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Tonic somatosensory responses and deficits of tactile awareness converge in the parietal operculum

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Although clinical neuroscience and the neuroscience of consciousness have long sought mechanistic explanations of tactile-awareness disorders, mechanistic insights are rare, mainly because of the difficulty of depicting the fine-grained neural dynamics underlying somatosensory processes.

Here, we combined the stereo-EEG responses to somatosensory stimulation with the lesion mapping of patients with a tactile-awareness disorder, namely tactile extinction.

Whereas stereo-EEG responses present different temporal patterns, including early/phasic and long-lasting/tonic activities, tactile-extinction lesion mapping co-localizes only with the latter. Overlaps are limited to the posterior part of the perisylvian regions, suggesting that tonic activities may play a role in sustaining tactile awareness. To assess this hypothesis further, we correlated the prevalence of tonic responses with the tactile-extinction lesion mapping, showing that they follow the same topographical gradient. Finally, in parallel with the notion that visuo-tactile stimulation improves detection in tactile-extinction patients, we demonstrated an enhancement of tonic responses to visuotactile stimuli, with a strong voxel-wise correlation with the lesion mapping.

The combination of these results establishes tonic responses in the parietal operculum as the ideal neural correlate of tactile awareness.

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Abbreviation: TE +/− = tactile extinction present/absent

Introduction

Identifying the neural correlates of conscious perception represents a major challenge for the neuroscience of consciousness.[1] When external stimuli are reported as perceived, neural responses increase in sensory regions,[2,3] they involve a more comprehensive network of areas[2,4] and early responses are accompanied by late sustained ones.[5–8] Late components have been documented using intracranial recordings in the processing of somatosensory, consciously perceived stimuli. Passive somatic stimuli evoke a tonic, bilateral, long-lasting and non-somatotopically arranged response confined to the perisylvian regions.[9–11] Due to the analogy with the features characterizing recurrent activity,[12] it has been proposed that tonic activity represents the neural signature of tactile awareness.[10]

Neuropsychological studies frequently describe a selective disorder of somatosensory awareness, named tactile extinction.[13,14] This is a clinical condition consisting of a failure to detect contralesional tactile stimuli when delivered simultaneously with ipsilesional ones. Intriguingly, the same patients improve their bilateral tactile detection when concomitant visual stimuli are delivered on their contralesional side.[14,15] Instances of brain damage involving the parietal lobe, and especially the perirolandic areas, have long been considered the anatomical correlate of tactile extinction.[13] More recently, tactile extinction has been reported in individual patients with right-brain damage to frontal and subcortical regions (the thalamus, basal ganglia, white matter and internal capsule).[13,16,17] The literature has yet to offer a mechanistic explanation of tactile extinction (beyond its anatomical localization) that is supported by quantitative evidence, but the recent literature on tonic somatosensory responses[9–11] has offered insights into the neural mechanisms underlying tactile awareness and—possibly—its disorders.

To quantitatively test the link between tactile awareness and tonic somatosensory responses, we combined two large datasets collected in different clinical populations. That is, stereo-EEG recordings collected in drug-resistant epileptic patients during the delivery of somatosensory, visual and bimodal stimulation were combined with the lesion mapping of post-stroke patients exhibiting tactile extinction, thus allowing us to make inferences about the normal functioning of conscious (tactile) perception. Our aim was to estimate the topographical overlap between tonic somatosensory responses and tactile extinction lesion mapping, to measure their reciprocal relationship, and finally to evaluate whether tonic somatosensory activities are modulated by a concomitant visual stimulus.

Materials and methods

Stereo EEG

Participants and data acquisition

Intracranial recording data were collected from 60 drug-resistant epileptic patients (27 male, 33 female, age 30 11) undergoing stereo-EEG implantation of depth electrodes for a presurgical evaluation. Two patients had bilateral implantation, 31 right and 27 left. Patients were fully informed regarding the stereo-EEG procedures, and informed consent was obtained. The present study was approved by the Niguarda Ethics Committee (ID 939-12.12.2013). For all patients, neurological examination was unremarkable, no sensory deficits were presented, and the seizure-onset zone was outside of the perisylvian areas. The procedures for electrode implantation are detailed in Cardinale *et al.*[18,19]

Stimulations

Patients underwent the following stimulations: (i) tactile stimulation: the median nerve contralateral to the implanted hemisphere was stimulated at the wrist, using 100 constant-current pulses (0.2-ms duration) at 1 Hz while the patient lay in bed with eyes closed. The stimulation intensity was set at 10% above the motor threshold; (ii) visual stimulation: patients wearing goggles received 100 bilateral visual stimulations (i.e. flashes) at 1 Hz, with an intensity of 3 cd/m^2; and (iii) bimodal stimulation: patients received 100 concurrent tactile and visual stimulations.

