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The electrophysiology of tactile extinction: ERP correlates of unconscious somatosensory processing

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Abstract

We examined the electrophysiological correlates of left-sided tactile extinction in a patient with right-hemisphere damage. Computer-controlled punctate touch was presented to the left, right or both index fingers in an unpredictable sequence. The patient reported his conscious tactile percept ("left", "right" or "both"). He showed extinction on 75% of bilateral trials, reporting only right stimulation for these. Somatosensory evoked potentials for unilateral stimulation showed early components over contralateral somatosensory areas (P60 and N110) for either hand. In contrast to the results observed for age-matched controls, the patient's P60 was smaller in amplitude for left-hand touch over the right hemisphere than for right-hand touch over the intact hemisphere. Bilateral trials with extinction revealed residual P60 and N110 components over the right hemisphere in response to the extinguished left touch. These results demonstrate residual unconscious somatosensory processing of extinguished touch. They also suggest that tactile extinction can be caused by attenuation rather than elimination of somatosensory responses in the damaged hemisphere, with an underlying deficit even on unilateral trials.

Keywords: Tactile extinction; Somatosensory; Hemisphere damage; Event-related brain potentials

1. Introduction

Extinction is a relatively frequent consequence of unilateral brain damage. Patients showing extinction can typically detect and report isolated stimuli in either hemispace, but will miss contralesional stimuli when presented concurrently with an ipsilesional competitor (see [5,7,13] for reviews). While extinction can be observed after several types of lesion [38], it is classically associated with damage in the territory of the right middle cerebral artery [12,14]. It can often manifest as one component of the neglect syndrome, but has been reported to dissociate from neglect in some cases [7]. A common suggestion (e.g. [10,12,13,26]) has been that extinction may reflect a pathological imbalance in attentional competition following the lesion. While a contralesional stimulus can still attract attention in isolation, it apparently loses a competition for attention with the concurrent ipsilesional stimulus during bilateral stimulation.

Recent studies have begun to examine the neural correlates of extinction ([14,15,25,26]; see [9,40] for reviews). Although extinction can be found within several different modalities (e.g. [5]) and even cross-modally (e.g. [11,29]), the majority of recent studies using neural measures have concerned just the *visual* modality (a few exceptions to this are considered later). Using event-related potential (ERP) and/or fMRI measures to study visual extinction, several recent studies have shown that, on the one hand, relatively early components of visual processing may be abnormal for contralesional stimuli in visual extinction (e.g. [25,26,42]); while, on the other hand, extinguished visual stimuli can evidently still undergo considerable unconscious residual processing that activates intact cortical visual areas, despite being undetected (e.g. [14,15,34,42]). Here, we address similar issues with ERP measures, but for the *tactile* modality instead.

Tactile extinction has frequently been described in the clinical literature (e.g. [4,8]) and has recently been investigated more closely with behavioural measures (e.g. [2,21,32,36,37]). Analogously to visual extinction, tactile extinction can be observed during bilateral stimulation using the clinical method of 'confrontation', whereby the examiner

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produces stimulation with his or her own fingers (e.g. light touch on either or both of the patient's hands). As with visual extinction, tactile extinction can also be observed with more formal computerised testing, or in more complex tasks that require the discrimination of particular features on either or both sides, rather than merely detection (e.g. [1]). Importantly, analogous to well-known behavioural results on implicit processing in visual extinction (see [14,26] for reviews), a few recent behavioural studies of tactile extinction have now shown that contralesional tactile events that are extinguished from awareness may nevertheless undergo a degree of residual unconscious processing (e.g. [1,6,24]; see also [23] for electrophysiological evidence on sub-threshold tactile stimulation in normals).

Here, we addressed the neural fate of extinguished tactile stimuli using ERP measures in a single-case study. Although ERPs have previously been used to study somatosensory deficits resulting from thalamic lesions [30], to our knowledge the current study provides the first application of ERP measures to tactile extinction (see [39] for a study involving tactile neglect). We recorded somatosensory ERPs (SEPs) from patient ED, who showed strong and consistent left-sided tactile extinction following a right-hemisphere stroke. This case was particularly suitable for ERP testing, because of the consistency of his extinction, still present 2 years after stroke; plus his compliance with the task over many trials; and the fact that somatosensory cortex was structurally intact on MRI (see below). After pilot testing without ERP measures, two full ERP sessions were conducted. Brief tactile pulses were delivered unilaterally or bilaterally to the patient's left and/or right index finger. The task was to report verbally the type of tactile stimulation experienced ("left", "right" or "both") on every trial. These verbal reports allowed separation of bilateral trials where the contralesional stimulus was extinguished (i.e. "right" response on bilateral trials) from trials where this stimulus was detected correctly ("both"). We could then compare bilateral trials with extinction (only the right-hand stimulus reported) to unilateral trials where only the right hand had been stimulated. SEPs and vocal response times were computed separately for unilateral left, unilateral right and bilateral trials with correct report, as well as for bilateral trials where the contralesional (left) stimulus was extinguished.

