Title: Blocking tactile input to one finger using anaesthetic enhances touch perception and learning in other fingers

Abbreviated title: Input loss enhances touch perception and learning

Authors: Dempsey-Jones, H1,2, Themistocleus, AC3,4, Carone, D5,6, Ng, TWC7, Harrar, V8,9, Makin, TR1,2

Affiliations:
1 Institute of Cognitive Neuroscience, University College London, London, UK
2 FMRIB Centre, Nuffield Department of Clinical Neuroscience, University of Oxford, United Kingdom, UK
3 Nuffield Department of Clinical Neurosciences, University of Oxford, UK
4 Brain Function Research Group, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, South Africa
5 Acute Vascular Imaging Centre, Radcliffe Department of Medicine, University of Oxford, UK
6 Laboratory of Experimental Stroke Research, Department of Surgery and Translational Medicine, University of Milano Bicocca, Milan Center of Neuroscience, Italy
7 Department of Anaesthesia, University College Hospital, UK
8 Visual Psychophysics and Perception Laboratory, School of Optometry, Université de Montréal, Canada
9 NSERC-Essilor Industrial Research Chair, Université de Montréal, Canada

Submitting and corresponding author:
Harriet Dempsey-Jones
Institute of Cognitive Neuroscience,
Alexandra House, 17-19 Queen Square,
Bloomsbury, London WC1N 3AZ
h.dempsey-jones@ucl.ac.uk
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None.
Abstract:

Brain plasticity is a key mechanism for learning and recovery. A striking example of plasticity in the adult brain occurs following input loss, e.g., following amputation, whereby the deprived zone is 'invaded' by new representations. Although it's long been assumed that such reorganisation leads to functional benefits for the invading representation, the behavioural evidence is controversial. Here, we investigate whether a temporary period of somatosensory input loss to one finger, induced by anaesthetic block, is sufficient to cause improvements in touch perception ('direct' effects of deafferentation). Further, we determine whether this deprivation can improve touch perception by enhancing sensory learning processes e.g., by training ('interactive' effects of deafferentation). Importantly, we explore whether the direct and interactive effects of deprivation are dissociable by directly comparing their effects on touch perception. Using psychophysical thresholds, we found that brief deprivation alone caused improvements in tactile perception of a finger adjacent to the blocked finger, but not to non-neighbouring fingers. Two additional groups underwent minimal tactile training to one finger either during anaesthetic block of the neighbouring finger, or sham block with saline. Deprivation significantly enhanced the effects of tactile perceptual training, causing greater learning transfer compared to sham block. That is, following deafferentation and training learning gains were seen in fingers normally outside the boundaries of topographic transfer of tactile perceptual learning. Our results demonstrate that sensory deprivation can improve perceptual abilities, both directly and interactively when combined with sensory learning. This dissociation provides novel opportunities for future clinical interventions to improve sensation.
Keywords: anaesthetic; deafferentation; plasticity; psychophysics; somatosensory
Blocking tactile input to one finger using anaesthetic enhances touch perception and learning in other fingers

Long-term sensory input loss (hereafter ‘deafferentation’) is known to trigger brain reorganisation. For example, individuals born without eyesight show occipital lobe activity for various non-visual tasks (e.g., auditory and tactile tasks: Sathian & Stillia, 2010; Sathian, 2005). Similarly, adults with upper-limb amputation recruit the missing hand area during movement of their intact hand (Makin et al., 2013; Philip & Frey, 2014). It is commonly assumed that the invading representations can directly benefit from the freed-up cortical territory, leading to functional advantages for perception and action (Bottari, Nava, Ley, & Pavani, 2010; Merabet & Pascual-Leone, 2010; Nava & Roder, 2011).

However, previous evidence supporting such functional advantages has been challenged (see review in Makin & Bensmaia, 2017). For instance, enhanced tactile perception in the blind may be due to greater experience with, or dependence on, touch (Grant, Thiagarajah, & Sathian, 2000; Heller, 1989); as opposed to the recruitment of visual areas by tactile processes (see Kupers & Ptito, 2014 for review). Vega-Bermudez and Johnson (2002) convincingly demonstrated that amputation of a finger does not confer tactile gains on the adjacent fingers (see also Oelschlager et al., 2014). Moreover, others have suggested deprivation-related reorganisation in adults has maladaptive sensory consequences (Flor et al., 1995; Haak, Morland, & Engel, 2015). Thus, the functional consequences of long term deprivation-related reorganisation remain unclear.

Studies investigating improvement of sensorimotor abilities by temporary, experimentally induced sensory deafferentation have been similarly inconclusive. While some studies showed tactile improvements across measures (Weiss et al., 2011; Werhahn et al., 2002), most studies have shown limited improvement in measures of touch perception (Bjorkman, Rosen & Lundborg, 2004; Bjorkman, Rosen, van Western, Larsson & Lundborg, 2009; Weiss et al., 2004) or motor performance (Floel et al., 2004; both sensory and
motor: Rosen et al., 2006), or no change in any touch measure tested (in a
healthy control group: Sens et al., 2013; see also Bjorkman, Rosen & Lundborg,
2004 for improvement in touch but not motor performance). A key consideration
when interpreting such reports is that perceptual changes may not be caused by
the deafferentation per-se, but instead by exposure to testing protocols
(unintentional ‘training’), or, by altered behaviour also triggered by the
deaferentation (see Discussion). Thus, it is difficult to piece apart the
contributions of deafferentation alone to perceptual changes from the currently
existing body of research.

Extending this concept, some groups have investigated whether deprivation-
related plasticity can be harnessed to explicitly boost sensory *training* effects.
For example, can deprivation enhance perceptual learning – the inherent ability
of sensory systems to improve in perception following repeated exposure to
stimuli or direct training (Gibson, 1969; Volkman 1858)? Or motor learning –
improvements in motor performance by practice or training (Schmidt & Lee,
2011)? Here again results were mixed, with reports that temporary
deaferentation either improves motor learning (Muellbacher et al., 2002;
Ziemann, Muellbacher, Hallett, & Cohen, 2001), or improves tactile learning
(Voller et al., 2006) but not motor learning (through rehabilitation: Rosen,
Bjorkman & Lundborg, 2006; Weiss, Miltner, Leipert, Meissner & Taub, 2011). In
vision, three days of monocular deprivation has been reported to enhance
contrast sensitivity training in the non-deprived eye (Shibata, Kawato,
Watanabe, & Sasaki, 2012). However, the question still remains whether these
gains represent ‘direct’ effects of deafferentation (e.g., resulting from increased
cortical representation: Merzenich et al. 1983; 1984) or are induced via
‘interactive’ effects of deafferentation (e.g., by facilitating on-going processes of
sensory plasticity such as perceptual learning).
Here we wished to determine whether sensory deafferentation to one finger can enhance tactile perception directly, as well as interactively – by improving the efficacy of a tactile training protocol. Further, we wished to investigate whether these direct and interactive effects of deafferentation are dissociable, delineating their separate contributions to perceptual gains. Since previous studies typically fail to include a deafferentation only control condition, to our knowledge, such a dissociation has not yet been successfully demonstrated.

We compared changes in tactile perception over time in three groups: one group experienced two (one-hour) pharmacological nerve blocks to the right index finger, carried out on subsequent days – the ‘block only’ group. In two additional groups, tactile training was performed on the finger next to the blocked (or sham blocked) finger – these were the block+train and sham+train groups, respectively. Tactile perception was tested at multiple time points before and after the blocks to examine the time-course of perceptual changes caused by deafferentation, and/or training.

We predicted that the block would cause enhancements of tactile perception largely (or completely) restricted to the finger adjacent to the deafferented finger. This could be achieved through the re-distribution of neuronal resources that have been freed up due to deafferentation (e.g., see Faggin et al., 1997; see Discussion). Critically, we predicted these ‘direct’ effects of deafferentation in the block only group would be largely finger specific, i.e., improvements of touch perception would be largely restricted to the deafferentation-adjacent finger. This follows from studies showing greatest physiological deafferentation changes for deafferentation-adjacent locations (e.g., recruitment of cortical territory proximal to the deafferented zone; Merzenich et al., 1984; 1983). See prediction Figure 1A for a visualization of the hypothesized results.

# Figure 1 approximately here #
Secondly, we predicted that training coupled with a sensory block (block+train group) would result in greater transfer of learning from the trained finger to the other fingers, as compared with sham block and training (sham+train group; see prediction Figure 1 panel B vs. C). A strong body of literature indicates that tactile learning transfers in a defined and highly consistent pattern, from the trained finger to the adjacent and homologous fingers only (humans: Dempsey-Jones et al., 2016; Harrar et al., 2014; Harris et al., 2001; rodents: Harris & Diamond, 2000; Harris et al., 1999; for review see Tame et al., 2016). This specific learning transfer pattern has been suggested to reflect topographic transfer in the somatosensory system, resulting from overlap in receptive fields (RFs; Harris et al., 2001). Critical to our prediction, learning has not been found to generalise to fingers other than the adjacent or homologous, presumably due to insufficient physiological overlap to permit transfer. Here we wished to determine if we could extend the boundary restricting the topographic spread of learning gains by deafferentation concurrent to training. Specifically, we investigated whether we could induce learning gains in the index and ring fingers of the untrained hand, fingers that do not normally showing benefits from learning transfer. Gains for these fingers would, therefore, be expected in the block+train group, but not the sham+train group. Such a change could occur because the direct effects of deafferentation change neighbourhood relationships between fingers in the somatosensory system (Faggin et al., 1997), thereby altering the transfer of learning (see Discussion).

