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Sensory Percepts Induced by Microwire Array and DBS Microstimulation in Human Sensory Thalamus

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Abstract

Background—Microstimulation in human sensory thalamus (ventrocaudal, VC) results in focal sensory percepts in the hand and arm which may provide an alternative target site (to somatosensory cortex) for the input of prosthetic sensory information. Sensory feedback to facilitate motor function may require simultaneous or timed responses across separate digits to recreate perceptions of slip as well as encoding of intensity variations in pressure or touch.

Objectives—To determine the feasibility of evoking sensory percepts on separate digits with variable intensity through either a microwire array or deep brain stimulation (DBS) electrode, recreating “natural” and scalable percepts relating to the arm and hand.

Methods—We compared microstimulation within ventrocaudal sensory thalamus through either a 16-channel microwire array (~400 kΩ per channel) or a 4-channel DBS electrode (~1.2 kΩ per contact) for percept location, size, intensity, and quality sensation, during thalamic DBS electrode placement in patients with essential tremor.

Results—Percepts in small hand or finger regions were evoked by microstimulation through individual microwires and in 5/6 patients sensation on different digits could be perceived from stimulation through separate microwires. Microstimulation through DBS electrode contacts evoked sensations over larger areas in 5/5 patients, and the apparent intensity of the perceived response could be modulated with stimulation amplitude. The perceived naturalness of the sensation depended both on the pattern of stimulation as well as intensity of the stimulation.

Conclusions—Producing consistent evoked perceptions across separate digits within sensory thalamus is a feasible concept and a compact alternative to somatosensory cortex microstimulation for prosthetic sensory feedback. This approach will require a multi-element low impedance electrode with a sufficient stimulation range to evoke variable intensities of perception and a predictable spread of contacts to engage separate digits.

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Keywords

neuroprosthetics; sensory encoding; brain machine interface; proprioception; artificial sensation; sensory prosthetic

Introduction

Routine clinical access to the human thalamus was developed for stereotactic surgical procedures. Both sensory (i.e., ventral posterolateral – VPL – or equivalently, ventrocaudal – VC) and motor (ventral lateral – VL – or equivalently, ventralis oral anterior/posterior – VOA/VOP) [1, 2] regions of the human thalamus have been extensively mapped during stereotactic procedures to treat tremor [3–5] and neuropathic pain [6–9]. Microstimulation in the sensory thalamus leads to well characterized, small perceived fields in the hands and face [5, 10]. Therefore, sensory thalamus may provide a compact, alternative site to somatosensory cortex for input of prosthetic or supplementary sensory information [11–16], such as that provided by a prosthetic limb with sensors [17–23].

In humans conscious identification of a sensory percept during intraoperative mapping requires prolonged (i.e., > 500 ms) sensory stimulation, similar to sensory exploration of an object [24, 25] whereas short, subconscious stimuli (i.e., < 500 ms) are subliminal [25]. Human experiments in sensory thalamus focused on conscious detection of stimuli, particularly the location and modality (i.e., pressure, temperature and whether painful), using stimuli of > 1–2 s [4–6, 26, 27]. Sensation and proprioception during a motor task are integral for task performance but typically occur at a subconscious level [14, 28, 29]. For example, motor control can be biased by short stimulation presentations of likely suprathreshold stimulation as well as salience and reward, representing the internal state of the brain [12, 30–32]. Microstimulation of sensory pathways may evoke an artificial prosthetic sensory input such as touch, pressure, or slip, which may be useful for somatosensory feedback or proprioception during motion [13, 14, 23, 33–35]. Further, it remains unclear how and where (i.e., peripheral vs central nervous system) artificial proprioception may be optimally inserted into the nervous system to facilitate perception of motion, likely dependent partially on clinical need [23]. Although multiple channels of microstimulation have been delivered in somatosensory cortex using small arrays [13, 14], the equivalent within sensory thalamus has not been performed in humans [18, 36].

Our hypothesis is that microstimulation through multiple microwires or DBS electrode contacts can produce separate, digit-specific perception as well as the perception of altered intensity. We explored this hypothesis through intraoperative experiments conducted during deep brain stimulation (DBS) electrode insertion into thalamus, and characterized percepts evoked by microstimulation within sensory thalamus through either a dispersed, multiwire microelectrode array [37, 38] or microstimulation through the larger contacts of a DBS electrode. Separate percepts on different digits could be evoked through different microwires, and the apparent intensity of the percept could also be modified with the lower resistance DBS contacts [34, 39, 40].