Previous experiments with young neurologically unimpaired participants (e.g. [16,17]) have found early SEP components (typically P45 and N90) in response to tactile stimuli identical to those used in the present study. Both components were elicited at electrodes over somatosensory areas contralateral to the stimulated hand, being strongly lateralised. The P45 is most likely generated in primary somatosensory cortex (S1; see [22,31] for MEG evidence on latencies of S1 sources). Although the cortical generators of the subsequent N90 component are not yet known, the fact that later SEP components such as the N140 (and their magnetic counterparts) have been linked to secondary somatosensory cortex (S2 [19,20,22]) suggests that the somatosensory N90 may also reflect early sensory–perceptual processing stages in modality-specific somatosensory areas, such as S1 or S2.

In the present patient study, we focused on early and highly lateralised sensory-specific SEP components, similar to those found in young normals (albeit with slightly longer latencies in the elderly patient and in age-matched normals; see below). For unilateral trials, we compared the early SEP components for left- and right-hand tactile stimuli. Of interest here was whether the amplitudes of SEPs would be attenuated for left-hand unilateral stimuli projecting to the damaged hemisphere in the patient, as compared with those for right-hand stimuli projecting to the structurally intact hemisphere (see [25,26] for analogous results concerning visual ERPs). In addition to this within-patient comparison, we also assessed whether or not age-matched control subjects showed analogous asymmetries in an identical paradigm. For the patient, we also examined early lateralised SEP components for bilateral trials, over the right hemisphere (triggered by left tactile stimuli), on those trials where left stimuli were extinguished. These components could then be compared to unilateral right trials (where no left-hand tactile stimulus had been presented) within the patient, to assess any unconscious residual response to the extinguished left touch. Finally, in principle the components for bilateral trials with extinction might also be compared to those on which no extinction arose (if there were sufficient of the latter trials), in an attempt to index any SEP signatures of conscious rather than unconscious perception.

If tactile information originating from the left hand was eliminated at an early stage of somatosensory processing on extinction trials in the patient, then early contralateral SEPs recorded over the right hemisphere should be attenuated or absent (relative to SEP components recorded on non-extinguished bilateral trials, or left unilateral trials). Right-hemisphere SEP waveforms should be similar to unilateral trials on which tactile stimuli were presented only to the right hand. By contrast, if substantial residual early somatosensory processing of contralesional tactile stimuli can be preserved in tactile extinction, one would expect to find early SEP components over the right hemisphere in response to the left-hand stimulation, even on bilateral trials where left stimuli were extinguished, similar to the right-hemisphere SEPs found for left unilateral stimulation. Note that although age-matched controls were included in this study, the patient also served as his own control for the critical comparisons.

2. Case details

ED is a right-handed, 69-year-old male. Eighteen months prior to ERP testing he suffered a right-hemisphere stroke. An MRI performed 5 weeks before ERP testing showed encephalomalacia and atrophy involving the right anterior temporal lobe, basal ganglia and thalamus (see Fig. 1 for detailed lesion reconstruction). When first observed, 9 weeks