Finally, and critically, we wished to show that extensive sensory gains in the block+train group were truly due to the interaction of deafferentation and training, and not simply due to deafferentation alone. This would be reflected in divergent patterns of sensory gains in the block+train group, as compared to the block only group. We predicted learning in the deafferent-adjacent finger of both groups (due to the direct effects of deafferentation). However, we anticipated significantly more learning in the remaining five fingers for the block+train group as compared to the block only group. Importantly, revealing a statistical divergence in the pattern of learning gains produced by these two groups would allow us to provide first evidence of a dissociation in direct and interactive effects of deafferentation.
Methods

Participants

Forty-seven participants were recruited for the study. One participant dropped out of the study, six participants were excluded due to ineffective anaesthesia, and four were removed from the analysis due to insufficient tactile perception (accuracy at chance on more than one finger at baseline testing). The remaining 36 participants were randomly allocated to one of three conditions based on order of sign-up (some final participants were directly assigned to groups to ensure age and gender matching across groups). There were three test groups of 12 participants each: block only (age, M = 26.25, SEM = 1.45; 7 females; 0 left-handers), sham+train (age, M = 27.17, SEM = 1.50; 7 females; 1 left-hander) and block+train (age, M = 29.92, SEM = 2.59; 5 females; 1 left-hander).

All participants provided written informed consent prior to participation. Ethical approval was granted by the NHS Health Research Authority, reference code: 13/SC/0502. Participants were reimbursed for their time. Exclusion criteria included: allergy to local anaesthetic, medical or physical issues causing impaired perception to the fingertips; history of neurological or psychiatric illness; history of drug abuse; major illness within the last three months; pregnancy; and needle phobia.
Experimental timeline

The study was conducted over 6-7 days. The experimental time-course is shown in Figure 2B. Day 1 involved a baseline test, followed by a real/sham block. Once an effective block was achieved (indicated by a sensitivity check, see below), trained groups underwent the first session of minimal tactile training to the right middle finger (i.e., concurrent block and training). During this time, the block only group was allowed a supervised break. Day 2 involved a real/sham deafferentation and sensitivity check, followed by a second training session (or another supervised break for the block only group), and finally the online test. Day 3 involved the offline test alone. The final retention test was given 3-4 days subsequent to the offline test. Please note: the nomenclature of the testing sessions indicates the anticipated state of deafferentation effects. For instance, ‘online’ infers there may have been some residual anaesthetic effects at the time of testing (given the predicted duration of the block, see below). ‘Offline’ indicates anaesthesia had ceased. ‘Retention’ indicates anaesthesia had ceased by an extended period.

#Figure 2 approximately here#

General procedures

During training and testing participants were blindfolded. They were instructed to prioritise accuracy over speed, and no time limit was imposed. Stimuli presentation was controlled by a computer running MATLAB (release 2013a, MathWorks, Inc., Boston, MA). During tasks, participants were asked to respond with a mouse using the index and middle fingers of the hand that was not being used for testing/training. Prior to the first testing session, participants in all groups were briefly familiarised with the testing protocol (~5 presentations of the largest grating, in randomly alternating orientations with accompanying verbal labels). Trained groups received a similar familiarisation prior to the first training (~5 presentations of task-relevant stimuli conditions, see below). Note: stimuli and task details for testing and training were similar to those described in our previous studies (see Harrar et al., 2014; Dempsey-Jones et al., 2016 for more details.)
Deafferentation interventions

All participants received the same deafferentation protocol. The intervention varied only in the substance injected, which depended on group assignment. With the participant’s right hand pronated, a trained physician inserted a 25-gauge sterile needle into the dorsolateral aspect of the base of the right index finger. One millilitre of solution was injected continuously as the needle was withdrawn. The same procedure was repeated on the other side of the base of the finger to achieve anaesthesia of the entire finger (a ‘ring block’). The two blocked groups received an injection of lidocaine hydrochloride 1% and the sham group received normal saline 0.9%. The volume, type and concentration of local anaesthetic used provided a block duration of approximately one hour (lasting up to three hours). This blocking procedure prevents afferent sensory input from the finger, while motor function is largely preserved (because the tendons allowing finger movement reside in the hand/ arm, outside the region of nerve block). In the current study, we did not include a ‘sham only’ condition (i.e., repeated testing alongside two sham blocks) to demonstrate the effect of testing alone on perceptual thresholds. This was because we have previously demonstrated in two previous studies (Dempsey-Jones et al., 2016; Harrar et al., 2014) that repeated testing does not cause selective changes in sensory thresholds of any one finger (gains are consistent across fingers over testing sessions, please see Supplementary Materials, part I for more).

Two sessions of blocking (on subsequent days) were included in the protocol to maximise the effect of deafferentation. Participants in all groups were informed that they were receiving local anaesthetic – but that the effects were variable, and therefore they may not subjectively perceive a complete anaesthetic effect (only one person in the sham group reported suspected administration of a sham block in debriefing).
Testing task

The testing task assessed perception of grating orientation using a set of seven plastic dome gratings (JVP domes, Stoelting, Wood Dale, IL). This test overcomes various pitfalls of other measures of tactile perception, such as two-point discrimination (see Van Boven & Johnson, 1994; Tong, Mao & Goldreich, 2013 for critique). The fingers tested were the index, middle and ring fingers of the left and right hands. Because training was administered on the right middle finger, our selection of these six testing fingers allowed us to probe for gains in three fingers known to benefit from learning transfer (the adjacent index and adjacent ring on the trained hand, and the homologous middle finger of the untrained hand), as well as two fingers of no topographic relation to the trained finger – that consequently do not show learning transfer gains (the index and ring fingers of the trained hand; see Introduction).

The gratings varied in groove width, with isometric groove spacing (i.e., grooves and ridges were equal in diameter). The spacings were 0.25, 0.5, 1.0, 1.2, 1.5, 2.5, and 3.5mm (with the smallest spacing being the hardest to feel, decreasing in difficulty with increased size). They were presented to the glabrous surface of the distal pad of the finger. Gratings were applied using a specially constructed apparatus designed to allow contact between the grating and the participant’s fingertip with constant pressure and position (Figure 2A). The gratings were applied for ~1s per presentation, with an inter-stimulus interval of ~2-3s.

On each trial of the testing task the experimenter would present one of the seven testing gratings to the participant’s fingertip, with the grooves oriented either parallel or perpendicular with respect to the medial-proximal axis of the participant’s finger. Participants were asked to respond using a two-alternative forced choice (2AFC) whether the dome was parallel (‘down’) or perpendicular (‘across’) (see Figure 2C).
In blocks one and two, each of the seven gratings was presented in a ten trial block (in a random order). Subsequently, the computer selected four grating sizes for additional data collection in a final block. These four gratings were selected to fall within the ‘interval of uncertainty’ of the psychometric function. That is, we targeted gratings with variable accuracy. This was done by excluding any gratings that produced 100% correct performance from the selection range (if applicable). If no gratings produced 100% accuracy, then any with 90% accuracy were excluded. We then selected randomly from the gratings that were left. Thus, for each finger, 3 from 7 gratings were presented in one block (10 trials), and 4 were presented in two blocks (20 trials), resulting in 110 trials in total per finger/test. Accuracy feedback (0-100%) was provided over headphones randomly, on approximately ⅓ of the blocks. Overall, the testing sessions lasted approximately one hour, with short intra-block breaks.

**Sensitivity check**

We used a short sensitivity check to determine whether we achieved a significant reduction in information from slowly adapting mechanoreceptors mediating the performance of orientation discrimination (Johnson, 2001; Van Boven & Johnson, 1994). As in the testing procedure, responses were two-alternative forced choice, so chance performance corresponded with 50% accuracy. The sensitivity check used an abbreviated version (~2 minutes) of the testing task, i.e., only 10 presentations of the largest grating (3.5mm). Effective reduction in perception was achieved: the sham+train group demonstrated 100% accuracy (SEM = 0; i.e., all participants performed with complete accuracy), the block only group performed at chance (54.09% accuracy; SEM = 3.78; accuracy non-significantly (ns) different from chance, as demonstrated by a one-sample t-test comparing accuracy to 50% chance, p = .437), as did the block+train group (52.27% accuracy; SEM = 5.00; also ns different from chance, p = .615). Independent-samples t-tests indicated there was no difference in accuracy between the blocked groups (p = .967), and that both blocked groups had significantly lower accuracy than the sham group (p < .001).
Training sessions were used to improve perception of tactile grating orientation. Although this task was originally considered to be resistant to training effects (Johnson & Phillips, 1981; Van Boven & Johnson, 1994), later studies have shown this task to robustly produce tactile perceptual learning following training (Dempsey-Jones et al., 2016; Harrar, Spence, & Makin, 2014; Sathian & Zangaladze, 1997). The trained finger was the middle finger of the right hand.

The task used for training differed from the testing task, to encourage participants to learn tactile features of the stimuli, rather than task requirements. On each trial, the grating was presented twice to the trained finger (using the same apparatus and timing as in testing). Participants were asked to report whether both presentations were oriented in the same direction (e.g., both down) or in different directions (e.g., down-across; also 2AFC, see Figure 2C). Feedback on accuracy was provided over headphones trial-by-trial to maximise learning (‘correct’/ ‘incorrect’).

The gratings used for training were selected for each participant to be two above and two below that individual’s perceptual threshold, as determined at baseline (Dempsey-Jones et al., 2016; Harrar et al., 2014). A larger range of (10) grating spacings was used for training to allow closer matching to the participant’s threshold (sizes were the same as the testing stimuli, with the addition of 0.75, 2.0 and 3.0).