Visual and tactile stimulations belong to the clinical routine commonly used during stero-EEG procedures on drug-resistant epileptic patients, and are intended primarily to characterize functionally the implanted leads and guide the subsequent surgery. The tactile stimulation is administered above threshold, so it is quite likely that proprioceptive components may contribute to the overall responsiveness. However, in a previous paper from our group,[9] we compared in a large population the responses to stimulations above and below the motor threshold, reporting how all the time courses observed in response to the former are still present in response to the latter, and with comparable topographical distributions.

Data processing

Data from all leads exploring the grey matter were decomposed into time-frequency plots using a complex Morlet wavelet decomposition. Because gamma-band activity (50–150 Hz) is considered the best reflection of neuronal activity,[20] gamma-band power was extracted in a time window from 100 ms before to 500 ms after the stimulation and subdivided into 60 non-overlapping 10-ms bins. For each post-stimulus time bin, gamma-band power was compared against baseline using a *t*-test (Bonferroni corrected). Recording leads were labelled as responsive only if three consecutive time bins had a gamma-band power significantly higher than baseline. Gamma-band power time courses of the responsive leads were clustered with a correlative *k*-means algorithm to group data regardless of their amplitude modulations. The ideal number of clusters was identified via a maximum silhouette criterion,[21] which evaluates the consistency within clusters of data. The silhouette values range from −1 to +1, where a high value indicates that the gamma-band power time course of responsiveness is well

matched to its own cluster and poorly matched to neighbouring clusters.

Because the phasic and tonic patterns within somatosensory responsiveness are not mutually exclusive,[9] we computed a tonicity index for each responsive lead to establish the prevalence of one component over the other. In particular, we used the gamma-band power (GBP) values obtained at 20 and 100 ms after the stimulation (i.e. the latencies corresponding to the peak of phasic and tonic components, respectively) to derive a combined index, as follows:

$$tonicity\ index = \frac{GBP(100\ ms) - GBP(20\ ms)}{GBP(100\ ms) + GBP(20\ ms)}. \quad (1)$$

Consequently, the tonicity index would range between –1 and +1, with negative values indicating a prevalent phasic component and positive values reflecting a prevalent tonic one.

Anatomical reconstruction and functional mapping

The individual anatomy of each patient and the coordinates of the leads exploring from the grey matter were reconstructed following the procedures detailed in Avanzini *et al.*[9] Once the individual anatomies were coregistered to a common brain template (164 k fsaverage), we computed functional maps that assigned to each node the values derived from all leads lying within a geodesic distance of 1 cm. We obtained the following maps:

(i) A cortical sampling density map, which represented the local density of recording leads. To calculate this index, we counted how many leads fell into each disc. Cortical regions with fewer than three recording leads per disc were filtered out and not included in the subsequent computations.

(ii) An overall responsiveness map, which represented the number of responsive leads as a percentage of the number of explored leads within a disc. This time-independent variable provided a picture of cortical responsiveness, with values ranging from 0 to 100%. Overall responsiveness maps were thresholded at 10% to reduce the impact of false positives.

(iii) A relative responsiveness map, which represented the number of leads exhibiting a specific temporal pattern as a percentage of the number of responsive leads within a disc. This variable indexed the degree to which an area responded with a specific temporal pattern. Relative responsiveness maps' results were thresholded at a $1/n$ value, where n represents the number of clusters, to show only areas in which the proportion of a single cluster exceeded the chance level.

(iv) A tonicity map, which represented the average tonicity index across the leads within a disc.

All maps were plotted using CARET software[22] and visualized on either a flattened hemisphere surface or an inflated one (Supplementary Fig. 1).

Tactile extinction lesion mapping

Participants

From a continuous series of 153 brain-damaged patients collected over a period of 8 years, we selected patients based on the following inclusion criteria: first-ever stroke, unilateral damage of cerebrovascular origin, spared unilateral tactile detection and neuropsychological assessment performed between 30 and 120 days after the stroke onset. Data from 46 right- and 32 left-brain-damaged patients were collected. Patients did not present severe language deficits, general cognitive impairment or mood disturbances that might preclude the assessments. Neuropsychological assessment was performed according to previous studies.[14,23] All patients provided written informed consent. The Ethical Committee of the ASLTO1-Turin approved the study (number 46485/13).

Tactile extinction evaluation

The patients were divided into two groups according to the presence/absence of tactile extinction (TE+/TE–). The groups were balanced for demographic factors and in terms of any of the investigated neurological and neuropsychological features (Supplementary Tables 1 and 2).