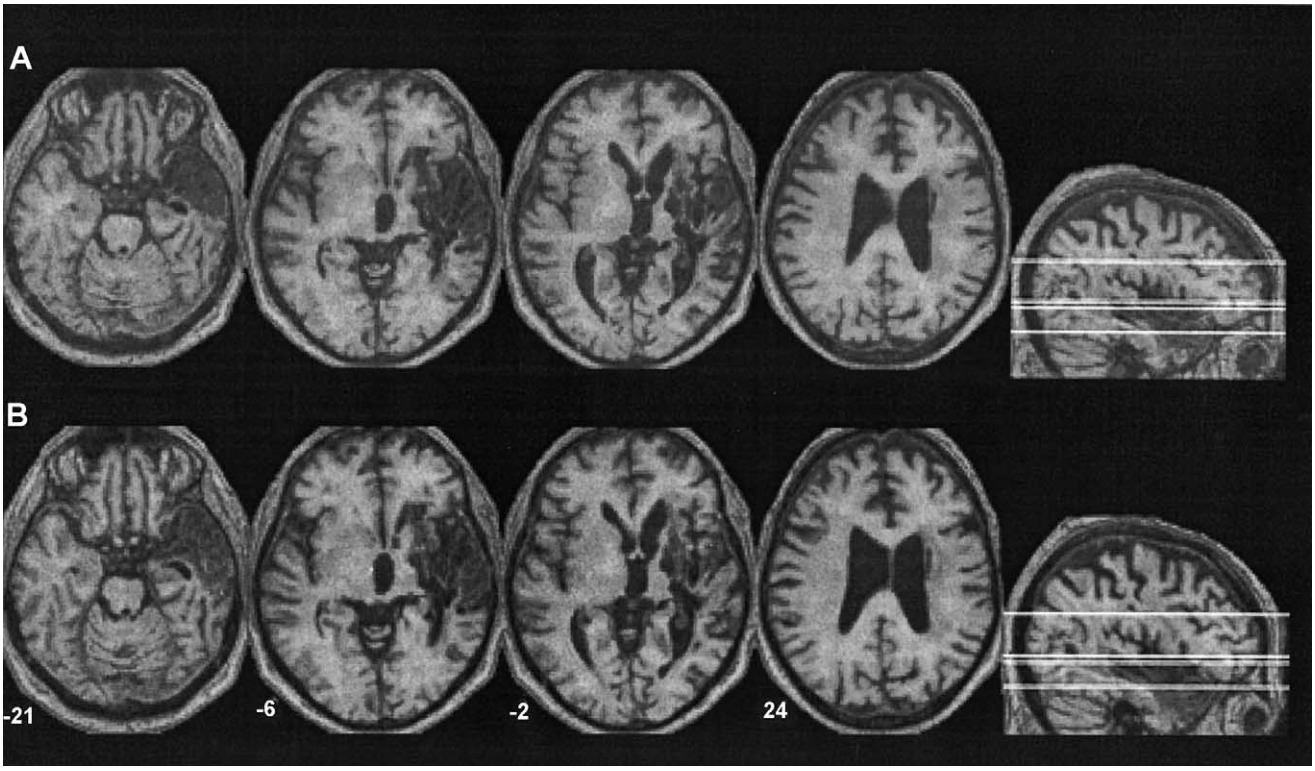

Fig. 1. (A) T-1 weighted MRI images for patient ED, showing the brain lesion. The levels of the transverse sections shown are indicated in the sagittal view at the right. (B) MRI after co-registration with the standard Montreal Neurological Institute (MNI) brain, via MRIcro software (http://www/psychology.nottongham.ac.uk/staff/cr1/mricro.html), using the linear normalisation functions of SPM99 (http://www/fil.ion.ucl/ac/uk/spm/spm99.html). The Talairach *z* co-ordinate for each transverse section is shown. On both the original MRI and the co-registered MRI, the lesion can be seen to involve, in the right hemisphere, the anterior temporal lobe, inferior insula, periventricular white matter, internal capsule, putamen, caudate and posterior thalamus. Posterior regions of the brain and parietal cortex were spared (see rightmost transverse section).

prior to ERP recording, he presented some left upper and lower limb weakness (score of 4 according to the MRC scale for grading muscle strength), but was able to walk with the aid of a stick and use the upper limb effectively. He showed a deficit in the left visual field (left hemianopia), more prominent in the upper quadrant. His somatosensory detection on the left hand was good when clinically tested with tactile, thermal, painful and proprioceptive stimulation, although the patient reported some subjective difference to the ipsilesional hand. Left visual neglect was evident clinically in ED's behaviour; for instance, he tended to miss left-sided doorways when walking in the ward. Neglect was also present in letter cancellation and line bisection sub-tests of the Behavioural Inattention Test [43]; respective scores of 29 with a normal cut-off of 32, and 4 with a cut-off of 7. Left neglect was also apparent in reading.

Reliable extinction on confrontation was present within touch, audition and during cross-modal confrontation with tactile stimuli on the left hand coupled with right tactile, auditory or visual stimuli. Of most interest for the present study is ED's tactile extinction. On manual confrontation with light touches on the dorsal aspects of the hands, ED showed consistent extinction of left touch during bilateral stimulation (over 90% misses). Tactile extinction was also reliably found in pilot work using computer-driven stimulation like that in the ERP sessions described below.

3. Methods

3.1. Stimuli, apparatus and procedure

Patient ED was tested in two sessions, separated by 2 months. He sat in a dimly lit soundproof experimental chamber, with a head-mounted microphone positioned in front of the mouth, facing a computer screen. A small cross at the centre of this screen served as fixation (see below). Tactile stimuli were presented to the lateral aspect of the middle phalanx of the left or right index finger, using two 12 V solenoids. These solenoids drove a metal rod with a blunt conical tip, making contact with the skin whenever a current was passed through the solenoid. The tactile stimulators were occluded so that the patient could not see the rod movements. Hands were placed on a table, 25° to the left or right of fixation, in their respective hemispaces, at a viewing distance of about 45 cm from the patients' eyes. White noise (62 dB SPL) was presented from a centrally located loudspeaker throughout the experimental blocks,

to mask any sounds made by the operation of the tactile stimulators.