Training consisted of 6 blocks (4 grating sizes/ block; 12 trials/ grating – where 1 trial consisted of 2 presentations of the grating stimuli, see above). There were two blocks of training, on the first and second days respectively. One training session lasted approximately 45 minutes, with short intra-block breaks. We used a short training as we aimed for minimal learning in order to avoid potential training ceiling effects when examining the added benefits of deafferentation (i.e., allowing any additional benefit of block+training to reveal itself in comparison to sham+training).
Determined perceptual thresholds

Tactile psychophysical thresholds for each finger and testing session were determined by plotting accuracy as a function of grating size across all levels of stimulus difficulty. The data was fitted with a Weibull curve using a least-squares function in MATLAB (two free parameters; gamma and lambda set at .05 and 0, respectively). The threshold for this psychometric function was interpolated from the grating size estimated to yield 82% accuracy.

Baseline thresholds for our sample were quantitatively and qualitatively similar to those collected from several independent samples that we have previously published using the same testing method and stimuli (Dempsey-Jones et al., 2016; Harrar et al., 2014); though note raw thresholds were higher than some previously published studies due to use of the method of constant stimuli for grating difficulty presentation, as opposed to a descending staircase that produces lower absolute thresholds (see Supplementary Materials, part II (Table S1) for raw thresholds and part III for further discussion).

Goodness of fit of the psychometric functions

In 4.8% of the cases (42 out of 864 cases: 6 fingers x 4 sessions x 36 participants = 864), the algorithm was unable to fit a curve to the data using the specified parameters. This occurred because the data to be fitted violated the assumptions of the Weibull curve beyond the defined tolerance limits (e.g., there was not a reasonable incremental increase in accuracy with increasing stimulus size). For these 42 cases, we attempted to refit the curve by removing a single outlying data-point (i.e., accuracy score for a single grating) if said point was deemed to be an outlier. To identify outlier data-points, we plotted all data for all participants and conditions onto a grand mean plot and removed a data-point if it fell outside +/- 3 standard deviations of the grand mean, and was thus considered an outlier. Removing single problematic data-points allowed us to fit a curve to the remaining data in all but 16 functions (1.9% of all original cases) that had to be excluded from further analysis.
Over the whole dataset, the psychometric functions predicted the data with good accuracy (average $R^2 = .72$, SEM = .01). However, some individual psychometric functions showed very poor fits to the data. We, therefore, removed functions with low $R^2$ ($R^2 < .15$; 7 cases from the remaining 848, leaving 841 cases), because values below this level represent very low fitting success considering the percentage of variance in the data explained by the psychometric function fit (Swanson & Birch, 1992). That is, these data-points were removed not to improve model convergence in the GEE, but rather because they did not represent valid thresholds as produced by the psychophysical thresholding procedure (GEE model convergence was good, see quasi likelihood under independence model criterion (QICC) values in Tables 1, 2 and 3). In the interests of reliability, an additional analysis was performed on the full dataset (without excluding these cases). This produced the same pattern of results as reported below.

Supporting the stability of our thresholds over time, we found that there was no difference in goodness of fit ($R^2$) across the four testing sessions, for any of the three groups ($.200 < p > .744$; i.e., curve fitting was equally successful). High consistency in mean and SEM values between our study and previous studies (from our laboratory and externally) also support the stability of our data and fitting procedures (see Supplementary Materials, part III).

**Normalisation of data**

Data was baseline normalised to best reflect change over sessions for each finger, independent of minor baseline threshold differences between fingers that were irrelevant to the results of interest (Vega-Bermudez & Johnson, 2001; Harrar et al., 2014; Dempsey-Jones et al., 2016; note: no baseline differences were found between groups for any finger, $137 < p > .438$). Normalisation was achieved by subtracting the baseline threshold from subsequent thresholds (individually for each participant and finger). Raw data is presented and visualised in the Supplementary Materials, part II; normalised data with individual case (single participant) data is also available in Supplementary Materials, part IV and online at: http://www.ucl.ac.uk/icn/research/supps/dempseyjones).
In all visualisations, we present actual means, rather than estimated marginal means (generated by the statistical analyses, see below) – to best represent the actual data values and variability.

**Analyses**

Generalised Estimating Equation (GEE) analyses were selected to examine the current dataset because such methods are better able to account for the interdependence between data as compared to ANOVA methods (by allowing explicit specification of the working correlation matrix between dependent variables), thus providing a better fitting model (Ballinger, 2004; though note we replicate our central results with ANOVA methods in the Supplementary Materials, part V, for comparability). Additionally, the GEE approach is also able to deal with missing data-points (e.g., from curves that did not generate, see above).

The threshold data were normally distributed: thresholds for all six fingers at all four sessions were assessed for normality using a Kolmogorov-Smirnov test, with 23/24 thresholds (6 fingers x 4 sessions) found not to be different from a normal distribution (all \( p > .05 \), aside from the right index finger in the online session; all 24 were \( p > .05 \) when corrections were applied for multiple comparisons).

GEE analyses were conducted using a linear scale model. This model was chosen for parsimony, as we had no a priori reason to specify a higher-order or more complex model. The working correlation matrix was set as exchangeable, rather than independent, to maximise the model fit (reflected by the QICC). Session was coded as an ordinal factor (not continuous – as there were not continuous gaps between sessions, allowing us to test deafferentation effects at specific critical times post-intervention; see experimental timeline in Figure 2). The GEEs were implemented with IBM SPSS Statistics, Version 22.0. (Armonk, NY).
For all analyses, results ($\chi^2$ and p values) are presented for major comparisons in text, and comparisons not relevant to hypotheses and other lower-order effects are presented in Tables 1-3.

**Comparisons**

The first ‘parent’ GEEs compared all fingers at all sessions – either within- or between-groups depending on the test – to determine whether there was any difference in the way the six fingers change over sessions, and justify our follow-up analyses. To ensure these interactions were not driven by changes in threshold caused by on-going anaesthesia (i.e., numbing of the right index finger in blocked groups at the online session), we repeated any comparison including such data with these values removed. There was no change in the pattern of results, all interactions remained significant (see Tables 1-3 in the Results section: comparisons repeated in this way are marked with a tilde (~)). To avoid this issue and enhance ease of interpretation, for our hypothesis-driven follow-up analyses we removed the online session data if the (injected) right index finger was being compared – looking then at the offline and retention sessions only. Further, since these follow-up analyses only used a subset of fingers at a time, we covaried out the raw baseline threshold to account for any inter-finger differences that could affect interpretation of our results (Van Breukelen, 2006; Vickers, 2001); unlike in the parent GEEs where this is not necessary, as finger is balanced across hands, and thus main effects of Finger are even. These follow-up analyses were conducted separately per session to explore how changes varied over time, and were thus Bonferroni corrected for multiple comparisons.

Please note: here we include our hypothesis-driven analyses only. These tests compare particular fingers from particular groups at a time, based on a priori predictions (e.g., comparing the index and ring fingers of the block+train group vs. the sham+train group to investigate for enhanced learning transfer). In the interests of completeness and transparency, we have, therefore, included a data-driven, exploratory analysis of learning in all fingers, for all groups in the Supplementary Results, part V. These data-driven analyses provide a converging picture of results to the hypothesis-driven tests (see Discussion).
Results

Direct effects of deafferentation: Selective learning in the deafferentation-adjacent finger (block only group)

We wished to investigate whether administration of anaesthetic block to the right index finger altered perceptual thresholds of the six tested fingers over sessions. Specifically, we predicted selective improvements on the deafferentation-adjacent finger – with no, or significantly reduced perceptual change on the other fingers as some non-selective, generalised improvement may be seen across all fingers due to repeated tactile testing alone (Dempsey-Jones et al., 2016; see Supplementary Materials, part I), or due to limited deafferentation related change in the non-adjacent fingers (see Discussion).

We found that there was indeed a difference in the way the fingers of the block only group changed in threshold over time. This was revealed by a 6 x 3 within-participants GEE analysis with factors Finger (left/ right index, middle, ring) and Session (online, offline, retention) that produced a significant interaction of Finger x Session ($\chi^2(10) = 111.41, p < .001$). See Table 1A for lower-order $\chi^2$ and p values, and Figure 3 for visualisations. Please note, comparing all six fingers in a 6 x 2 GEE returned only a trending difference ($p = .075$): this may indicate a loss of power due to removing data, or, may suggest that selectivity of deafferentation gains may not be complete (see Discussion).

Next, we wished to directly contrast changes in the deafferentation-adjacent finger and the remaining five fingers of the hand – to determine whether gains were significantly larger for the right index finger compared to the other fingers, indicating relative selectivity. To do so, we collapsed over these five fingers to create an average threshold. Collapsing over fingers was deemed appropriate given, critically, these five fingers changed in the same way over time (i.e., there was a non-significant interaction of Finger x Session, $p = .167$; see Table 1B).
As predicted, we found there were greater perceptual gains in the deafferentation-adjacent finger than in the remaining five fingers of the hand. This difference, however, reduced by the long-term testing session (3-4 days post intervention). This was indicated by a within-participants GEE performed for each session with one factor, Finger (deafferentation-adjacent, average of remaining 5). This produced a main effect of Finger that was significant at the offline session (p = .003), but reduced to a trend at the long-term retention test (at Bonferroni corrected α = .025, p = .061; see Table 1, Ci and Cii). Descriptive statistics for the offline session indicated that the direction of this main effect was as expected, with greater learning decreases seen in the deafferentation-adjacent finger (M = -0.37, SEM = .23) than the remaining fingers (M = 0.23, SEM = .11). Please note. Results are presented for individual participants (one data-point per condition/participant) in the Supplementary Materials, Part IV.