Methods and materials

Intraoperative human subjects research

All patients undergoing ventral intermediate (VIM) DBS to treat essential tremor at Duke University Medical Center were offered the opportunity to participate in the study. Studies were conducted following review and approval by the Duke University Institutional Review Board, and all subjects provided written informed consent after reviewing the goals and potential risks of intraoperative research with study staff. Of 20 patients that consented to participate 2 withdrew prior to study completion, 1 was withdrawn by the investigator for lack of time, and 17 participated in the study; there were 6 patients in which technical malfunction prevented completion (all with microwire microstimulation), leaving 11 patients who completed the study (6 with microwires, 5 with DBS electrodes).

The research was performed while the patient was awake and interacting prior to placing the therapeutic DBS electrode into VIM thalamus for treating tremor. Initially a clinical single unit recording electrode (FHC Inc., Bowdoin, ME) was introduced and an initial track through the VC sensory thalamus was mapped for sensory activity, responsiveness and depth, 2–3 mm posterior to the planned VIM treatment track [10]. Subsequently, a 16 channel microarray (bundle of 35 μm Pt/Ir microwires; Ad-Tech Medical Instrument Corp, Racine, WI) was placed where active cell firing in response to focal skin stimulation in the hand or face was present, as determined by the single microelectrode within the VC sensory nucleus, generally 2–3 mm in front of posterior commissure (PC) and 1–2 mm superior to the anterior commissure (AC) -PC line [10, 37, 38]. In later studies the Medtronic 3389 DBS electrode was placed into the VC sensory nucleus at the same location. In both cases either the microarray or DBS electrode was left in a fixed location 1 – 2 mm above the AC-PC line. The individual microwires or electrode contacts were tested for as long as the patient tolerated the experimental study (typically ~ 30 min). Once the research was concluded the DBS electrode was placed into the planned VIM track anterior to the sensory nucleus and tested for tremor control using macrostimulation. Patients were frequently examined during and after the surgery by multiple physicians, focusing on any new neurological changes or deficits (ie, such as residual paresthesias or sensations), which may have outlasted the microstimulation.

During initial microstimulation the threshold for perception of the stimulus on a single channel was determined using 2 s duration trains of 100–200 Hz 0.2 ms charge-balanced biphasic pulses (using bipolar electrode configurations for microwire arrays, and monopolar for DBS leads with respect to a reference or counter electrode). The threshold was determined by slowly varying the amplitude using a staircase method. The patient was asked to describe the perceived area of sensation, noted in detail on a diagram (i.e., Figs 2, 3 and 5), including on the skin surface or below the surface. The patients were also asked to describe the modality, using several possible categories: mechanical (including touch and pressure), movement (including vibration and movement across the skin), temperature (warm or cool), and tingling (electric current, tickle) [10, 39, 41]. These categories were described to the patients several times throughout the study, including definitions of these

natural responses, but there was no prompting by the research team to emphasize one category versus another, to allow the patient to spontaneously describe the best fit category.

Naturalness was assessed using a 5-point subjective scale, varying from totally natural (5) to totally unnatural (1), based on comparison to the perception of light touch generated by a 10 g von Frey hair touching the skin. We then contracted this 5 point scale to a 0–1 scale equivalent for plotting. At levels of 0.8 X to 1.4 X threshold, different patterns of stimulation were tested to assess whether these patterns led to either a different modality or more or less “naturalness” than constant 200 Hz stimulation. Patterns tested were ramps of increasing frequency (from 10 Hz to 200 Hz over 2 s), ramps of decreasing frequency simulating a rapidly adapting response (from 200 Hz to 10 Hz over 2 s), single frequencies from 10 Hz to 300 Hz, and “flutter” patterns (consisting of 2-pulse bursts of 200 Hz stimulation delivered at a rate of 10 or 25 Hz). The spatial description of the perceived response was mapped according to the channel stimulated and the pattern.