Each experimental session consisted of nine blocks (60 trials per block). Tactile stimuli were delivered with equal probability and in random order to the left, right or simultaneously to both index fingers (20 trials per block for each of unilateral left, unilateral right and bilateral trials). Each trial started with a 200 ms presentation of a white fixation cross at the centre of the computer screen. After 200 ms, this fixation cross turned red for 200 ms (to capture attention at the screen centre and remind the patient of the necessity to maintain central gaze direction) and then it turned back to white. This white fixation cross remained on the screen until a vocal response was recorded. One thousand milliseconds after the fixation cross turned from red to white, tactile stimuli were delivered either unilaterally or bilaterally for 200 ms.

The patient's task was to report the tactile stimuli verbally ("left", "right" or "both"). Vocal response latencies were measured with a voice key (latencies in excess of 2000 ms were not entered into the reaction time analyses). Vocal responses were also coded on-line by the experimenter sitting outside the experimental chamber, who pressed a key corresponding to the patient's response. On those 7% of all trials where the patient failed to give a spontaneous response, he was asked whether he detected any tactile stimulus on the preceding trial. On 60% of these trials, the answer was "no" and these trials were coded separately ("none"). The next trial was initiated 1000 ms after the experimenter had entered the response category for the preceding trial. The patient was instructed to report the tactile stimuli as quickly and accurately as possible, and to maintain central eye fixation throughout the blocks (monitored with EOG, see below). Two training blocks (consisting of 60 trials each) were delivered at the beginning of each of the two sessions to familiarise the patient with these task requirements.

Two neurologically unimpaired age-matched male control participants (aged 67 and 65 years, respectively) were tested under identical circumstances, except that these participants completed only a single experimental session, consisting of two training blocks followed by 10 blocks with EEG recording.

3.2. EEG recording and data analysis

EEG was recorded with Ag–AgCl electrodes and linked-earlobe reference from FPz, F7, F3, Fz, F4, F8, FC5, FC6, T7, C3, Cz, C4, T8, CP5, CP6, P7, P3, Pz, P4, P8 and Oz (according to the 10–20 system), and from OL and OR (located half-way between O1 and P7, and O2 and P8, respectively). Horizontal EOG (HEOG) was recorded bipolarly from the outer canthi of both eyes. The impedance for all electrodes was kept below 5 kΩ. The amplifier bandpass was 0.1–40 Hz. EEG and EOG were sampled with a digitisation rate of 200 Hz and stored on disk.

EEG and HEOG were epoched off-line into 600 ms periods, starting 100 ms prior to, and ending 500 ms after the onset of tactile stimulation. Trials with eyeblinks and movement-related artefacts (as indicated by EEG waveforms exceeding ±80 μV at any recording site in the 500 ms interval following stimulus onset), as well as trials without vocal responses or with incorrect vocal responses to unilateral stimulation, were excluded from analysis. Separate averages waveforms were derived for unilateral left, unilateral right and bilateral stimulation trials. Bilateral trials were averaged separately for trials where the patient responded correctly ("both") and for trials where the left stimulus was extinguished ("right" response to bilateral stimulation). The total number of trials contributing to the four resulting average waveforms (collapsed across both sessions) for patient ED was 208 and 244 for unilateral left and unilateral right trials, and 198 and 63 for bilateral extinguished and bilateral correct trials, respectively. For the two control participants, who did not show any extinction, averaged waveforms were derived for unilateral left and unilateral right stimulation trials, as well as for bilateral stimulation (these latter waveforms are not shown or discussed below). All averages were computed relative to a 100 ms baseline preceding stimulus onset.

For statistical analyses within the patient, the two sessions were further subdivided into sub-sessions of three successive blocks, yielding an overall total of six sub-sessions. Separate mean reaction times (RTs) and ERP waveforms were computed for each of these sub-sessions for unilateral left, unilateral right and bilateral extinguished trials. The number of trials contributing to the average ERP waveforms for each sub-session ranged from 26 to 48, with an average of 36 trials per waveform. Because bilateral trials without any extinction (i.e. stimulation on both sides correctly reported by the patient) were infrequent, no analogous sub-session analyses could be meaningfully performed for those trials.