Interactive effects of deafferentation: Enhancement of learning transfer in the block+train vs. sham+train group

We next wished to explore the interactive effects of deafferentation and training on perception. To do so, we compared perceptual changes over session in the block+train group vs. the sham+train group.

As predicted, we found that deafferentation altered training-related learning gains, as compared to training alone. This was revealed by a 6 x 3 x 2 mixed GEE analysis with within-participants factors Finger (left/right index, middle, ring) and Session (online, offline, retention) and between-participants factor Group (block+train, sham+train) that produced a significant Finger x Session x Group interaction ($\chi^2$ (10) = 38.42, p < .001; see Table 2A for lower-order $\chi^2$ and p values, and Figure 3 for visualisations).
We then wished to explore whether, consistent with our predictions, deafferentation caused enhanced transfer of tactile perceptual learning. Specifically, did deafferentation enhance transfer to the index and ring fingers of the left (untrained) hand – as these are fingers that do not normally show gains from learning transfer (see Introduction).

Consistent with our hypothesis, we showed that there was more learning in the left index and ring fingers in the block+train group compared to the sham+train group, but this effect had also reduced by the final (long-term) testing session. This was revealed by a mixed 2 x 2 GEE performed for each session with factors Finger (left index, left ring) and Group (block+train, sham+train). This revealed there was a significant main effect of Group for the offline session (at $\alpha = .025$, $p = .018$), but this became non-significant by the long-term retention test ($p = .425$; see Table 2, Bi and Bii). Looking at the descriptive statistics for the offline session, we saw that the direction of the main effect was as predicted – with greater threshold decreases (improved perception) in block+train group (averaged across fingers, $M = -0.39$, SEM = .13) than the sham+train group (also averaged, $M = -0.27$, SEM = .13).

Dissociation of direct and interactive effects: Block only vs. block+train group

Finally, we wished to demonstrate that the direct and interactive effects of deafferentation were truly dissociable in the pattern of perceptual gains they produce. As predicted, we found that the thresholds of the block only and block+train groups did change differently over fingers and sessions. This indicated that sensory improvements in the block+train group were attributable to both the effects of training and the block (not the block alone), and these interactive effects were, thus, statistically distinguishable from the direct effects of the block alone seen in the block only group.

This was revealed by the results of a 6 x 3 x 2 mixed GEE analysis with within-participants factors Finger (left/ right index, middle, ring) and Session (online,
offline, retention) and between-participants factor Group (block only, block+train)
that produced a significant Finger x Session x Group interaction ($\chi^2 (10) =
26.29, p = .003$), see Table 2C for lower-order $\chi^2$ and $p$ values, and Figure 3 for
visualisations.

We then examined whether the difference between these two groups aligned
with our specific hypotheses. As discussed in the Introduction, we had predicted
threshold gains for the deafferentation-adjacent (right middle) finger in both the
block only and block+train group. However, we predicted gains would be largely
selective to this finger in the block only group. In contrast, we expected there
would be widespread gains across the hand in (up to) all five remaining fingers
in the block+train group – due to the interaction of training and deafferentation.
As predicted, we found greater learning gains across these five fingers in the
block+train group as compared to the same fingers of the block only group. As
with previous results, however, this effect reduced by the long-term test.

This was revealed by a 5 x 2 mixed GEE with the factors Finger (left/ right index,
left middle and left/ right ring) and Group (block only, block+train), conducted for
both the offline and retention sessions. These analyses revealed the main effect
of Group was significant for the offline test (at $\alpha = .025$, $p = .006$), but reduced to
a trend by the long-term retention test ($p = .062$; see Table 2, Di and Dii).
Descriptive statistics at the online test indicated that, consistent with
expectations, there was greater threshold drop (and thus, improved perception)
in fingers of the block+train group (averaged over fingers; $M = -0.38$, SEM = .08)
than the block only group (also averaged; $M = 0.05$, SEM = .09). Group did not
interact with Finger at the offline or retention tests (.841 and .406, respectively),
indicating all five fingers were ns different in threshold at either session, i.e.,
there was consistency in tactile perception between fingers at both tests (also
see Table 2D).

In addition to our hypothesis driven analyses (above), we also performed data-
driven (within-groups) analyses on each group separately to investigate in more
detail how each finger changed individually across sessions for each group. Due
to their exploratory and descriptive nature, we report these results in the Supplementary Materials (part VI). The results of these data-driven analyses reflected the hypothesis driven tests. Finally, we present a description of the point at which significant changes in threshold occurred for each finger (for each group), termed the ‘time to learn’ analysis; see Supplementary Materials (part VII).

Discussion

It is now widely supported that sensory input loss causes changes in brain organisation. In contrast, whether and how reorganisation functionally shape perception has remained unclear (Makin & Bensmaia, 2017). Perceptual gains could be triggered by the direct effects of sensory loss (recruitment of deafferented cortex: Merzenich et al., 1983a). They could also occur by facilitation of concurrent sensory input that co-occurred with the deafferentation e.g., training (Ziemann, Muellbacher, Hallett & Cohen, 2001; Muellbacher et al., 2002; Rosen, Bjorkman & Lundborg, 2006; Shibata, Kawato, Watanabe & Sasaki, 2012), or changes in behaviour to compensate for deafferentation e.g., exploration behaviour using the deprived sensory organ, after the sense of touch had been restored (Polley, Chen-Bee & Frostig, 1999). Upper-limb amputees present a classic example of this duality, since amputation causes both input loss and dramatic behavioural change (Makin et al. 2013; Hahamy et al. 2015; 2017 see also Kupers & Ptito, 2014).

Here we aimed to disentangle this ambiguity by determining the relative contributions of deafferentation and concomitant sensory training on perceptual gains. Using psychophysical measures, we found that temporary finger deafferentation directly enhanced tactile perception of the deafferentation-adjacent finger. We also demonstrated that sensory block concurrent to tactile training caused widespread transfer of learning to untrained fingers – beyond what was seen with sham block, and beyond the normal topographic spread of tactile learning (Dempsey-Jones et al., 2016; Harrar et al., 2014). Our results
suggest that deafferentation enhances perception both directly and interactively (by boosting the effects of sensory training) – resulting in distinct profiles of sensory gains. This dissociation expands possibilities for the use of deafferentation for boosting sensory perception or promoting rehabilitation training following sensory insult or injury.

How could deafferentation directly impact tactile perception?

What mechanisms might support selective gains in sensory thresholds in the deafferentation-adjacent finger? Cortical and subcortical deafferentation-related changes are likely inherently linked (Kambi et al., 2014). Here we focus our discussion on documented changes in primary somatosensory cortex (SI), which have been studied most extensively – allowing a more comprehensive mechanistic understanding of deafferentation-related physiological changes.

SI reorganisation after deafferentation is largely driven by alterations of the excitation-inhibition balance and Hebbian plasticity processes. Merzenich and colleagues revealed that several months after finger amputation (or median nerve transection) the cortical territory previously representing the deafferented finger(s) was subsumed by the adjacent fingers (Merzenich et al., 1983a; Merzenich et al., 1984; see also Pons et al., 1991; see Feldman & Brecht, 2005 for results in rodents). In rats, Faggin and colleagues (1997) showed deafferentation-related changes across the somatosensory system occurring almost immediately following anaesthetic whisker block. The rapid timescale of these changes suggests reorganisation is supported by the unmasking of pre-existing connections (‘silent cells’) between adjacent cortical areas (Margolis et al., 2012). Unmasking may occur due to disinhibition, which is known to be important in maintaining distinct borders between representations (SI: Jones, 1993; Paullus & Hickmott, 2011; M1: Jacobs & Donoghue, 1991). Thus, deafferentation causes near-immediate increases in processing resources for spared sensory inputs. Supporting this, training-related increases in cortical areal extent correlate with perceptual gains in tactile learning studies (Recanzone, Merzenich, Jenkins, Grajski, & Dinse, 1992), suggesting deafferentation could cause similar gains by increasing cortical representations.
The selective gains we document on the right middle finger are unlikely to have occurred as a result of repeated exposure to our testing procedure. Although not shown here, we have previously demonstrated in two independent samples that testing the right and left index, middle and ring fingers using an identical protocol over multiple testing days causes limited, but importantly, equivalent (i.e., non-selective) gains in perception for all six fingers (Dempsey-Jones et al., 2016; Harrar et al., 2014, full details in Supplementary Materials, part I).

Physiological literature suggests that while the majority of deafferentation effects occur for bodily locations directly adjacent to the deafferentated zone, effects are not restricted to adjacent locations – with reduced changes being documented further afield (Merzenich et al., 1984) almost instantaneous to deafferentation (in whiskers, Faggin et al., 1997). While our a priori results and exploratory analyses (see Supplementary Results, part VI) suggest selectivity of gains, selectivity may not be complete (see trend in the Block only results). Thus, it may be that with longer deafferentation (e.g., over 2 hours, as here), we may see gains in fingers other than the deafferentation adjacent finger. Given the results of physiological studies (above), however, we expect effects to be most pronounced in the adjacent finger – regardless of deafferentation duration.

**How could deafferentation interact with training to cause learning gains?**

Our second key prediction was that deprivation can drive sensory gains by modulating the processing of sensory input concurrent to input loss (here, training effects) – thereby resulting in a divergent pattern of gains for touch perception, compared to deafferentation alone. More specifically, we predicted deafferentation would cause training-related learning gains to transfer beyond the normal extent of topographic transfer. Previous studies using similar designs have demonstrated learning transfer causes a specific and restricted pattern of learning gains, with transfer from the trained finger to the adjacent and homologous fingers alone (and not to other fingers outside these topographic relational categories; Harrar et al., 2014; Dempsey-Jones et al., 2016).