Microwire stimulation technique

The first group of patients ($n = 6$) underwent sensory thalamic microstimulation using the 16-channel Ad-Tech microwire array (individual microwire impedance of ~ 400 k Ω) attached to a high-compliance (100 V) switching headstage (SH16, Tucker-Davis Technologies, Alachua, FL), using initially a variety amplitudes, from 10 μ A up to ~ 75 μ A at 0.2 ms duration biphasic pulses (Fig. 1). Each of the 15 contacts was then tested using bipolar stimulation with reference to a single designated microwire, initially using 100 Hz to 300 Hz constant frequency stimulation, incrementing the current from 10 μ A up to 75 μ A as needed to evoke a clearly perceived sensory response. Due to the high (and variable) electrode impedance of the microwires the constant current mode was used. We focused on testing each of the multiple microwires for any response and the threshold for that response, particularly searching for microwires showing a different or unique projected field than ones initially tested, then having the patient describe the naturalness. Due to time constraints it was not possible to routinely test multiple stimulation patterns consistently using the microwires.

DBS macrostimulation

The second group of patients ($n = 5$) underwent microstimulation through individual contacts of the four-channel Medtronic 3389 DBS electrode in monopolar mode (with respect to a distant reference or counter electrode) within the sensory nucleus, starting at 100–200 mV amplitude (here defined in constant voltage mode since the DBS contact impedance was ~ 1.2 k Ω). Similar to the microwire stimulation, the threshold for awareness of the sensation, location, and “naturalness” of the sensation were recorded for each contact. Since there were fewer channels to test and the ability to detect a threshold with the larger electrode was more straightforward than with microwire stimulation, these experiments focused on testing different patterns of stimulation at levels just above and below the perception threshold. Once clearly defined the patient described in detail the perceived modality and degree of “naturalness”. Further, the patients were asked to rate the intensity of the stimulus compared to threshold on a 1–10 scale (10 being the most intense, threshold

typically a 1 or 2). Threshold was defined as the presence of a clear, perceived sensation, hence in many instances a subthreshold response was also perceived but with less certainty.

Statistical analysis

Results are reported as means $\pm$ standard error, and statistical significance was defined at $\alpha = 0.05$. We measured statistical differences using ANOVA, with Tukey's Honestly Significantly Different (HSD) test to assess multiple comparisons. Linear mixed-effects models were used to compare stimulus amplitude required to achieve a threshold percept across stimulation patterns, as well as percept intensity across stimulation amplitudes (JMP Pro 13, SAS Institute, Cary, NC). Additionally, cumulative logit models with proportional odds assumption were used to define the relationships between stimulation amplitude, intensity, patterns, and paresthesia naturalness (on a scale of 5 possible indices from totally natural to totally unnatural, contracted to a 0–1 scale for ease of illustration).

Results

All study patients tolerated the research protocol and the additional intraoperative time. The study patients did not experience any infections and routine, postoperative brain CT scans did not reveal any hemorrhage. In spite of placing either the microwire bundle or the DBS electrode directly into the VC sensory nucleus there were no residual sensations, spontaneous tingling or other side effects described by the research subjects during the perioperative period on detailed neurological exams, similar to the experience in VC stimulation to treat chronic pain [9, 42].

Microwire stimulation

Threshold responses during microwire stimulation were perceived as either a light touch or a mild tingling, in the range of 25–75 μA (average: $45.8 \pm 18.8 \mu\text{A}$, $n = 26$ responses in $n = 6$ patients) (Figures 2, 3). The area of perceived sensation from stimulation of a single microwire was typically small. In 5/6 patients ($n = 55$ distinct responses, including microstimulation across different microwires and various patterns), the evoked percepts from different microwires were located on the hands or forearm. In 1/6 of the patients the percepts (4 distinct responses) were primarily on the face and jaw (a small region around the corner of the mouth, similar to those described in [10]). Of the 55 total responses referred to the upper extremity there were 24 focused on a single fingertip, 4 responses with 2 and 5 responses with 3 adjacent digit tips, 2 responses spread across 4 digits, one on 5 digits, and 19 located within either the palm or the forearm (Figs. 2 and 3). The individual microwires disperse several millimeters apart when in the brain (Fig. 1), leading to these distinct responses when testing specific microwires [38]. The colors and hatching in Figs. 2 and 3 represent the response to different microwires in three separate patients, indicating that it was feasible to evoke various areas of sensation on separate digits with separate microwires. The specific details of each microwire stimulation are described in the figure legends. The average size of the percepts was $\sim 14 \text{ cm}^2$ ($n = 55$ responses) ranging from $\sim 1 \text{ cm}^2$ (a single fingertip) to $\sim 120 \text{ cm}^2$ (on the forearm), based on the qualitative diagrams noted in Figs. 2 and 3. Most responses (55%) were “natural” to the patient, described as pressure or touch, or

tingling; none were painful and there was no spontaneous description of the perception as representing vibration. Most responses were referred to the surface of the fingers or palm.