Peak amplitudes of early SEP components for patient ED (P60 and N110; these latencies being apparent from the practice data) were quantified within two analysis windows centred on the peak latencies of these components (P60: 50–70 ms post-stimulus; N110: 100–120 ms post-stimulus). Peak amplitude differences between different stimulation conditions (unilateral left, unilateral right and bilateral extinguished) were analysed at lateral contralesional (left) and ipsilesional (right) electrodes. Differences in mean vocal RTs for unilateral left, unilateral right and bilateral extinguished trials were also assessed. These were evaluated by repeated-measures ANOVAs and paired *t*-tests, across sub-sessions. The *t*-tests for unequal sample sizes were used to compare RTs obtained from the infrequent bilateral trials without extinction, versus from the other trial types. Greenhouse–Geisser adjustments to the degrees of freedom were performed when appropriate and the adjusted *P*-values are reported. For completeness, non-parametric Wilcoxon matched-pair signed-rank tests were also implemented for paired comparisons.

4. Results

4.1. Behavioural performance

Table 1 shows the percentage of particular vocal responses to unilateral left, unilateral right and bilateral tactile stimuli for patient ED. Left tactile stimuli were extinguished (only the right reported) on 75.8% of bilateral trials. Unilateral left stimuli were correctly detected on 87.4% of all trials, although 11.1% of unilateral left tactile stimuli were neglected ("none" response). In contrast, unilateral right stimuli were virtually always detected successfully. This pattern of results was similar for the first and second experimental sessions (extinction rate on bilateral trials: 70% versus 81%; rate of neglected unilateral left stimuli: 6% versus 16%, for the first and second sessions, respectively). For the two control participants, stimulus classification was virtually perfect (100 and 99.3% correct responses overall).

Table 2 shows mean vocal RTs for patient ED on bilateral correct, bilateral extinguished and unilateral left or right trials. Responses were reliably slower for bilateral correct trials than for all other trial types (all $t > 3.5$; all $P < 0.02$). RTs obtained for unilateral left, unilateral right and bilateral extinguished trials were analysed with a repeated-measures ANOVA. A main effect of stimulation condition was obtained ($F(2, 10) = 6.64$; $P < 0.04$). Subsequent paired t-tests revealed that responses to unilateral left stimuli were significantly delayed relative to responses to unilateral right stimuli ($t(5) = 3.36$; $P < 0.02$), indicating a possible contralesional disadvantage even without bilateral competition. Responses to left unilateral stimuli were also significantly slower than responses on bilateral extinguished trials ($t(5) = 4.55$; $P < 0.01$). In contrast, the latency of "right" responses was not significantly different on bilateral extinguished and unilateral right trials ($t(5) < 1$), thus providing no evidence for an implicit redundant-targets effect (c.f. Marzi et al.'s visual study [27]), although note that a somewhat different response (verbal) was required here). Non-parametric Wilcoxon tests confirmed the same pattern of RT results in the patient.

For both control participants, vocal RTs on bilateral trials (647 and 655 ms) were slower than RTs on unilateral trials, and responses to unilateral left-hand stimulation (541 and 523 ms) were faster than responses to unilateral right-hand stimulation (585 and 576 ms), unlike the patient. This pattern was highly consistent across experimental blocks and RT differences between stimulation conditions were statistically reliable for both participants (all $t > 3.7$; all $P < 0.02$).

Table 1
Frequency (%) of different responses to unilateral left, unilateral right and bilateral stimulation trials in patient ED

Response stimulation	"Left"	"Both"	"Right"	"None"
Left	87.4	0.3	1.2	11.1
Bilateral	1.1	21.7	75.8	1.4
Right	0.8	0.3	98.6	0.3

Table 2
Mean vocal RT (ms) for the different stimulation conditions in patient ED

Bilateral correct	961 ± 30.0
Bilateral extinguished	798 ± 15.5
Unilateral left correct	848 ± 14.0
Unilateral right correct	776 ± 12.4

The values are given as mean ± S.E. RTs for bilateral trials are displayed separately for trials where a correct response ("both") was recorded, versus bilateral trials where the left stimulus was extinguished ("right" response to bilateral stimulation).

4.2. Somatosensory event-related brain potentials

Fig. 2 shows SEPs recorded from patient ED at lateral electrodes over the left and right hemispheres, in response to correctly detected unilateral tactile stimuli presented to the left hand (solid lines) or to the right hand (dashed lines). As can be seen from these waveforms, an initial distinct

