and specific than in the previous tractography study performed 3 years after stroke (see Fig 1C).

Discussion

Systematic investigations of the human ventrolateral thalamic nucleus have heretofore been limited, partly because of a lack of tools available to examine the isolated function of this compact structure in vivo and the typically larger lesions that affect more than one nucleus of the thalamus. We were able to examine a patient with a rare focal lesion of a single nucleus of the thalamus, the VL, to assess the role of this nucleus in human brain function. By taking advantage of recent developments that allow for in vivo delineation of the human thalamic nuclei using structural MRI and DTI,[25–27] we explored the perceptual consequences

Table 2. **Examples of Some of the Stimuli and Spontaneous Verbal Responses Regarding the Somatosensory Percepts from the Test-Retest Sessions That Were Conducted 6 Years after Stroke**

Auditory Stimulus	Response		
	Session I	Session II	Session III
Choir singing	"A lot! That's enough!"	DNT	"Yes"
Computer beep	"Yeah"	DNT	"Around my ear"
Growl	DNT	"Yes"	"Yes"
Gorilla	"A little"	DNT	"Not much"
Missile launch	"Yes"	DNT	"Yes"
Pouring liquid	DNT	"Yes, constant"	"Yes"
Radio announcer	"Yes"	DNT	"Yes"
Woman's laughter	DNT	"Yes, forearm"	"Yes"
500Hz tone	"Yes"	"Yes"	"Yes"
1,500Hz tone	"Hand"	"Yes"	DNT

DNT = did not test.

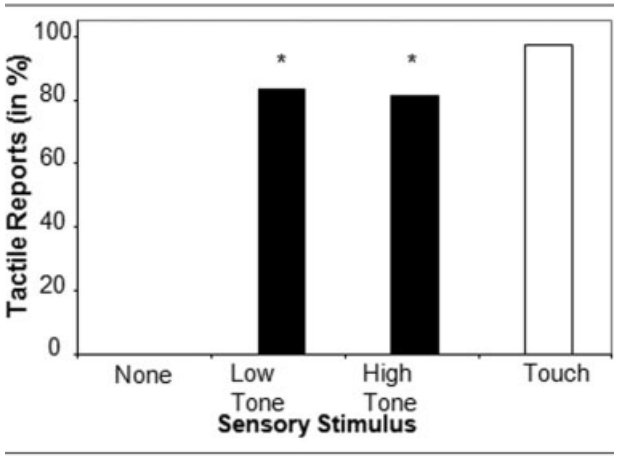

Fig 3. Data from an experiment illustrating illusory sensations of touch from different frequency tones. Asterisks *indicate illusory tactile sensations in response to sounds at* $p < 0.05$.

and axonal connectivity changes of restricted brain damage to the VL. Our longitudinal results suggest that a significant amount of functional and neural reorganization occurs after a lesion confined to the VL of the thalamus.

The initial damage and subsequent neural reorganization systematically influenced sensory perception. First, the patient demonstrated antiextinction, in which the patient detected contralesional somatosensory events significantly more when paired with an ipsilesional one. This antiextinction phenomenon, which lasted approximately 1.5 years after stroke, may reflect the initial stages of sensory coupling and reorganization via strengthened cortical callosal connections or altered thalamic ones. Subsequently, the patient experienced illusory tactile sensations induced by sound, which may reflect even further weakened thalamocortical pathways, as our DTI results suggest, or altered corticocortical pathways as a consequence of reorganization from deafferentation. For example, the deprived cortical input from the VL may have consequently strengthened some direct connections between the auditory and somatosensory cortices,[33] thereby producing the sound-touch synesthesia. This account of strengthened or overactive connections between different cortical structures in producing synesthesia is consistent with other neural accounts of this perceptual phenomenon.[34] Regardless of the exact neural mechanisms, this phenomenon of brain-damage–induced feelings of sound suggests that other forms of synesthesia, in which reportedly neurologically normal individuals feel,[30,31,35,36] taste,[37–39] or see[34,40–42] something qualitatively different than the actual sensory input, may be due to cross-wiring in the brain, especially subcortically.[30]