DBS stimulation

The second group of patients ($n = 5$) underwent placement of the DBS electrode directly into the VC sensory thalamus at the laterality planned for VIM stimulation for tremor control (ie, 13.5 – 15.5 mm off the midline). The mean threshold for clear and consistent detection of a response was 263 ± 56 mV at 200 Hz (Fig. 4) and often the patients also perceived stimulation at 0.8 X threshold amplitude, but with less consistency. At the threshold level patients easily described a perceived sensation that did not fade either within the 2 s stimulation time or on subsequent stimulus presentations, confirming the electrode location to be within VC (whereas DBS within VIM has a higher threshold and the perception fades rapidly) [41]. The log-transformed sensory thresholds varied significantly across stimulation patterns ($p < 0.0001$), with higher thresholds at lower stimulation frequencies (Fig. 4). These thresholds were determined individually for each specific pattern, using ramping above and below threshold for consistent detection of the sensory response.

Figure 5 shows representative distributions of sensations generated by different contacts at the threshold level of stimulation, indicating overlap but some clear differences in the perceived region of response (i.e., hatches and solid/dots in various parts representing different contacts with monopolar stimulation). Stimulation through each of the 4 contacts led to a response, often overlapping within a single patient, within the upper extremity or face. These perceived field responses were much larger than those noted with the microwires (Figs. 2–3). Out of a total of 147 separate trials, 121 trials elicited a sensation that the patient could describe, including 16 in the fingers, 13 in the fingers and/or hand, 39 extending from the fingers to the arm, 1 including the face and arm, 3 with the face and fingers, 11 in the hand and arm, 26 primarily in the arm, and 12 in the face. Overall, 64% of the sensory responses showed an arm component, whereas 68% of responses showed either hand or finger inclusion, while 13% included face representation. Subjects reported stimulation-induced sensations during 90.3% of all trials with amplitudes equal to or greater than the measured sensation threshold, and sensation intensity correlated positively with stimulation amplitude ($p = 0.0006$), using the “1–10” point description of stimulation intensity. As noted in Fig. 6 the increased stimulation amplitude (particularly above threshold) led to a significantly diminished perception of “naturalness” ($p < 0.01$).

Perceived sensory modality elicited by the DBS microstimulation showed (out of 146 responses in $n=5$ patients): 6% were characterized as mechanical (touch or pressure), 22% as movement or vibration, 18% as a temperature change, and 54% as tingling. In 1 patient the majority of responses were also described as painful whereas in the other 4 patients none were described as painful.

Patterning of stimulation and perception of “naturalness”

We compared the quality (“naturalness”) of perceived sensation across several stimulation patterns and frequencies (Fig. 7). The degree of “naturalness” varied with the pattern of stimulation (Fig. 7; $p < 0.01$). The ramped-frequency patterns showed a similar spread of

“naturalness” compared to simple 50, 100, and 200 Hz constant stimulation. However, the (non-physiological) increasing frequency ramp showed slightly more naturalness than the presumably more physiological decreasing frequency ramp (i.e., rapidly adapting pattern), with the flutter pattern exhibiting much less “naturalness”. Figure 8 compares the spread of descriptions of “naturalness” across subjects with similar stimulation patterns and intensities. There was considerable heterogeneity as to what patients labeled as “natural” with the same stimuli (Fig. 8) and usually with similar regions of evoked percepts.