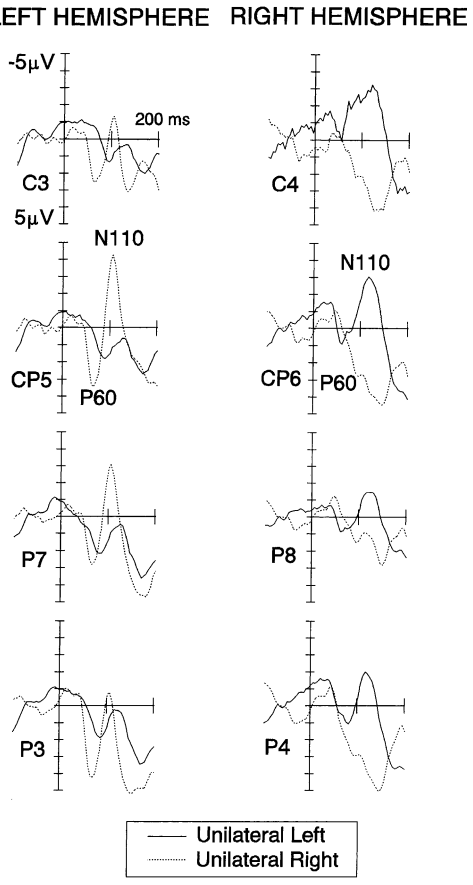

Fig. 2. SEP waveforms in extinction patient ED, recorded at lateral electrodes over the left (intact) and right (lesioned) hemisphere in response to unilateral tactile stimuli delivered to the left index finger (solid lines) or to the right index finger (dashed lines). Waveforms are shown within the 200 ms interval following stimulus onset relative to a 100 ms pre-stimulus baseline, with positive amplitude values plotted downwards and negative amplitudes plotted upwards.

positive-going component with a peak latency of about 60 ms (P60) was followed by the first negative component with a latency of about 110 ms (N110), at electrodes contralateral to the stimulated hand. These components were maximal at centroparietal electrodes (CP5/6), were more pronounced contralesionally (left hemisphere), but can also be seen at recording sites located over the lesioned right hemisphere. These two early SEP components elicited by unilateral tactile stimuli for patient ED were very similar, in terms of morphology and scalp distribution, to the SEPs obtained in response to identical stimuli for the age-matched control participants (as shown in Fig. 3). They were also similar to SEPs (P45, N90) previously observed for younger participants (c.f. [16,17]), although component latencies were somewhat delayed both for ED and the age-matched controls. Interestingly, both components appear to be attenuated for left-hand stimulation as compared to right-hand stimulation for patient ED, but not for the control participants.

Fig. 2 suggests that early SEP components observed for patient ED over the left hemisphere, by stimulation of the contralateral (right) hand, were larger in amplitude than the corresponding components elicited over the right hemisphere via stimulation of the left hand. This is further illustrated in Fig. 4, which shows SEPs elicited *contralaterally to*

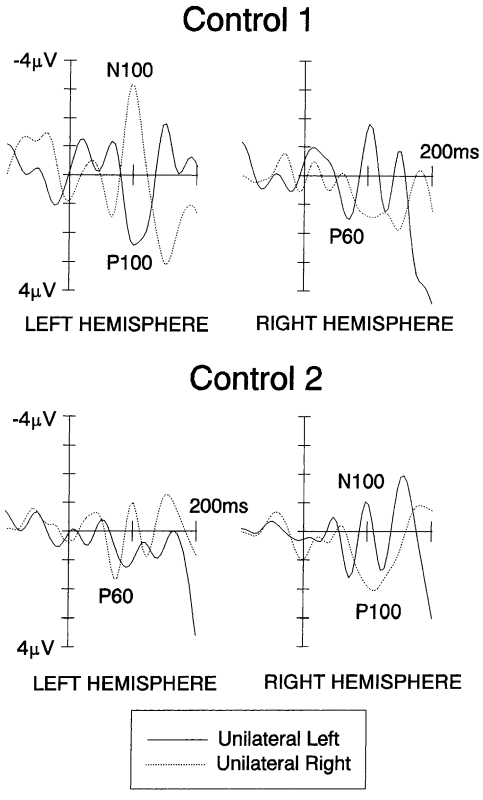

Fig. 3. SEP waveforms for two neurologically unimpaired age-matched control participants, recorded at lateral electrodes over the left and right hemispheres (CP5 and CP6) in response to unilateral tactile stimuli delivered to the left index finger (solid lines) or to the right index finger (dashed lines).