To screen for tactile extinction, the patients were blindfolded and the experimenter manually delivered tactile stimuli in the form of brief ecological touches. The touch consisted of the application of slight pressure with the examiner's index finger on the patient's hand dorsum or fingers. Touches ($n = 60$) could occur on the contralesional (affected) hand ($n = 20$), on the ipsilesional (intact) hand ($n = 20$) or simultaneously on both hands ($n = 20$). Patients were asked to verbally report where they felt the touches, that is, on either one hand or both hands. To be classified as TE+, patients had to fail to perceive the stimulus on the contralesional affected hand in >30% of the bilateral trials but correctly report >80% of the unilateral contralesional touches and 100% of the unilateral ipsilesional ones. This clinical assessment was based on previous studies of tactile extinction.[13,23–26]

Tactile extinction emerged in 32 patients (28 right- and four left-brain-damaged) but did not appear in the other 46 patients (18 right- and , 28 left-brain-damaged).

Because only four left-brain-damaged patients exhibited tactile extinction, we then focused on the right-brain-damaged sample, whose neurological/neuropsychological features are provided in Supplementary Table 1. Clinical data relative to left brain-damage are reported in Supplementary Table 2.

Visuotactile experimental task

In the visuotactile experimental task (performed in a subsample of 17 TE+ patients) tactile stimuli could be delivered unilaterally or bilaterally, either alone or simultaneously with visual stimuli. Patients were asked to focus on the tactile stimulation while ignoring the visual one and to report where they felt the tactile stimuli (i.e. on either the contralesional or ipsilesional hand or on both hands). Tactile stimuli were transcutaneous electrical stimuli consisting of constant-current square-wave pulses delivered by two electrical stimulators (DS7A, Digitimer) to each hand dorsum (i.e. between the index and the middle finger), using two pairs of surface bipolar electrodes (1 cm between electrodes). The stimulus duration was 0.2 ms, and the stimulation intensity was adjusted according to the individual sensory-threshold level. Visual stimuli were brief flashes (50 ms in duration) delivered through a red-light-emitting diode (5 mm) mounted close to the stimulated portion of the patient's hand (i.e. ∼3 cm from the stimulated portion of the hand).

Note that before starting the experimental procedure, the patients' ability to report unilateral and bilateral tactile stimuli with their eyes closed was reassessed using exactly the same transcutaneous electrical stimuli employed during the tactile detection task. A total of 20 tactile stimuli were delivered, five to the contralesional affected hand, five to the ipsilesional intact hand and 10 bilaterally, in a random fixed order.

During the task, unilateral and bilateral stimuli were delivered by two constant-current stimulators: (i) in a tactile-stimulation-only condition, in which no visual stimuli occurred; and (ii) in a visuotactile-stimulation condition, in which tactile stimuli were combined with visual stimuli appearing close to the hand. In the tactile-stimulation-only condition, we collected a total of 24 trials: 10 bilateral target trials, 10 unilateral target trials delivered on the contralateral hand and four unilateral non-target trials delivered on the