Discussion

We tested the hypothesis that microstimulation of the VC thalamic sensory nucleus can provide a platform for delivery of exogenous sensory information with digit-level specificity and the capability to encode slip and intensity. Our results confirm that the spatial resolution of microstimulation can be limited to several, separate digits using stimulation of individual microwires. Microstimulation through the DBS electrode evoked mostly natural responses and the intensity of the perception could be encoded with the amplitudes of stimulation. These results mirror those of human somatosensory cortex microstimulation, including the levels of current needed to evoke threshold responses as well as the naturalness and quality of the responses, except that we more commonly noted digit-specific perceptions in the thalamus [13].

However, the small microwires in the array ($\sim 35 \mu\text{m}$ Pt/Ir) cannot be routinely targeted to cover specific (or all) digits, as their positions cannot be individually controlled, and they have the drawback of high impedance, limiting current delivery. In contrast, stimulation through the DBS contacts evoked only large sensory percepts in the upper extremity and demonstrated minimal spatial spread across the width of sensory thalamus to cover specific digits. Perception intensity could be encoded with increasing stimulation intensity (but at the expense of spatial resolution and “naturalness”). Surprisingly, patterns designed to mimic rapidly adapting sensory receptors (i.e., fast to slow) produced less natural responses than either constant frequency stimulation or increasing frequency ramps, although a large percentage of sensory responses were somewhat natural across all patterns.

With the 2 s duration stimulus trains we focused on conscious perception of quality and location of the induced percept [5], but this prolonged stimulus mimics an “exploratory” mode to determine texture and quality of perceived sensation. In contrast, subconscious (i.e., < 500 ms duration) stimuli are likely to be more physiological and may be of use to guide motor action or intent [12, 24, 25]. Shorter duration stimuli may also mimic subconscious motor sensations occurring during movement to help guide or direct specific aspects of motion, and may not be easily separable from motor kinematics [33, 35, 43]. The brain’s internal use of a referent control of perception [28] or more traditionally, an efference copy, are concepts which describe how intrinsic sensory patterns may be tied to motor outputs during action [14, 29, 44, 45]. For example, insertion of a patterned stimulus to indicate a “false” proprioceptive response during a movement may alter the intended trajectory or performance of a movement, but encoding appropriate proprioceptive stimuli at the single unit and field potential level to facilitate motion represents a daunting challenge for brain-

machine interfaces [22, 46, 47]. Likewise, brain state, salience and reward may further bias motor intent and action [30].

These results clearly demonstrate that a fixed microwire array within the sensory nucleus can produce perceptions in multiple different regions, particularly across the hand and in different digits. However, the location of these regions was highly variable and the uncontrolled dispersion of the microwire array does not allow selection of specific fingers or regions to provide uniform coverage of the hand, for example. Since it is possible to record from the microwires and determine receptive fields directly, this may help select individual wires within the microwire bundle for testing (although there was insufficient time in this protocol), and larger or additional microwires could be added to the bundle to improve the stimulation amplitude range, enhance dispersion and predictable spatial orientation of the perceived fields. However, even with recording from receptive fields there may be a mismatch between these recordings and the perceived area of response [41, 48].

The usual exploration performed during thalamic surgery involves moving a single electrode along a vertical track to identify specific nuclear location, borders, and neuronal properties [4–6]. In contrast, sensory neuroprosthetics in either the thalamus or sensory cortex will require placement of a fixed multichannel electrode [13, 17, 21, 33, 39, 47], perhaps after preliminary searching for the optimal site with sufficient resolution for the intended spatial coverage (i.e., digits). The hand occupies only ~ 3 mm of medial-lateral sensory territory in the thalamus, but occupies > 5 cm length along the somatosensory cortex [13, 49]. Multiple microarrays along various digit representations of the sensory cortex may be more reliable to have specific and reliable digit stimulation from the postcentral gyrus [12, 16, 49, 50]. The compactness of thalamic sensory representation may provide an advantage in this regards, if a suitable electrode design can be developed with sufficient dispersion and large enough contacts to provide stability and low impedance to provide a large range of stimulation intensities. For example, a new 32–40 contact DBS electrode in development may meet the required specifications [51]. Likewise, larger diameter microwires (~ 100–150 μm diameter) may provide both lower resistance (to enhance stimulation capability) and increased stiffness for reproducibility of placement once released from a common cannula.