However, the acquired synesthetic percepts experienced by this patient differ in many ways from those reported in most developmental forms of synesthesia. First, the sensations experienced by the patient tend to be simpler than the complex sensations experienced by developmental synesthetes. Developmental synesthetes may feel complex shapes, such as pyramids in response to tastes,[30] or experience complex tastes, such as "bacon" or "apple" in response to words.[38,39] In contrast, our patient reports only basic somatosensations such as tingling or pressure. Second, the sensory modalities affected in our patient differ from those usually involved in developmental synesthesia. Namely, our patient experiences touch in response to sounds (auditory-somatosensory), whereas most forms of developmental synesthetes experience color from letters (visual-visual) or vision from sound (visual-auditory).[31,40,43] In fact, feeling touch from another sensory modality is extremely rare in developmental synesthesia, with only three cases to our knowledge in the literature (one described in Luria,[36] another case in Cytowic,[30] and the third case in Simner and colleagues[31] and Simner and Holenstein[35]). Interestingly, a recent report demonstrates that developmental digit-color synesthetes refer touch sensations to distant parts of their bodies more than nonsynesthetes.[44] In conjunction with other reports of acquired synesthesia (eg, simple visual percepts evoked by sound[45–48]), our results suggest that acquired forms of synesthesia may influence the affected sensory modality only in limited ways and only after months to years following the initial brain damage (compare with a patient who perceived visual events in response to touch[49]).

In addition to demonstrating a previously unknown role for the VL in sensory processing, the results from this patient suggest that connections between the thalamus and other brain areas may be important for sensory plasticity after brain damage. Our results suggest that local disruption of the thalamus causes large-scale changes in remotely connected regions of the brain, perhaps including enhanced excitatory connections between auditory and somatosensory cortex leading to the patient's synesthesia. The synesthesia may have also been caused by altered interthalamic connections (or transcallosal connections originating in the thalamus) that facilitate the processing of afferent sensory information when normal processing is impaired. Despite the exact nature of these altered connections between brain regions, such changes can clearly have a wide spectrum of behavioral effects, from antiextinction to synesthesia. Although further converging evidence will be necessary to definitively demonstrate whether such remote changes take place, as well as the more precise role of the VL in sensory processing, this single-case study nonetheless provides tremendous insight into the consequences of VL thalamic brain damage. As best described by this patient, she is "sensitive to sound, on my skin as it were. This is true of the left side (the affected side) and it's especially noticeable in the hand