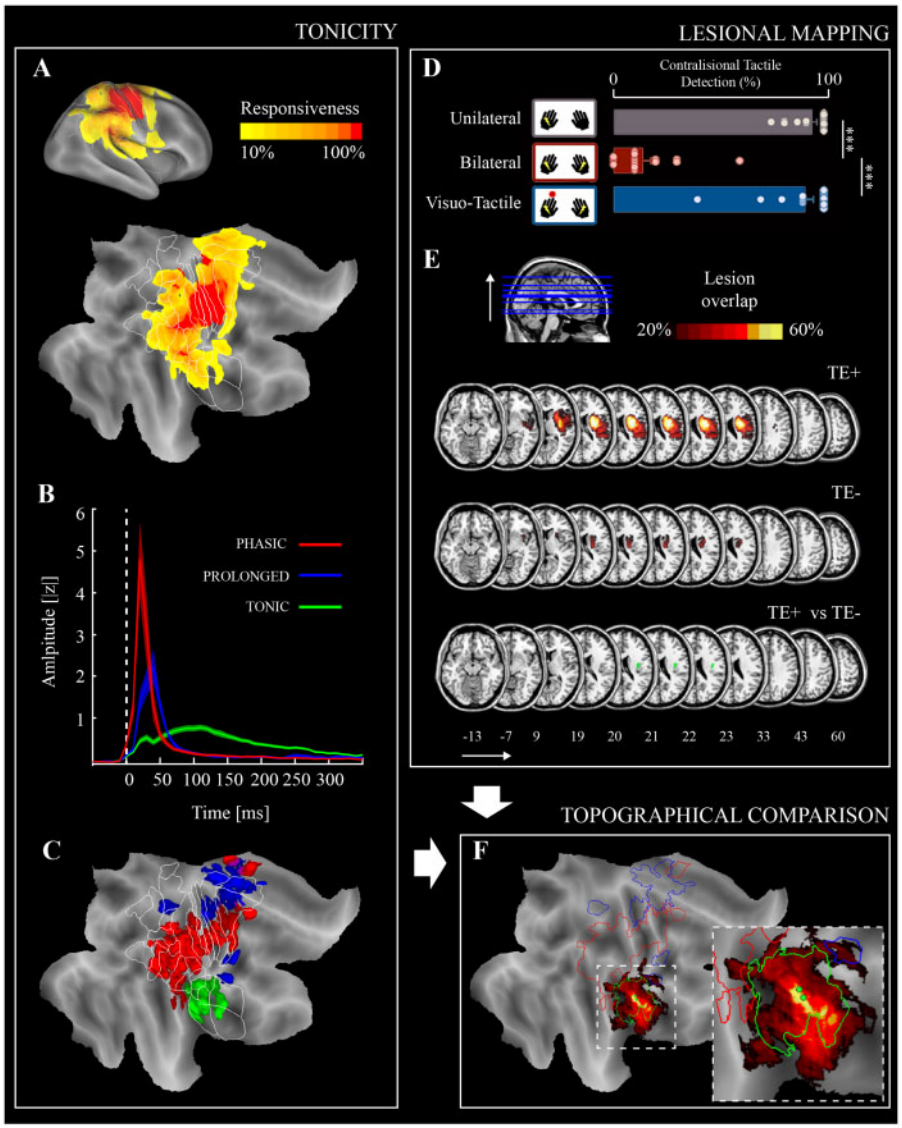

Figure 1 Co-localization of somatosensory tonic responses with tactile extinction lesion mapping. (**A**) Overall responsiveness map for the right hemisphere (responsive leads as a percentage of locally explored leads). Only nodes with values exceeding 10% are shown. (**B**) Time courses (centroids standard error, SE) of the three clusters: phasic in red, prolonged in blue and tonic in green. The average silhouette of such clustering was equal to 0.364. (**C**) Relative responsiveness map (leads belonging to one cluster as a percentage of total number of locally responsive leads) of the three clusters for the right hemisphere. Only nodes with values exceeding 33% are shown. The colour code is as in **B**. (**D**) Behavioural results for TE+ patients. The three task conditions (i.e. unilateral in grey, bilateral in red and visuotactile in blue) are graphically represented on the *left*. Histogram represents the percentage of tactile detection across conditions. Asterisks indicate significance levels (Wilcoxon test, $^{***}P < 0.0005$). Bars indicate standard error of the mean. Dots represent individual patients. (**E**) The lesion mapping is reported for the 28 TE+ patients (*top row*) and for the 18 TE– patients (*middle row*). Colour bars were kept balanced in relative terms (6–16 of 28 patients for TE+, 3–10 of 18 patients for TE–). The *bottom row* reports the statistical comparison between the TE+ and TE– patients. Local maxima were located in the rostral parietal operculum (OP3; respectively, $z = 3.852$, $P < 0.01$, MNI coordinates: 39, –9, 21, and $z = 4.072$, $P < 0.01$, MNI coordinates: 40, –9, 22), which corresponds to the area of maximal overlay for TE+ lesional mapping. Axial slices are numbered according to the MNI z-coordinate. (**F**) TE+ lesion mapping is shown together with the borders from **C**. Green dots indicate the local maxima obtained from the comparison between the TE+ and TE– patients.

ipsilateral hand. The visuotactile-stimulation condition consisted of 28 trials: 10 bilateral visuotactile target trials, in which bilateral tactile stimuli were simultaneously delivered with visual stimuli appearing close to the contralesional hand, eight non-target trials and 10 bilateral tactile trials conducted to verify the persistence of tactile extinction in the absence of visual stimuli.

Non-target trials were introduced to control different confounds. Unilateral visuotactile trials ($n = 4$), consisting of ipsilesional tactile stimuli and concomitant visual stimuli appearing close to the contralesional hand, aimed to exclude the possibility that the patients reported a bilateral tactile sensation when only the ipsilesional hand was stimulated and visual stimuli occurred on the contralesional side. Visual trials ($n = 4$), consisting of coloured LEDs without electrical stimulation, aimed to exclude the possibility that the patients reported a tactile sensation on their contralesional hand whenever visual stimuli occurred close to their contralesional hand.

To address whether the patients' contralesional tactile detection percentage was modulated by the experimental manipulation, we performed Wilcoxon tests (two-tailed).