Compared to Heming et al. [39] we followed a different strategy but with similar goals. In this study, we found a larger proportion of more natural or almost/possibly natural responses in both the microstimulation groups, possibly because we restricted all of the stimulation data to be acquired within the middle of the VC sensory nucleus, rather than at the VIM/VC border, and most responses were collected with stimulation intensities close to threshold. As the stimulation intensity increased, the patient perceived the evoked response as being less natural, but this may also provide an excellent clue for intensity control since larger amplitudes may be more easily discriminated. Similar to Heming et al. [39], we were surprised that the more physiological patterns (particularly ramp down and flutter) were perceived as less natural than simple constant 100–200 Hz stimulation, or the increasing frequency ramp. These results also mirror the clinical use of sensory thalamic stimulation for chronic deafferentation pain, where typically > 1.5V – 2.0V is employed to maintain clinical paresthesias for pain control, in parallel to spinal cord stimulation, typically at ~ 60–75 Hz [7–9, 42].

It is not clear if the subjective perception of natural sensations are required for delivery of useful exogenous sensory input, such as that obtained from pressure sensors on a prosthetic hand, as most patients may be able to learn the meaning of an “unnatural” signal during training, such as different frequencies to code intensity [35]. However, clear digit representations will likely be needed with some reliability, which may not be possible with the random microwire insertion we used in this study. With a denser wire bundle and larger, stiffer wires there may be a greater possibility to accrue reproducible responses on multiple digits. Improved stimulator circuitry may also facilitate a graded response for intensity modulation. Further, a perception of slip may be induced with a delay between separate digit stimulation, once a larger array is mapped out to represent multiple digits, which is important for a prosthetic hand to hold variously weighted items (with a control loop for slip leading to enhanced force).

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Thalamic Sensory Microstimulation

Human thalamic microstimulation simulates input of prosthetic sensory data.

Stimulation through microwire and DBS electrodes replicate hand and finger percepts.

Patterning of stimuli alters the naturalness of the evoked percept.

Intensity encoding is possible but with reduced naturalness.

Limitations include defining specific percept location and duration of stimuli.

Figure 1. A picture of the 16-channel microwire array (right), together with a Medtronic DBS lead (left; 3389). The scale bar is 1 cm. Note that the microwire array also spreads within the brain, as noted on prior fluoroscopic pictures [38].

Figure 2.

These 4 illustrations of the right hand show the threshold level pattern of perceived sensory fields using different contacts (in bipolar stimulation) of the microwire array, in the same patient. Overall, there were 8 microwires with a distinct, bipolar response and 7 with no response (using microwire #1 as a local counter electrode). The size of the projected fields was small, $\sim 1\text{--}3\text{ cm}^2$. Stimulation of microwire #7 resulted in a projected field in the right thumb (Fig. 2A) with a perception of traveling electrical current (in the direction of the arrow) at 100 Hz and 10 μA whereas microwire #4 stimulation was described as a small area of “falling asleep” on the two medial fingertips (Fig. 2B) at 100 Hz and 35 μA . Stimulation of microwire #16 resulted in tingling the ulnar aspect of the palm and extending slightly up the forearm at 100 Hz and 25 μA (Fig. 2C). Additionally, microwire #5 also resulted in a mild tingle on the medial aspects of the palm at 100 Hz and 13 μA , whereas microwire #4 led to a “prickling” sensation on the small cross-hatched area on the index fingertip (pink) at 100 Hz and 35 μA (Fig. 2D) and microwire #5 gave a mixture of tingling on the thumb and two forefingers at 100 Hz and 35 μA (small pink circles, Fig. 2D). Some of the microwire responses were repeated with similar distribution of the perceived field on the second trial.

Figure 3.