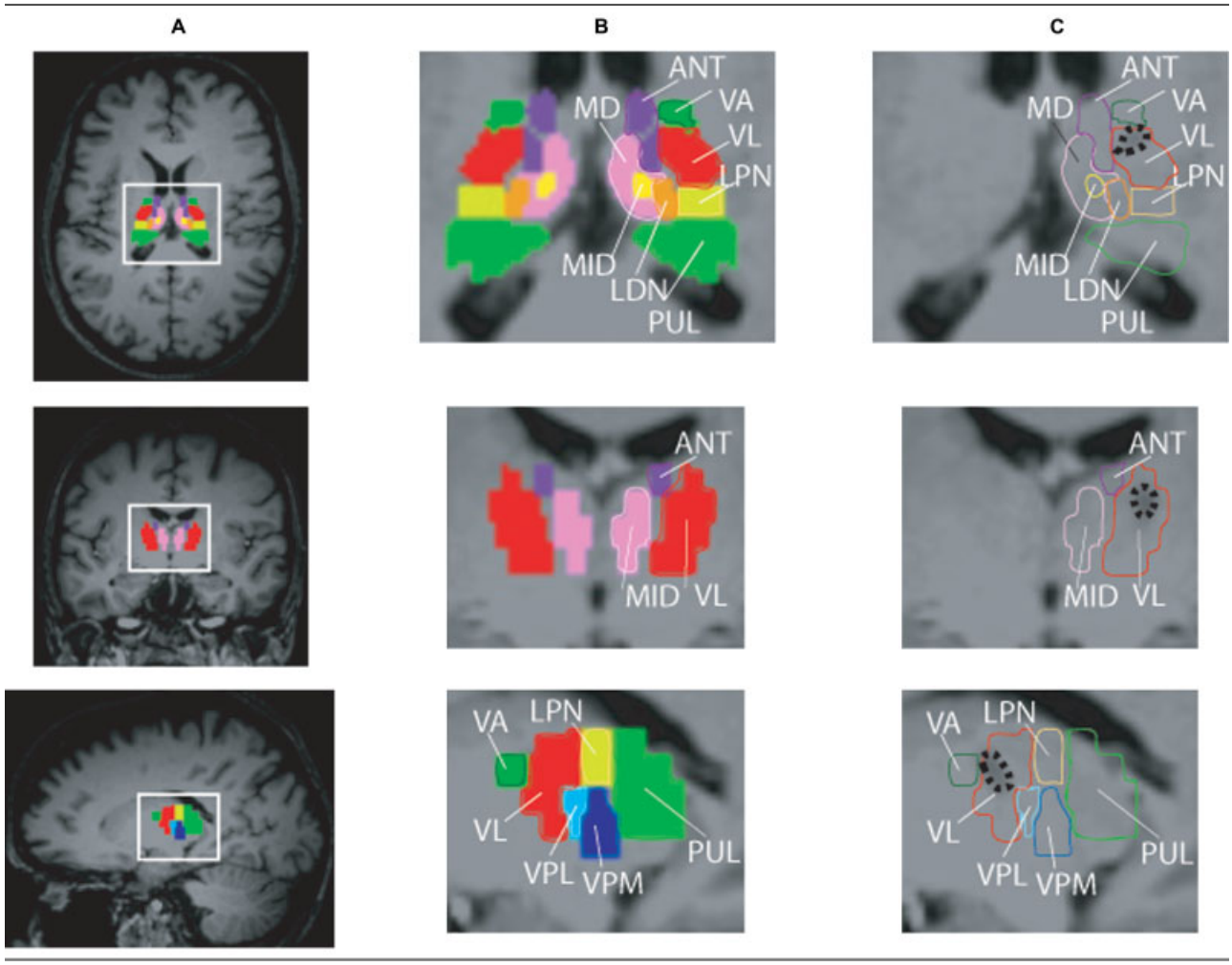

Fig 4. Relationship between the thalamic nuclei and the patient's lesion. (A) Parcellation of the patient's thalamus in Talairach space. Her brain was normalized and the thalamic nuclei were color coded in the axial (top; x = *15mm), coronal (middle;* y = −*11mm), and sagittal planes (bottom;* z = *14mm). (B) Enlarged view of the thalamic parcellation. (C) The thalamic parcellation* (colored outlines) *and lesion location* (dashed black line). *The lesion falls entirely within ventrolateral nucleus* (red outline). *ANT = anterior nucleus; LDN = laterodorsal nucleus; LPN = lateroposterior nucleus; MD = mediodorsal nucleus; MID = midline nucleus; PUL = pulvinar nucleus; VA = ventroanterior nucleus; VL = ventrolateral nucleus; VPL = ventral posterolateral nucleus; VPM = ventral posteromedial nucleus.*

maybe because that part of the body is more involved in everyday activities (of an academic)….Maybe the left side is using this sensitivity to vibration to extract information it can't get in other ways." In future studies, we plan to use other behavioral and neuroimaging methods, such as functional MRI, to shed light on the neural substrates of this fascinating perceptual phenomenon.

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