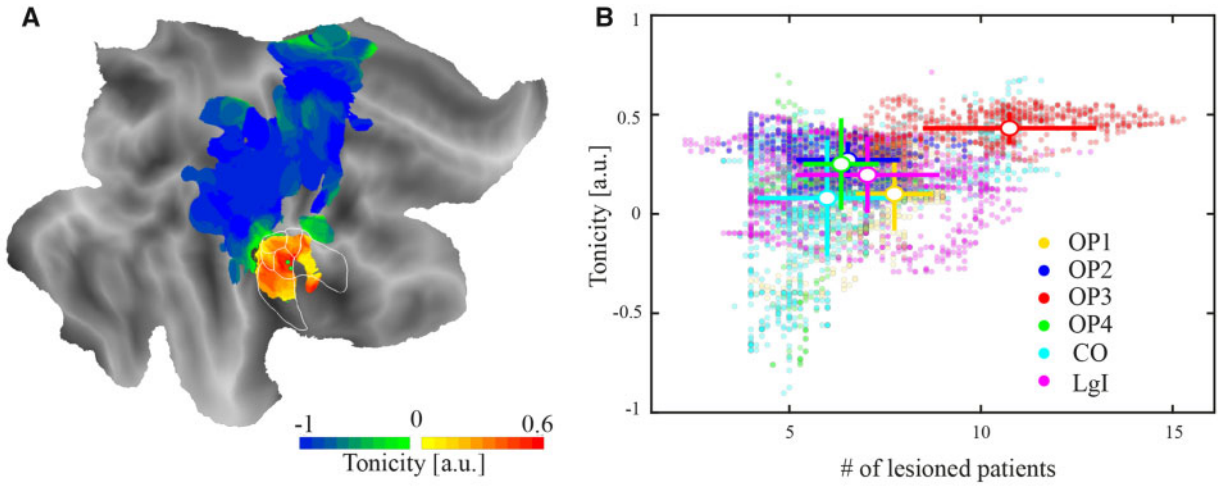

Figure 2 Tonicity index and lesionality follow the same topographical gradient. (**A**) Values of the tonicity index are plotted on a flat map (right hemisphere). Positive values indicate that the tonic component prevails relative to the phasic one: they are strictly confined to the perisylvian region, with a hotspot in OP3. Green dots indicate the local maxima obtained from the comparison between the TE+ and TE– patients (see also Supplementary Fig. 4). (**B**) Voxel-wise distribution of (TE+ lesion mapping, tonicity index). For each subregion, mean values are indicated along with standard deviation on both axes.

Lesion mapping

Patients' brain lesions were manually delineated with MRIcron[27] onto a normalized MRI template (ch2.nii) from the Montreal Neurological Institute using the identical or closest-matching transversal slice of each individual. Lesion delineation was blindly performed by CF and FG. The overlay percentage maps for each group were calculated from all the lesions and superimposed on a template.

A lesion comparison (i.e. voxel-based lesion-symptom mapping) between the TE+ and TE– patients was implemented using non-parametric mapping.[27] The between-group comparisons were obtained using the Liebermeister test (and permutation thresholding with 1000 iterations for multiple comparisons correction). Quantitative estimates of grey and white matter involvement were obtained by superimposing the AAL anatomical template[28] and the Natbrainlab white matter template.[29]

Comparative analyses

Within areas showing tonic responses, we correlated the tonicity index with the TE+ lesion mapping on a voxel-by-voxel basis.

To estimate whether a concomitant visual stimulus modulated somatosensory responses in the perisylvian region, we compared the number of leads responding to bimodal and tactile stimulations. Subsequent analyses were limited to the leads responsive to bimodal stimulation. We computed a timewise *t*-test [false discovery rate (FDR) corrected] comparing the gamma-band power (GBP) time courses following the two stimulations. For each lead, we then calculated the prevalence of the tonic increase over the phasic increase, as follows:

$$[GBP_{VT}(100\ \text{ms}) - GBP_{VT}(20\ \text{ms})] - [GBP_{T}(100\ \text{ms}) - GBP_{T}(20\ \text{ms})]. \quad (2)$$

Finally, we split the previous measure into its two subcomponents, namely the tonic increase ($GBP_{VT\text{-}100\ \text{ms}} - GBP_{T\text{-}100\ \text{ms}}$) and the phasic increase ($GBP_{VT\text{-}20\ \text{ms}} - GBP_{T\text{-}20\ \text{ms}}$), and mapped them separately within regions of the tonic cluster. We evaluated the voxel-wise correlation against the TE+ lesion mapping for both phasic- and tonic-increase maps.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Results

The coverage ensured by stereo-EEG patients was extensive for the entire cortical surface, with sparse undersampled regions occupying only the occipital and frontal poles, and for some areas in the cortical crown due to surgical constraints (Supplementary Fig. 2). Contralateral median nerve stimulation activated a wide cortical network, including the primary somatosensory cortex (SI), premotor, motor and parietal cortices and the posterior perisylvian region, in line with Avanzini *et al.*[9] (Fig. 1A). Three clusters of responsiveness were identified. A phasic, short-lasting and early-latency cluster (in red) pertaining to the SI, premotor and parietal cortices; a prolonged cluster (in blue) peaking around 50 ms pertaining mainly to the dorsal and ventral premotor regions; finally, a tonic cluster was present exclusively in the posterior perisylvian region (in green) (Fig. 1B and C). Results of the left hemisphere exhibited a highly similar pattern, as shown in Supplementary Fig. 3.