Subsequently, we wished to determine if we could expand this transfer boundary. We predicted that the interactive effect of training and deafferentation would result in transfer of learning to the index and ring fingers of the untrained
hand (which typically do not learn under normal circumstances i.e., no
deafferentation). Consistent with our prediction, we found the extent of learning-
transfer was greater in these fingers when training was coupled with sensory
block, compared to when coupled with sham block.

This boost in learning transfer may have resulted from the direct effects of
deafferentation: for instance, invasion of the deafferented finger territory by the
deafferentation-adjacent finger(s) (see above) may have altered the pattern of
learning transfer by changing topographic neighbourhood-relationships in the
somatosensory system. In such a case, fingers could become ‘adjacent’ after
deafferentation – where they weren’t before, thus modulating the way learning
can transfer between fingers (Harrar et al., 2014; Dempsey-Jones et al., 2016;
please see Supplementary Materials, part VIII for a discussion of the locus of
tactile training effects within the somatosensory system). Given training is also
known to cause an increase in the areal extent of the trained skin surface
(Detorakis & Rougier 2014; Jenkins et al. 1990; Xerri et al. 1994; see
Buonomano and Merzenich, 1998 for review) this could contribute to the way in
which deafferentation and training interact to boost perception.

Training may also harness Hebbian plasticity processes triggered by
deafferentation – causing enhanced training-related gains, e.g., long-term
depression (Allen, Celikel & Feldman, 2003) and/ or potentiation (Gambino &
Holtmaat, 2012). This is consistent with previous rodent work suggesting
deafferentation-related modulations of neuronal selectivity and tuning are
altered by concurrent behaviour (and the subsequent patterns of sensory input
these behaviours cause: Polley et al., 1999). Indeed, increased training efficacy
could account for the widespread transfer of learning, and subsequent sensory
gains across the hand we show here (see Zeiler & Krakauer, 2013 for a similar
theory of interactive effects of post-stroke plasticity and learning).

Alternatively, enhanced transfer of learning gains following anaesthetic block
may reflect deafferentation-related alterations in RF properties. Tactile training
has long been associated with changes in RF properties in SI (e.g., the
shrinking and migration of RFs towards the trained area and (some) adjacent
areas: Jenkins, Merzenich, Ochs, Allard & Guic-Robles, 1990; Recanzone,
It has been suggested that RF overlap may critically drive the transfer of tactile learning (Harrar et al. 2014; also see Harris, Harris & Diamond, 2001). Thus, the increased overlap of RFs representing the spared, neighbouring fingers (Merzenich et al. 1983a) might facilitate enhanced learning transfer following deafferentation that we demonstrate here.

Deafferentation and experience-dependent plasticity

While we demonstrate direct and interactive effects of temporary deprivation are distinct in the patterns of sensory gains they produce, we believe these processes are likely supported by a related mechanism. We previously emphasised the role of habitual behaviour in shaping SI organisation and, subsequently, transfer patterns of tactile learning (Dempsey-Jones et al., 2016; also see Ejaz, Hamada & Diedrichsen, 2015). Our current findings highlight the need to consider behavioural changes (especially with non-deafferented (spared) body-parts) in understanding deafferentation related plasticity (Makin et al., 2013). Indeed, it is possible that undocumented behavioural changes subsequent to deafferentation could contribute to the ‘direct’ sensory improvements we report. For example, since we did not restrict the movements of our participants in the block only group during and post deafferentation, they may have increased reliance on their deafferentation-adjacent finger due to the altered state of their hand. Indeed, deafferentation could combine with hand-use related to our testing or training protocols, as well as naturalistic behaviour in the experiment breaks and following cessation of testing (while residual deafferentation effects lingered). The use of the mouse to respond in our study, for instance, could have provided tactile feedback to the index and middle fingers (of both hands during testing, and the left hand during training, if applicable). This may have lead to a reduction in tactile thresholds on these two fingers due to unintentional ‘training’ (though this appears unlikely given non-significant tactile gains in the left/ right index finger – used with the mouse – in either the block only or the sham+train groups).

Given the potential influence of undocumented tactile stimulation, we suggest that sensory improvements in the block only group could also have resulted, in
part, from the interaction of deafferentation and sensory experience. It may, therefore, be more appropriate to term direct and interactive effects as ‘weakly interactive’ and ‘strongly interactive’ effects of deafferentation and training. This finding emphasises the tight link between deprivation-driven and experience-dependent plasticity. In this way, our results compliment those from studies of visual deprivation (e.g., Duffy & Mitchell, 2013; Lunghi, Emir, Morrone & Bridge, 2015) and demonstrate that even transient somatosensory input loss can reset sensory pathways to a more plastic state.
Brain plasticity is critical for learning, adapting to change and recovering from injury. Previous research suggests that loss of sensory input could ‘free up’ brain territory to be used for other purposes (e.g., to support tactile perception in the blind). Despite decades of research, solid behavioural evidence is lacking. Here we show that plasticity following sensory deprivation can indeed be harnessed to enhance perception and learning in adults. Our results reveal that by removing touch input to a single finger (using anaesthetic), touch sensation improves on the neighbouring finger (the ‘direct’ effects of sensory loss). We also show that anaesthetic to one finger can boost sensory training applied to its neighbouring finger, causing widespread learning gains across the hand (as compared to training without anaesthetic, or anaesthetic alone). We term these enhanced learning outcomes the ‘interactive’ effects of sensory loss. Importantly, our results indicate for the first time that these direct and interactive processes produce different patterns of sensory improvements. This study highlights that sensory exposure concurrent to acute sensory loss is critical in shaping our perception; though further research is needed to reveal how sensory loss and sensory inputs may interact at a chronic timescale, and whether deprivation effects vary over time. Our findings reveal a new way by which plasticity can be exploited to improve perception, for example to optimise rehabilitation, combat perceptual loss in ageing and boost our natural human capacities towards superior sensory perception.
References


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Table 1.

Group x Finger x Session

\[ \chi^2(5) = 11.67, \quad p = .040^* \]
\[ \chi^2(4) = 6.47, \quad p = .155 \]
\[ \chi^2(1) = 8.90, \quad p = .003^* \]
\[ \chi^2(1) = 3.52, \quad p = .061 \]

Group x Finger

\[ \chi^2(2) = 7.97, \quad p = .019^* \]
\[ \chi^2(1) = 1.70, \quad p = .193 \]

\[ \chi^2(4) = 6.47, \quad p = .167 \]

Finger x Session

\[ \chi^2(10) = 111.41, \quad p < .001^* \]
\[ \chi^2(4) = 6.47, \quad p = .167 \]

\[ \chi^2(1) = 3.52, \quad p = .061 \]

Finger x Group

\[ \chi^2(1) = 3.52, \quad p = .061 \]

\[ \chi^2(1) = 3.52, \quad p = .061 \]

Session x Group

\[ \chi^2(1) = 3.52, \quad p = .061 \]

\[ \chi^2(1) = 3.52, \quad p = .061 \]

QICC

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**Figure and table captions**

**Figure 1.** Prediction figure: schematic representation of hypothesised changes in touch perception from pre- to post-intervention in the three groups: **A. Block only** (i.e., ‘direct’ effects of deafferentation, top panel), **B. Block+train** (i.e., ‘interactive’ effects of deafferentation, middle panel) and **C. Sham+train** (training only control, bottom panel). Values are baseline normalised (threshold-baseline), thus zero represents baseline perceptual threshold, and threshold decreases from zero represent improved perception (negative numbers). We predicted **A.** In the block only group, direct deafferentation effects would produce sensory gains that were mostly selective to the deafferentation-adjacent (right middle) finger; **B.** In the block+train group, interactive effects would lead to gains that were much more widespread, i.e. learning for (up to) all six tested fingers; **C.** Finally, in the sham+train group, we predicted limited learning in the trained finger, with possible transfer of learning to the homologous finger, due to the effects of the minimal training paradigm alone. Fingers that were predicted to improve significantly are marked with an asterisk and a block-coloured line (*), those that are expected to show some limited improvement that may not reach significance with a hash and dashed line (#), fingers predicted not to change significantly are indicated by grey lines. On the hand ‘legend’, fingers marked with a circle and ‘B’ denote a blocked finger, those marked with ‘S’ denote a sham-blocked finger, and the circle marked ‘T’ denotes a trained finger (if applicable).

**Figure 2.** **A.** Apparatus for presentation of experimental stimuli (tactile dome gratings) – views from the top and side. **B.** Schedule of testing and training for the three groups. Please note: in the testing task, ‘all fingers’ refers to all six fingers tested, i.e., the index, middle and ring fingers of the left and right hands. **C.** Schematic description of the testing and training tasks, with grating orientations. **D.** Example psychometric functions from two representative participants of the block only group (tactile ‘threshold’ corresponds with the interpolation of 82% accuracy on the y axis). The psychometric functions show threshold improvement for the (deafferentation-adjacent) right middle finger from the baseline to retention tests, i.e., the direct effects of sensory block on the
adjacent finger. Improvement in perception is reflected by a drop in grating orientation threshold (lower grating size values on the x axis).