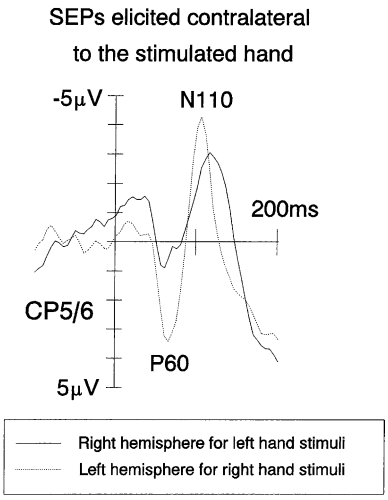

Fig. 4. SEP waveforms in extinction patient ED recorded in response to unilateral tactile stimuli, at electrodes CP5/6 contralateral to the stimulated hands. The solid line shows SEPs to left tactile stimuli recorded from CP6 (right hemisphere) and the dashed line represents SEPs in response to right tactile stimuli recorded from CP5 (left hemisphere).

the stimulated hand at electrodes CP5/6, separately for stimulation of the right hand (left hemisphere; dashed line) and stimulation of the left hand (right hemisphere; solid line). Although P60 and N110 components are apparent for both types of stimuli, these components (especially the P60) were larger in amplitude over the left hemisphere for right-hand stimulation, than over the right hemisphere for left-hand stimulation. This observation in patient ED was substantiated by statistical analyses, revealing a significant P60 amplitude difference between contralateral SEP responses to right-hand stimulation versus left-hand stimulation at CP5/6 ($t(5) = 2.74$, $P < 0.05$; Wilcoxon signed-rank test: $Z = 2.0$, $P < 0.05$). The difference in N110 amplitudes elicited contralaterally by right versus left tactile stimuli, visible in Fig. 4, failed to reach overall statistical significance ($t(5) = 1.17$). Contralateral N110 components were, however, numerically larger for right-hand stimulation relative to left-hand stimulation in both experimental sessions.

This observation that an early SEP component, elicited within 60 ms after stimulus onset, was reliably attenuated in response to tactile stimulation of the contralesional (left) hand suggests that some left-hand deficit may be present even on unilateral trials, although it becomes most manifest behaviourally on bilateral trials (see [15,26], for analogous ERP evidence in visual rather than somatosensory extinction). Unlike patient ED, the age-matched control subjects did not show any systematic amplitude differences for the contralateral P60 component in response to right-hand stimulation versus left-hand stimulation (Fig. 3; see also [16,17] for similar findings). For these control subjects, a positive component (P100) was elicited over the ipsilateral hemisphere in response to unilateral tactile stimuli (see Fig. 3), again in line with previous observations for younger participants [16,17]. It thus appears likely that

the large positive-going deflection peaking at about 140 ms post-stimulus for patient ED, in response to unilateral right stimuli over the right hemisphere (Fig. 2, right) might represent a substantially delayed ipsilateral P100 component in the patient.

While these purely unilateral trials are of interest, one main aim of the present study was to examine the fate of extinguished stimuli on bilateral trials in the patient. To investigate this, we compared SEPs elicited on bilateral trials with the left stimulus extinguished, against SEPs recorded for trials where only a unilateral right stimulus was presented (and detected). It should be noted that these trials were identical with respect to the patient's reported conscious percept (of "right" tactile stimulation only), but differed with respect to the presence or absence of an undetected tactile stimulus on the left hand. Fig. 5 shows ERPs elicited at left and right lateral electrode sites on bilateral extinguished trials (thick dashed lines) and on correctly detected unilateral right trials (solid lines), together with ERPs obtained in bilateral correct trials (thin dashed lines; see below for further discussion).

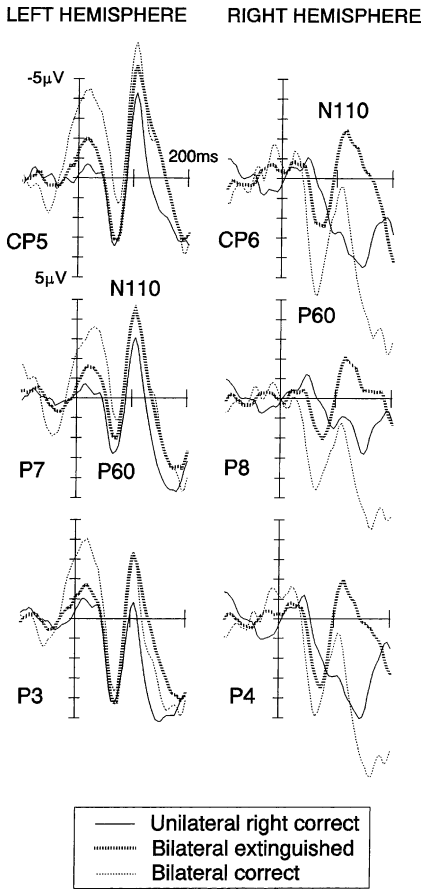

Fig. 5. SEP waveforms in extinction patient ED recorded at lateral electrodes over the left (intact) and right (lesioned) hemisphere, on trials where a unilateral right stimulus was detected successfully (unilateral right correct; thin solid lines), on bilateral stimulation trials where the left stimulus was extinguished (bilateral extinguished; thick dashed lines), and on bilateral stimulation trials where the left stimulus was detected successfully (bilateral correct; thin dashed lines).