Figure 3A shows the response of microwire # 6 stimulation resulting in the blue area in the index finger and palm (extending up the forearm) at 300 Hz and 50 μ A, whereas at 300 Hz and 75 μ A there was a slight increase in the width of the band (purple area). Figure 3B (from the same patient as Fig. 3A) shows microwire #1 resulted in a perceived field (pink hatching) along the ulnar aspect of the hand at 300 Hz and 50 μ A, which felt similar to the 10 gram von Frey filament as a natural, light touch. Microwire #10 led to a mild, electric shock sensation perceived in the palm and extending slightly up the forearm at 300 Hz and 75 μ A (green cross hatching) whereas microwire #7 showed a perceived response in the palm at 300 Hz and 50 μ A (yellow cross hatching). Figures C and D are from another patient, with Fig. 3C showing microwire #8 stimulation resulting in a perceived field (“tickle”) across several dorsal fingertips (yellow shading) at 100 Hz and 50 μ A and microwire #9 stimulation causing a stripe of tingle sensation across the dorsal aspect of the middle finger at 100 Hz and 75 μ A. Figure 3D shows microwire #11 resulting in a small area of electric-like sensation on the dorsal aspect of the middle finger (red cross-hatched area) at 100 Hz and 35 μ A intensity, microwire #12 stimulation causing a similar small area of tingling (green hatched area) at 100 Hz and 50 μ A and microwire #13 leading to a similar area with a different perception of “electric-like” sensation at 100 Hz and 40 μ A. Note the nearly single digit or part of a digit representation in all 4 examples. The size of the responses vary from $\sim 1 \text{ cm}^2$ (D) to much larger area of $\sim 15 \text{ cm}^2$ (A).

Figure 4.

The log-transformed sensory thresholds for various patterns passed through individual contacts of the Medtronic 3389 DBS electrode placed in VC sensory nucleus. Each pattern was tested independently to derive the threshold value for each patient by ramping up (see Methods) then averaged across patients by the specific patterns. Thresholds were significantly lower during 50 to 200 Hz constant stimulation and the ramped frequency stimulation patterns than those measured during stimulation at †10 Hz ($p < 0.028$, Tukey's HSD), ‡ 20 Hz ($p < 0.075$, Tukey's HSD), or § Flutter at 10 Hz ($p < 0.048$, Tukey's HSD).

Figure 5.

These diagrams illustrate different patterns of perceived responses with microstimulation through the 3389 DBS electrode from a single patient, with varying frequency patterns and amplitudes shown. Figure 5A shows 10 Hz flutter responses, with #1 (yellow, largest) at 1.4 X threshold (of 800 mV), #2 at 1.0 X threshold (blue hatches), #3 at 1.2 X threshold and #4 at 0.8 X threshold (minimal to no response). Figure 5B shows the response to 20 Hz stimulation (threshold = 975 mV) with #1 at 1.4 X threshold (yellow), #2 at threshold (gray area), and #4 at 1.2 X threshold (blue dots) (no perception at 0.8 X threshold). Note the enlarging perceived field from threshold to 1.4 X threshold and increased intensity. Figure 5C illustrates the response at 10 – 200 Hz ramp up stimulation (threshold at 230 mV) with #1 at 1.2 X threshold (yellow) nearly equivalent to #2 at 1.4 X threshold whereas at threshold (blue hatches) there was a smaller response area. Figure 5D shows the response to 50 Hz stimulation (threshold 250 mV) with #1 at 1.0 X threshold (pink), #2 at 1.4 X threshold (yellow/orange) and #4 at 1.2X threshold (dots). These are representative examples, showing slight enlargement of the perceived field (and increased intensity) with higher stimulation values relative to threshold.

Figure 6.

For each subject a variety of different intensity stimuli were applied using the DBS macroelectrode, varying from just below perception (0.8 X threshold) to suprathreshold (1.4 X threshold). The level of “threshold” was set at a stimulation intensity such that the patient was certain of a response and could easily describe the quality and perceived field, so in many cases the 0.8 X threshold was still detectable, but with less certainty than 1.0 X threshold. There was a clear decrease in the naturalness of the perceived response as the stimulation was increased, across the $n = 5$ patients. This gradation towards less “natural” may enhance the intensity discrimination.

Figure 7.

This diagram shows the effect of stimulation pattern on perceived naturalness, at 1.2X threshold stimulation intensity, for the $n = 5$ patients undergoing stimulation using the DBS macroelectrode. Note that the low freq (10–20 Hz in particular) and the flutter gave the highest degree of unnatural percepts whereas the 50, 100, 200 Hz and ramps gave the most natural percepts (see text description for significance values).

Figure 8.

This diagram shows the relative percentage of all stimulation patterns that the patients classified on a scale between natural and totally unnatural for the $n = 5$ DBS macrostimulation patients, in terms of the perceived effects of stimulation with the DBS electrode contacts, across patients. Note the wide variability in how sensations are perceived between patients.