As expected from the clinical evaluation and shown in Fig. 1D, although TE+ patients correctly detected contralesional tactile stimuli delivered unilaterally (94.61 8.40%), they systematically failed to detect contralesional touches during bilateral stimulation (14.12 15.02%), with a significant decrease in the contralesional tactile detection ($z = 3.62$; $P = 0.0003$). Crucially, in the visuotactile trials TE+ patients recovered tactile detection (91.17 15.76%), with a significant enhancement relative to the one of the bilateral trials ($z = 3.62$; $P = 0.0003$). Note that the patients correctly responded to all non-target trials. Thus, only the target trials were included in the analysis.

Regarding lesion mapping (Fig. 1E), the extent of the lesion volume did not differ between the TE+ and TE– groups [$t(44) = 1.84$, $P > 0.05$]. In the TE+ patients, the lesion overlay occupied the entire perisylvian territory, with a maximum centred on the rostral parietal operculum. TE– lesion mapping was more widespread, with the maximum overlay centred on the internal capsule and the corticospinal tract. Voxel-based lesion-symptom mapping analysis using binary scores for the presence or absence of tactile

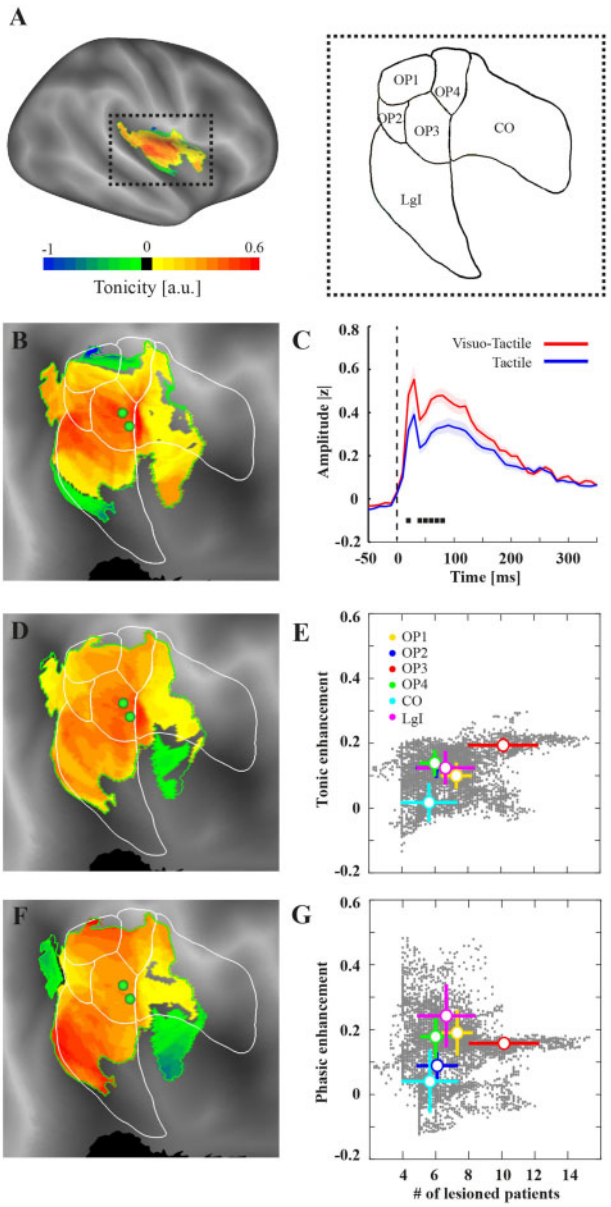

Figure 3 Modulations induced by visuotactile stimulation onto phasic and tonic components. (**A**) Differential values of the tonicity index between bimodal and tactile stimulation are plotted on an inflated map of the right hemisphere. The *right* panel reports the outlines of the six investigated cytoarchitectonic subdivisions. (**B**) Same data as in **A**, plotted on a flat map of the perisylvian regions. (**C**) Gamma-band power time courses for tactile (in blue) and visuotactile (in red) stimulation for all the leads ($n = 130$) responsive to visuotactile stimulation and exploring the perisylvian region (OP1–4, LgI, CO). Statistical significance (FDR corrected) was found for both phasic (20 ms, $P_{20ms} = 0.034$) and tonic intervals (from 40 to 80 ms, *P*-values ranging from 0.009 to 0.031). (**D**) Continuous map of the tonic increase within the perisylvian region. (**E**) Voxel-wise distribution of TE+ lesion mapping, increase of tonic activity. For each subregion, mean values are indicated along with standard deviation on both axes. A significant and positive correlation was found ($r = 0.347$, $P < 0.0001$). (**F**) Continuous map of the phasic increase within the perisylvian region. (**G**) Voxel-wise distribution of TE+ lesion mapping, increase of phasic activity. For each subregion, mean values are indicated along with standard deviation on both axes. Absence of correlation was found ($r = –0.059$, $P < 0.0001$).

extinction showed that lesions involving voxels within the rostral parietal operculum were significantly associated with the presence of tactile extinction. Finally, the TE+ lesion mapping closely co-localized with the spatial distribution of the tonic cluster, keeping out of the territories exhibiting phasic and delayed responses (Fig. 1F). The lesion mapping relative to left brain-damage is reported in the Supplementary Fig. 4.