Figure 3. Change of tactile sensory thresholds over testing sessions in the three groups: A. Block only (i.e., ‘direct’ effects of deafferentation, top panel), B. Block+train (i.e., ‘interactive’ effects of deafferentation, middle panel) and C. Sham+train (training only control, bottom panel). Data are baseline normalised values (threshold-baseline); see Supplementary Materials, part II for raw data and part III for individual participant data (one point per condition/ participant). Actual means are used (not estimated marginal means from the GEE). Zero represents baseline perceptual threshold, and decreases from zero represent improved perception (negative numbers). Fingers that changed significantly in threshold over session, i.e., that showed a significant main effect of Session (see Table S3 in the Supplementary Materials) are marked with an asterisk (e.g., the right middle finger of the block only group) and a block coloured line. Fingers showing trending change are marked with a hash (#) and a dashed line. On the hand ‘legend’, fingers marked with a circle and ‘B’ denote a blocked finger, those marked with ‘S’ denote a sham-blocked finger, and the circle marked ‘T’ denotes a trained finger (if applicable). Please note: for the blocked groups, the threshold for the right index finger is not represented for the period during which this finger was anaesthetised (i.e., at the online test).

Table 1. Complete statistical details for the within-participants Generalised Estimating Equation (GEE) Analyses presented in-text for the block only group. Columns A-C contain GEE analyses: A. for all six fingers and three sessions, which indicates fingers change differently over finger and session; B. Analyses with the deafferentation-adjacent finger removed reveals the remaining fingers change in the same way over sessions (i.e., collapsing values over these fingers is appropriate); C. Hypothesis-driven, follow-up tests. This reveals significant differences between the trained finger vs. five remaining fingers (a main effect of Finger) in the offline session (Ci.), reducing to a trend by the long-term retention sessions (Ci.; see in-text for direction of this Finger main effect and its interpretation). Follow-up GEEs in column C were Bonferroni corrected for multiple comparisons ($\alpha = .25$). * indicates a significant difference.
(at $p = .05$ and $p = .025$ for interactions and follow-up tests, respectively).

~ indicates this comparison was re-run without data for the injected finger while anaesthetic effects may have still been apparent (right index finger, online session): interaction remained $p < .05$.

Table 2. Complete statistical details for the between-participants Generalised Estimating Equation (GEE) analyses presented in text for between-group comparisons. Columns A-B contain analyses presented for the trained groups: 

A. For all six fingers and three sessions – revealing a difference in the way thresholds change over session for the fingers; B. Hypothesis-driven, follow-up tests between the left index/ ring of the block+train vs. sham+train groups, which indicate a significant group effect (main effect of Group) in the offline (Bi.) but not long-term retention sessions (Bii.; see in-text for direction of Group main effect and its interpretation). Columns C-D contain analyses presented for the blocked groups: C. For all six fingers and three sessions – also revealing a difference in threshold change over session between fingers. D. Hypothesis-driven, follow-up tests between the five fingers tested (no deafferentation-adjacent finger) for the block only group vs. the block+train group – revealing a significant group effect (main effect of Group) at the offline (Di.), but not retention sessions (Dii.; see in-text for direction of this Group main effect and its interpretation). Follow-up GEEs in columns B & D were Bonferroni corrected for multiple comparisons ($\alpha = .25$). * indicates a significant difference (at $p = .05$ and $p = .025$ for interactions and follow-up tests, respectively). ~ indicates this comparison was re-run without data for the injected finger while anaesthetic effects may have still been apparent (right index finger, online session): interaction remained $p < .05$. 
Figure

A. Direct effects of deafferentation: Block only group

B. Interactive effects of deafferentation: Block+train group

C. Training only control: Sham+train group
A. Direct effects of deafferentation: Block only group

B. Interactive effects of deafferentation: Block+train group

C. Training only control: Sham+train group
Supplementary Materials

Part I. Supplementary Results: ‘Testing only’ control group, independent dataset

In the current study we compare a deafferentation only group (‘block only’), a deafferentation and training group (‘block+train’), and a sham deafferentation and training control group (‘sham+train’). We did not include a ‘sham only’ condition, where participants underwent a protocol of repeated testing alongside two ‘sham’ blocks (akin to the ‘block only’ group). A major consideration in this decision was that we have previously run two studies examining the effects of repeated tactile testing alone on the tested fingers i.e., without training (a ‘testing only’ control: Harrar et al., 2014; Dempsey-Jones et al., 2016). In both previous studies, we have established that repeated testing alone does not cause selective change in touch thresholds for any one finger. This allows us to interpret the effects of the nerve block in the block only group indirectly. It also means repeated testing cannot explain isolated improvement of the right middle finger in the block only group. Given these replicated findings, a ‘sham only’ group would arguably not be additionally informative here.

Here, for the interest of readers, we provide further details of the analysis of one such ‘testing only’ control group from one of the aforementioned independent datasets (Dempsey-Jones et al., 2016). In this study, participants underwent an identical tactile testing procedure to that used in the current study (same stimuli, design and equipment). This testing, however, was carried out over a week, involving five tests (one in addition to the testing applied in the present study, i.e., even greater exposure to testing).

Analysis of this testing only control group showed that, as had been predicted, there was some limited improvement in threshold (as a result of repeated testing) but this improvement was not different between fingers. This was revealed by a within-participants ANOVA with factors Finger (right/ left index, middle, ring) and Session (1-5) that produced a significant main effect of testing Session (F (2,14) = 10.12, p = 0.003), a significant main effect of Finger (F (5,40) = 3.94, p = .005), but no interaction of Finger x Session (F (5,41) = 0.76, p = .758). See Figure 2C, Dempsey-Jones et al., 2016. This consistency across fingers supports the role of our intervention in causing selective change in the right middle finger in the block only group (also see similar results in Harrar et al., 2014).
Part II. Table S1. Raw (non-normalised) data for all experimental groups, I. the block only group, II. The block+train group and III. The sham+train group. Mean values are shown in the left four columns and standard error of the mean (SEM) values in the right four columns. ‘block’ indicates a deafferented finger, ‘sham’ a sham-deafferented finger and ‘train’ a trained finger, where applicable.

I. Block only

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</table>
Part III. Grating orientation values against aspects of methodology

With regard to the absolute values of these thresholds, procedures using descending staircases typically appear to produce lower threshold values (Sathian & Zangaladza, 1996; 1997; Van-Boven & Johnson, 1994) than those using randomised presentation of difficulty levels (e.g., the method of constant stimuli, as in the current study; also see Harrar et al., 2014; Dempsey-Jones et al., 2016). Studies using presentation orders midway between staircase and randomisation report midrange thresholds (e.g., adaptive or Bayesian staircase procedures: Peters et al., 2009; Wong et al., 2011; 2013).

Given the potential link between apparent threshold values (as well as other methodological/ participant factors like age: Stevens & Patterson, 1995; gender: Peters et al., 2009), ‘absolute’ threshold values may be difficult to interpret with respect to physiological factors such as innervation density (see discussion in Johnson and Phillips, 1981; Peters et al., 2009). For this reason, we prefer not to speculate on the physiological meaning of our absolute threshold values (e.g., whether our intervention pushes perception below a level set by peripheral receptors, into, for example, the range of hyperacuity: Sathian, Deshpande & Stilla, 2013) but interpret relative threshold change with respect to baseline alone.
We propose a relationship between method of grating presentation (re. order of difficulty levels) and the absolute value of thresholds: if descending staircases are coded as 0 (least randomised), adaptive/ Bayesian staircases as 5 (mid-level randomisation) and method of constant stimuli as 10 (full randomisation), there is a trending correlation between index finger threshold and presentation method (Spearman’s rho = .498, p = .099, N = 12 studies). All threshold values represent grating resolution in millimetres (mm). Please note that these studies use different values for threshold interpolation and are thus only approximately comparable (differences of between 1-9%). Also note the studies with most participants (marked in green, N>20), have thresholds most similar to those of the current study.

Table S2. We propose a relationship between method of grating presentation (re. order of difficulty levels) and the absolute value of thresholds: if descending staircases are coded as 0 (least randomised), adaptive/ Bayesian staircases as 5 (mid-level randomisation) and method of constant stimuli as 10 (full randomisation), there is a trending correlation between index finger threshold and presentation method (Spearman’s rho = .498, p = .099, N = 12 studies). All threshold values represent grating resolution in millimetres (mm). Please note that these studies use different values for threshold interpolation and are thus only approximately comparable (differences of between 1-9%). Also note the studies with most participants (marked in green, N>20), have thresholds most similar to those of the current study.

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<tbody>
<tr>
<td>D1</td>
<td>N = 8</td>
<td>N = 7</td>
<td>N = 14</td>
<td>N = 7</td>
<td>N = 15</td>
<td>N = 8</td>
<td>N = 97</td>
<td>N = 3</td>
<td>N = 10</td>
<td>N = 55</td>
<td>N = 24</td>
<td>N = 21</td>
<td>N = 36</td>
</tr>
<tr>
<td>D2</td>
<td><del>0.80 (</del>−1) average D2/D3 (most D2)</td>
<td>0.89 (.05)</td>
<td>.98 (.12)</td>
<td>~1.00</td>
<td>1.10 (.09)</td>
<td>~1.23-1.26</td>
<td>~1.40-1.60</td>
<td>~1.70</td>
<td>1.60-1.80 average (9 on D2, 1 on D4)</td>
<td>1.70-1.80</td>
<td>1.70 (.08)</td>
<td>1.85 (.07)</td>
<td>1.84 (.08)</td>
</tr>
<tr>
<td>D3</td>
<td>0.93 (.05)</td>
<td>1.43-1.51</td>
<td>1.75</td>
<td>2.02 (.11)</td>
<td>2.10 (.07)</td>
<td>2.12 (.09)</td>
<td>As above</td>
<td>1.9</td>
<td>2.19 (.12)</td>
<td>2.39 (0.8)</td>
<td>2.38 (.09)</td>
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<tr>
<td>D4</td>
<td>1.06 (.10)</td>
<td>1.67-1.62</td>
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<tr>
<td>D5</td>
<td>1.44 (.15)</td>
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<tr>
<td>Threshold interpolation value</td>
<td>d' = 1.34 (approx. 75% acc.)</td>
<td>75% acc.</td>
<td>d' = 1.35 (approx. 75% acc.)</td>
<td>75% acc.</td>
<td>75% acc.</td>
<td>71% acc.</td>
<td>d' = 1 (76% acc.)</td>
<td>d' = 1.35 (~75% acc.)</td>
<td>d' = 1 (76% acc.)</td>
<td>d' = 1 (76% acc.)</td>
<td>82%</td>
<td>82%</td>
<td>82%</td>
</tr>
<tr>
<td>Presentation order</td>
<td>Descending Stair.</td>
<td>Descending Stair.</td>
<td>Unclear (may be descending stair.)</td>
<td>Descending Stair.</td>
<td>Descending Stair.</td>
<td>Staircase with reversals</td>
<td>Unspecified</td>
<td>Baysian algorithm</td>
<td>Baysian algorithm</td>
<td>Baysian algorithm</td>
<td>MOCS</td>
<td>MOCS</td>
<td>MOCS</td>
</tr>
<tr>
<td>Previous tactile testing or training?</td>
<td>Yes (various unrelated grating exps.)</td>
<td>No</td>
<td>No</td>
<td>Yes (4 prior grating exps.)</td>
<td>No</td>
<td>Yes (prior tactile discrim. task: 468 trials)</td>
<td>Unclear</td>
<td>Yes (2 unrelated tactile exps.)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

^ older sample (M = 39 yo)
* our laboratory

D1 = 1.00 (.06)
D2 = 0.89 (.05)
D3 = 0.93 (.05)
D4 = 1.06 (.10)
D5 = 1.44 (.15)
Part IV. Figure S1: Individual participant data (one data-point per participant/condition).

A. Direct effects of deafferentation: Block only group

B. Interactive effects of deafferentation: Block+train group

C. Training only control: Sham+train group
Figure S1. Change of tactile sensory thresholds over testing sessions in the three groups: A. Block only (i.e., ‘direct’ effects of deafferentation, top panel), B. Block+train (i.e., ‘interactive’ effects of deafferentation, middle panel) and C. Sham+train (training only control, bottom panel). Data are baseline normalised values (threshold-baseline), see Supplementary Materials, part II-III for raw data. Actual means are used (not estimated marginal means from the GEE). Zero represents baseline perceptual threshold, and decreases from zero represent improved perception (negative numbers). Fingers that changed significantly in threshold over session, i.e., that showed a significant main effect of Session (see within-participants GEE Results in Table 3) are marked with an asterisk (e.g., the right middle finger of the block only group). On the hand ‘legend’, fingers marked with a circle and ‘B’ denote a blocked finger, those marked with ‘S’ denote a sham-blocked finger, and the circle marked ‘T’ denotes a trained finger (if applicable). Please note: for the blocked groups, the threshold for the right index finger is not represented for the period during which this finger was anaesthetised (i.e., at the online test). For raw data for all participants and conditions please see: http://www.ucl.ac.uk/icn/research/supps/dempseyjones.
Part V. Supplementary results: Replication of our central (GEE) results using analysis of variance analysis (ANOVA) methods

Here we replicate our key, hypothesis-driven results using ANOVA methods for comparability with previous studies that utilise this method of analysis. However, please note that, statistically, the GEE is a more appropriate method for the analysis of interdependent data (e.g., multiple fingers/ sessions per participant), as compared to repeated-measures ANOVA (Ballinger, 2004; see further discussion in the main text).

One particular benefit of the GEE framework is the ability to deal with missing cases. The GEE uses modelling of within- and between-participants variance to predict missing case values and, subsequently, does not require them to be filled using an arbitrary criterion. For our ANOVA analysis we did not replace empty cases in our dataset e.g., with averages created within groups or participants, resulting in a smaller sample size per comparison/test.

In the main text, we hypothesise that deafferentation concurrent to training (block+train) enhances training effects by increasing the transfer of tactile learning. This transfer of learning to untrained fingers is predicted to be greater than that resulting from training effects alone (i.e., greater transfer in the block+train group versus the sham+train group).

To support these predictions, we tested whether the block+train group showed more learning in the index and ring fingers of the left (untrained) hand than the same fingers of the sham+train group. These fingers do not normally show gains from learning transfer following training alone (see data-driven results for the sham+train group, and previous literature: Dempsey-Jones et al., 2016; Harrar et al., 2014). The results supported our prediction, as revealed by a mixed GEE comparing learning gains on these two fingers (left index/ ring) between the block+train and sham+train groups.

Subsequently, we have now repeated this comparison with a mixed ANOVA, which revealed that the pattern of results held. The factors in this ANOVA were Finger (2 levels: left index, left ring), Session (3 levels: online, offline, retention), and Group (2 levels: block+train, sham+train). As in the main text, baseline normalised values were used, with the baseline covaried out (see van Breukelen, 2005; Vickers, 2001).
Supporting our GEE results, there was a significant main effect of Group, $F(1,15) = 5.39$, $p = .035$, $\eta^2_p = .26$. Also consistent with the GEE, no other main effects or interactions were significant ($.269 < p > .968$; please see Figure 3 in the main text for visualisation). As the GEE revealed no main effect or interaction with finger, gains were consistent between the two fingers for both groups.

As our second main hypothesis, we predicted that learning gains in the block+train group were indeed due to the interaction of training and deafferentation, rather than simply to deafferentation alone. Critically, we demonstrated differences between the block+train group and the block only group that supported this prediction.

More specifically, to reveal this result we examined whether tactile acuity was greater for the fingers of the block+train group, as compared to the block only group (we excluded the deafferentation adjacent finger, which was predicted to learn in both block groups). Using a mixed GEE we demonstrated widespread and equivalent gains across all fingers as a result of training and deafferentation – with more restricted gains from deafferentation alone (though these were also equivalent across fingers). That is, there was greater learning in the five fingers (all except the right middle) for the block+train group, as compared to the block only group – and learning was the same between all fingers, within either group.

We repeated this comparison with a mixed ANOVA, which produced the same pattern of results. The factors of this ANOVA were Finger (5 levels: left/ right index, left middle, left/ right ring), Group (2 levels: block+train; block only), Session (2 levels: offline, retention); other details consistent with the ANOVA above, and main text.

Supporting the GEE results, we found a significant main effect of Group, $F(1,17) = 5.71$, $p = .029$, $\eta^2_p = .25$ – where there were greater gains in the block+train group than the block only group. Also as in the main text GEE analysis, no other main effects or interactions were significant ($.210 < p > .936$). Thus gains were consistent across fingers, for both groups.
Part VI. Data-driven (hypothesis-free) analysis – Statistical assessment of significant learning gains in each finger, separately for each group

In addition to our hypothesis driven analyses (above), we also performed data-driven (within-groups) analyses on each group separately to investigate in more detail how each finger changed across sessions in the three groups. This was because our hypothesis-driven results compared specific subsets of fingers and groups. Consequently, this did not provide a complete picture of whether any one finger (within any one group) showed significant learning gains.

We, therefore, performed one GEE per group and interpreted the resulting main effect(s) of Session for each finger (Wald Chi-Square test), i.e., was there a change in threshold across the four sessions, for one finger at a time. As these final tests were exploratory and descriptive in nature, an uncorrected p value was used, results are presented in Table 3 (though summarised in text below) and we draw limited interpretations from the outcomes. These comparisons used raw (non-normalised data) to best assess change from baseline over sessions (as opposed to normalised data which would allow only comparisons of difference scores, i.e., reflecting the amount of change per session). For interest, we also characterise the timeline of learning for the individual fingers using a further exploratory “time to learn” analysis (i.e., at what session do learning gains occur; see also Dempsey-Jones et al., 2016). However, since these timing results do not directly relate to our main hypotheses, they will not be presented in the main text (please see Supplementary Materials, part VI for details).

Block only group
In the block only group, our data-driven comparisons provided converging support for the selectivity of learning gains of the deafferentation-adjacent finger – seen in the hypothesis-driven tests. Selectivity was revealed by a significant main effect of Session for the deafferentation-adjacent finger alone (p = .041; see Table 3A for statistics regarding non-significant change in the remaining fingers).

Block+train group
Looking at the block+train group, we found that there was learning across almost all fingers of both hands. This was revealed by a significant main effect of Session for five of the six fingers (.001 < p > .049): all fingers except for the left index finger that showed non-
significant perceptual gains over sessions (p = .252; see Table 3B). It, therefore, remains unclear whether interactive effects of deafferentation and training are somewhat finger-selective, or whether they are global (i.e., to all fingers) and we are simply underpowered here to reveal significant perceptual changes (vs. baseline) in the left index finger. While the left index finger showed non-significant change from baseline, the previous analysis still holds that there are significantly more gains on this finger for the block+train group vs. the sham+train group, still supporting enhanced transfer.

**Sham+train group**

In the sham+train group, we found evidence of small, but non-significant improvements in the trained and homologous fingers (p = .099 and p = .055; see Table 3C) – consistent with our prediction of minimal learning and learning transfer in this group (see Introduction). No fingers, however, showed significant learning gains.