The tonicity index map—which quantitatively assessed the degree of tonic components in a given cortical site—confirmed that late responses were prevalent only in the perisylvian region (Fig. 2A). More interestingly, the tonicity index peaked in the rostroventral portion of the parietal operculum (i.e. OP3; see Eichkoff *et al.*[30,31]), thus matching the lesion sites specific to the TE+ patients (Fig. 2A, green dots). Starting from this observation, we investigated whether lesionality (i.e. the degree of lesional mapping) and the tonicity index covaried within the perisylvian regions (Fig. 2B). The two indices were strongly associated, indicating that tonic responses and lesions inducing tactile extinction were not only co-localized but also followed the same topographical gradients (Pearson's $r = 0.326$; $P < 0.0001$). Regarding individual cytoarchitectonic areas (see also Supplementary Fig. 5), OP3 (in red) distinctly showed the highest tonicity index and lesion scores, whereas all the remaining areas showed similar values.

To investigate the mechanisms sustaining the recovery of the bilateral tactile function for the TE+ patients through visuotactile stimulation (Fig. 1D), we examined the stereo-EEG responses to visual stimuli and bimodal stimulations. In the perisylvian regions (left and right hemisphere), the number of leads responding to the visual stimulation was negligible (6 of 756). Nevertheless, the number of leads responsive to the visuotactile stimulation increased relative to those responsive to the tactile stimulation (Supplementary Table 3).

Comparing the gamma-band power time courses for visuotactile and tactile stimulation, differences in both phasic (20 ms, $P_{20ms} = 0.033$) and tonic intervals (from 40 to 80 ms, *P*-values from 0.008 to 0.031) of the somatosensory response emerged (Fig. 3C). Mapping the relative increase of tonic versus phasic activity, almost the entire perisylvian region presented a relative increase of the tonic component, with OP3 exhibiting the higher values, in line with the spatial gradient of TE+ lesionality (Fig. 3B). Considering the tonic and phasic increases separately (Fig. 3D–G), the correlation with the lesion mapping showed that tonic enhancement was significantly and positively associated with TE+ lesionality (Fig. 3E; $r = 0.347$, $P < 0.0001$), with OP3 maintaining a leading role in both measures. Contrarily, although statistically significant, a virtually null relationship was found for the phasic enhancement (Fig. 3G; $r = –0.059$, $P < 0.0001$).

Discussion

In the present study, we demonstrated a close link between the presence of tonic somatosensory responses and tactile awareness. In particular, we combined behavioural evidence and lesional mapping from neurological patients exhibiting tactile extinction and stereo-EEG recordings in drug-resistant epileptic patients during tactile peripheral stimulation. Although the enrolment of different populations might be seen as a detriment because only correlative observations can be derived, we coalesced the unique insights offered by post-stroke patients in the behavioural perturbation with those provided by stereo-EEG patients in terms of fine-grained spatiotemporal dynamics.

There are three main findings: (i) both tonic responses and TE+ lesion mapping are localized in the posterior part of the perisylvian regions; (ii) within the perisylvian regions, the degree of tonicity and lesionality covary, with the hotspot of both markers localized in OP3; and (iii) the presentation of concomitant visual stimuli enhances both phasic and tonic components, but only the latter follows the topographical distribution of TE+ lesion mapping.

Co-localization of tonic responses and tactile extinction lesion mapping

Our localization of tactile extinction substrates, which shows that the right rostral parietal operculum and posterior insula represent the hub of tactile awareness, is in line with previous findings.[13,14] From a neuropsychological perspective, the almost complete overlap between TE+ lesion mapping and regions exhibiting somatosensory tonic responses suggests that tonic activity is associated with tactile awareness whereas phasic responses play a minor or no role.

It is well-known that the parietal operculum subserves higher-order somatosensory functions in mammals. The caudal portion, traditionally named SII (secondary somatosensory cortex) and corresponding to OP1,[30,31] was proposed by de Haan and Dijkerman[32] as the last stage of the so-called 'cylinder block,' that is, the basic somatosensory processing unit. Within this structure, OP1 would be responsible of conveying the somatosensory information to a variety of brain regions.[32] In turn, it has been reported that the rostral portion (OP3–4) fulfils a specific role in sensorimotor integration finalized for motor control.[33–35] This functional difference between the caudal and rostral portions of the parietal operculum is reinforced by their connectional heterogeneity. In particular, OP1 is closely connected to the postcentral gyrus, intraparietal sulcus and deep thalamic nuclei.[36–38] The rostral parietal operculum, in turn, has closer anatomical and functional connections with the precentral gyrus and the motor/premotor and inferior frontal cortices.[36–38] In addition, the rostral parietal operculum receives denser information from the non-somatic thalamic nuclei (e.g. medial dorsal) deeply involved in attentional processes.[36]

Tonic responses and tactile extinction lesion mapping covary within the parietal operculum

Beyond localization, tonicity and lesionality also follow the same spatial gradient, exhibiting a significant and positive correlation with the areal peaks in OP3. This result is also corroborated by the observation that OP3 is the cortical site mostly differentiating the lesion mapping between patients with and without tactile extinction.

Our finding that the rostral parietal operculum plays a critical role in tactile awareness is in line with previous studies indicating that it is the only cortical area outside the SI associated with impaired touch perception[39] and that its activation occurs regardless of the stimulation modality (e.g. pinprick versus light touch versus pressure).[40] In addition, several studies investigating the neural functional correlates of sensory attenuation[41–43] have highlighted the role of the parietal operculum in differentiating the perceived intensity of self-generated and externally generated somatosensory stimuli. It can be tentatively suggested that this action-dependent modulation of tactile processing is due to the concomitant somatosensory and motor processing taking place in the rostral parietal operculum, thus reinforcing the prominent role that this area, and its peculiar tonic responsiveness to somatosensory stimuli, likely plays in mediating tactile awareness.

More generally, the correlation between tonicity and TE+ mapping in the perisylvian regions reinforces the hypothesis that tonic activity serves as a ground for tactile awareness.

Tonic responses and tactile extinction behaviour comodulate upon visuotactile stimulation

Similar to the TE+ patients' tactile perception,[14] somatosensory responses are enhanced by concomitant visual and tactile stimuli. Interestingly, the phasic and tonic enhancements follow different forms of topographical organization, and only the latter parallels the TE+ lesion mapping. Because the parietal operculum does not respond to flashes in isolation, the enhancement of tonic activity observed during visuotactile stimulation could be ascribed to the capacity of visual inputs to increase the responsiveness of the perisylvian region when combined with tactile inputs, leading to a stronger tonic component and a greater likelihood of reaching the perceptual threshold. Such a view, if applied to the case of TE+ patients, may explain the mechanisms underlying the recovery of tactile detection upon visuotactile stimulation. In this context, the role of attentional factors in mediating tactile extinction recovery has to be mentioned. On one side, tactile extinction *per se* has been interpreted as a (sensory-specific; i.e. tactile) attentional disorder.[13] The view of a non-primary sensory deficit is implicitly confirmed by the results of our behavioural study for TE+ patients, who successfully identify contralesional unilateral stimulations. On the other side, parietal operculum is densely connected with parietal and premotor centres involved in the cortical control of attention,[44] and its activity is modulated evenly by attention, with the rostral sectors being more strongly modulated by attentional factors.[45] This evidence parallels both the lesional mapping contrasting the TE+ and TE– patients and the enhancement of tonic responses driven by an additional visual stimulus.

Conclusions

We demonstrated that tonic responses to tactile stimuli co-localize, covary and comodulate with the neural substrates underlying disorders of tactile awareness. Starting from these findings, tonic activities represent the ideal fingerprint of tactile awareness. Indeed, they could constitute the mechanistic counterpart of previously reported late EEG components reflecting the access to perceptual awareness,[5,6,46] and at the same time tonic activity fits well with the model of local recurrent activities.[12]

Although recurrent networks have been documented mainly for the visual system,[12] it has been hypothesized that they also operate during the processing of both auditory[47] and somatosensory stimuli.[48] Thus, one could hypothesize that tonic activities are a common mechanism underlying conscious perception across modalities and that they are worth investigating against the lesion mapping of related disorders of consciousness.

Our data indicate that deficits of tactile awareness, which often characterize post-stroke patients, may be related to a deficient/absent tonic response to somatosensory stimulations. In turn, tonic responses could be enhanced by concomitant visual stimuli, counteracting the impaired perception. This view enhances the discussion of the neural machinery sustaining perceptual awareness. Further, our results are valuable for neurorehabilitation, because they support the use of protocols relying on intact sensory channels to improve the impaired domains, and for neuroprostethics, because they identify the neural spatiotemporal features that must be vicariated to prompt the improvement of impaired functions.

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Competing interests

The authors report no competing interests.

Supplementary material

Supplementary material is available at *Brain* online.

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