**Table S3. Generalised Estimating Equation (GEE) analyses for the exploratory analyses.**

The top rows contain comparisons of all six fingers and four sessions. These tests indicate that there were indeed differences in the way fingers changed over sessions (i.e., significant Finger x Session interactions), for all groups. The bottom row demonstrates which individual fingers changed significantly in threshold across the course of testing (i.e., which showed a significant improvement in threshold from baseline; as reflected by a significant main effect of Session). Given the data-driven nature of these results, tests are uncorrected for multiple comparisons and limited conclusions are drawn from the outcomes. ~ indicates this comparison was re-run without data for the injected finger while anaesthetic effects may have still been apparent (right index finger, online session): interaction remained p < .05.
### Difference scores

<table>
<thead>
<tr>
<th>Group</th>
<th>Finger (6: all), Session (3: all)~</th>
<th>Finger (6: all), Session (3: all)~</th>
<th>Finger (6: all), Session (3: all)~</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
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<tr>
<td>Group (1: Block only), Finger (6: all), Session (3: all)~</td>
<td>$\chi^2 (5) = 250.83$, $p &lt; .001^{**}$</td>
<td>$\chi^2 (5) = 25.33$, $p &lt; .001^{**}$</td>
<td>$\chi^2 (5) = 44.40$, $p &lt; .001^{**}$</td>
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<tr>
<td>B</td>
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<tr>
<td>Group (1: Block+train), Finger (6: all), Session (3: all)~</td>
<td>$\chi^2 (5) = 29.24$, $p &lt; .001^{**}$</td>
<td>$\chi^2 (5) = 46.13$, $p = .001^{**}$</td>
<td>$\chi^2 (5) = 440.51$, $p &lt; .001^{**}$</td>
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<tr>
<td>B</td>
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<tr>
<td>Group (1: Sham+train), Finger (6: all), Session (3: all)~</td>
<td>$\chi^2 (3) = 3.05$, $p = .384$</td>
<td>$\chi^2 (3) = 29.24$, $p &lt; .001^{**}$</td>
<td>$\chi^2 (3) = 138.90$, $p &lt; .001^{**}$</td>
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<td></td>
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<tr>
<td>QICC</td>
<td>130.21</td>
<td>126.75</td>
<td>127.41</td>
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### Raw scores (data-driven comparisons)

<table>
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<tr>
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<th>F</th>
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<tbody>
<tr>
<td>R index</td>
<td>$\chi^2 (3) = 0.57$, $p = .902$</td>
<td>$\chi^2 (3) = 10.10$, $p &lt; .001^{**}$</td>
<td>$\chi^2 (3) = 4.32$, $p = .229$</td>
</tr>
<tr>
<td>R middle</td>
<td>$\chi^2 (3) = 8.27$, $p = .041^{*}$</td>
<td>$\chi^2 (3) = 10.09$, $p = .018$</td>
<td>$\chi^2 (3) = 6.28$, $p = .099^{*}$</td>
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<tr>
<td>R ring</td>
<td>$\chi^2 (3) = 4.24$, $p = .237$</td>
<td>$\chi^2 (3) = 7.88$, $p = .049^{*}$</td>
<td>$\chi^2 (3) = 2.73$, $p = .436$</td>
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<tr>
<td>L ring</td>
<td>$\chi^2 (3) = 1.31$, $p = .726$</td>
<td>$\chi^2 (3) = 9.27$, $p = .026^{*}$</td>
<td>$\chi^2 (3) = 5.95$, $p = .114$</td>
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<tr>
<td>L middle</td>
<td>$\chi^2 (3) = 3.75$, $p = .290$</td>
<td>$\chi^2 (3) = 11.05$, $p = .011^{*}$</td>
<td>$\chi^2 (3) = 7.61$, $p = .055^{*}$</td>
</tr>
<tr>
<td>L index</td>
<td>$\chi^2 (3) = 6.19$, $p = .103$</td>
<td>$\chi^2 (3) = 4.09$, $p = .252$</td>
<td>$\chi^2 (3) = 4.83$, $p = .185$</td>
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Part VII. Supplementary Results: The timeline of learning gains

To follow up from the within-participants Generalised Estimating Equation (GEE) analyses presented in the main text, and characterise the timeline of learning for the individual fingers, we used an exploratory “time to learn” analysis (see Dempsey Jones et al. 2016). This analysis determines how long it took for each finger to significantly improve in threshold with respect to its baseline. Paired-sample t-tests were used to compare the baseline threshold to the threshold of the next session. If this was non-significant, the subsequent session was compared to baseline, until a significant difference was identified. Given the descriptive nature of this analysis, an uncorrected alpha value was used (p = 0.05) and interpretations were cautious. Only fingers that were identified as having a significant main effect of Session in the within-participants, two-way GEE analyses (see main text Results section, and Table 3 of the main text) were followed up with the time to learn analysis – as these were the only fingers for which there was a statistically verifiable change from in thresholds across sessions. Note these results are included here in the Supplementary Materials because we had no predictions regarding when particular fingers would show significant gains. This is a data-driven analysis, provided for interest only.

Block only group

The two-way GEE of the block only group (Finger x Session) revealed a significant main effect of the right middle finger only (see main text). Using the time to learn analysis, we found that the threshold of the right middle finger improved at the retention test (p = .006), though it was already trending towards improvement at the offline test (p = .096). This analysis suggests that the behavioural effects of temporary deafferentation may emerge and develop over the course of a few days. This suggestion is consistent with the findings of Shibata et al. (2012) who found deafferentation enhanced visual contrast sensitivity training between 5-8 days after the intervention, but not before or after this time. The delayed threshold drop we report here, however, may also simply indicate that more power is needed to detect a subtle change in perception, occurring earlier in the time-course. Please note, while this result indicates that gains are at their most different from baseline in the retention session for the deafferenation-adjacent finger, the difference between the deafferenation-adjacent finger and the remaining five fingers (averaged) is maximal at the offline session (see main text for details).
Block+train group

For the block+train group, the two-way GEE (Finger x Session) revealed five from six fingers tested showed a significant main effect of Session (see main text). These were the right index, right middle, right ring, left middle and left ring fingers (with no significant gains in the left index finger only). Once again, to probe the time-course of this learning, we performed the time to learn analysis for each of the fingers that showed a main effect. We found that the homologous left middle finger had already improved when tested during the online session (p = .004). The trained right middle finger (p = .002), right ring finger (p = .017), and left ring finger (p = .028) had significantly learned by the offline session. The deafferented right index finger (adjacent to the trained finger) only showed significant learning by the final retention session (p = .008). This apparent delay in learning may be due to deafferentation effects that vary over time (Merzenich et al., 1984) or to delayed transfer of tactile perceptual learning. Indeed, transfer in tactile learning has been shown not to always occur immediately, or necessarily at the same rate for all fingers. In our previous study (Dempsey-Jones et al., 2016), we show that while the trained finger learned on the day of training (i.e., showed significant change from baseline thresholds at this time), learning transfer did not occur until one or two days following the initial training (varying by finger). Thus, a delay in transfer is not unexpected. Particularly, in the deafferented right index finger, central or peripheral effects due to deafferentation might have interfered with normal processes of learning transfer to exaggerate normal lags in learning transfer.

Sham+train group

As there were no significant main effects of Session (i.e., no threshold values that differed significantly from each other, see main text), the time to learn analysis was not performed for the sham+train group.
Part VIII. Discussion of the locus of the transfer of perceptual learning within the somatosensory system

As discussed in the main text, the topographic organisation of the somatosensory system is integral to our interpretation of the pattern of transfer of perceptual learning. Some suggest perceptual learning occurs in sensory cortex e.g., through plastic changes in tuning properties of sensory neurons (Adab & Vogels, 2011; Jehee, Ling, Swisher, van Bergen, & Tong, 2012; Schoups, Vogels, Qian, & Orban, 2001; Shibata, Watanabe, Sasaki, & Kawato, 2011). These accounts predict tactile learning that either does not spread (Dinse et al., 2006, though see critique in Dempsey-Jones, 2016) or spreads in a topographic pattern (humans: Dempsey-Jones et al., 2016; Harrar et al., 2014; Harris et al., 2001; rodents: Harris & Diamond, 2000; Harris et al., 1999). Other theories suggest perceptual learning occurs in higher-order areas that read-out from sensory cortex e.g., parietal or decision making areas (Huang, Lu, & Dosher, 2012; Kahnt, Grueschow, Speck, & Haynes, 2011; Law & Gold, 2008; Petrov, Dosher, & Lu, 2005); see Harrar et al., (2014) for further discussion. Regardless of the precise locus of learning, transfer of tactile perceptual learning must occur as a function of topographic organisation (or reorganisation following deafferentation). Thus, the pattern of learning transfer we report here is consistent with several contemporary perceptual learning theories.

Transfer of tactile learning has also been suggested to occur ‘globally’ (to all fingers tested). However, many such studies only examine transfer to one finger, typically the finger homologous to (Kaas, van de Ven, Reithler, & Goebel, 2013; Nagarajan, Blake, Wright, Byl, & Merzenich, 1998; Sathian & Zangaladze, 1998; Spengler et al., 1997) or adjacent to the trained finger (Nagarajan et al., 1998; though see Arnold & Auvray, 2014). Such designs do not allow for separation between global and topographic accounts. Those that have attempted to dissociate these two drivers of transfer indicate the spread of spatial tactile learning is best characterised by SI topography (Dempsey-Jones et al., 2016; Harrar et al., 2014; Harris, Harris, & Diamond, 2001).