As can be seen from Fig. 5, early SEP components in patient ED were generally larger over the left (intact) hemisphere than over the right (lesioned) hemisphere, consistent with the unilateral data shown in Figs. 2 and 4. Nevertheless, and more importantly, tactile stimuli delivered to the left hand on bilateral extinguished trials clearly still elicited contralateral P60 and N110 components over the right hemisphere (thick dashed lines in right graphs of Fig. 5), even though these stimuli could not be consciously detected. By contrast, these components were entirely absent over the right hemisphere in response to unilateral right stimuli (Fig. 5, solid lines in right graphs).

A repeated-measures ANOVA on ERPs elicited in response to bilateral extinguished versus unilateral right stimuli in patient ED, at right-hemisphere electrodes C4, CP6 and P4 (with electrode location as an additional factor), revealed a main effect of stimulation condition on N110 amplitudes ($F(1, 5) = 16.0$; $P < 0.01$). This reflects the presence of an N110 component over the right hemisphere for bilateral extinguished trials, versus the absence of this component for unilateral right trials. Wilcoxon signed-rank tests confirmed this difference for each of these three electrodes (all $Z = 2$; all $P < 0.05$).

An analogous ANOVA performed for P60 peak amplitudes yielded a marginal effect of stimulation condition ($F(1, 5) = 5.85$; $P = 0.06$), consistent with a contralateral P60 being elicited by extinguished left tactile stimuli in addition to the N110. Wilcoxon signed-rank tests revealed reliably larger P60 amplitudes for bilateral extinguished relative to unilateral right trials at C4, CP6 and P4 (all $Z \geq 1.8$; all $P < 0.05$).

In contrast, the P60 elicited over the left hemisphere was virtually identical for bilateral extinguished and unilateral right trials (Fig. 5, left), which underlines the fact that this component is triggered by stimulation of the contralateral (right) hand. While the left hemisphere N110 may appear in the figure to be somewhat larger for bilateral extinguished relative to unilateral right trials (suggesting some possible impact of the extinguished left stimulus on this ipsilateral component), this difference could not be substantiated by statistical analyses.

The pattern of SEP results shown in Fig. 5, thus indicates that extinguished left tactile stimuli receive sufficient unconscious residual processing to still generate P60 and N110 components over the right hemisphere. Although unilateral right and bilateral extinguished trials led to the same conscious reports from patient ED (i.e. of "right" stimulation only), they appear to differ substantially with respect to tactile processing in somatosensory areas of the right hemisphere, as revealed by the SEP data.

Comparison of Figs. 2 and 5 suggests that P60 and N110 components were elicited over the right hemisphere both on unilateral left trials (Fig. 2, solid lines in right graphs) and on bilateral extinguished trials (Fig. 5, thick dashed lines in right graphs). These early lateralised SEP components were similar in terms of their latency and morphology in these two

stimulation conditions. If any trend existed, this was actually for P60 amplitudes to be numerically somewhat larger on bilateral extinguished trials, although this was not reliable ($t(5) < 1$). Thus, the early contralateral SEP component for left-hand stimulation recorded over the right hemisphere appeared at least as large for extinguished left touch on bilateral trials, as for felt touch on unilateral left trials. These observations underline that extinguished left tactile stimuli still receive residual processing in the contralateral (right) somatosensory cortex.

Because the extinction rate for patient ED was around 75%, there were relatively few trials where bilateral trials were correctly detected and this fact precluded any meaningful formal statistical comparison of SEPs for bilateral correct versus bilateral extinguished trials. Nevertheless, we show the mean patterns for completeness. Fig. 5 includes SEPs elicited by bilateral correct (thin dashed lines) and bilateral extinguished trials (thick dashed lines) at left and right lateral electrodes. While P60 and N110 amplitudes appear similar for the two types of trials at left electrodes, the right-hemisphere P60 component (which was elicited by tactile stimulation delivered to the left hand, as shown above) appeared larger on trials where left stimuli were correctly detected, as compared to trials where these stimuli were extinguished (Fig. 5, right). Although relatively few trials contributed to the SEP waveforms for bilateral correct trials, this amplitude enhancement of the P60 relative to bilateral extinguished trials was present in both experimental sessions. This may provide preliminary, suggestive evidence for a possible difference even in the early somatosensory processing of tactile signals from the left hand, that could relate to the presence versus absence of tactile extinction on particular bilateral trials.

5. Discussion

We examined the neural correlates of extinction using ERP measures, in a similar manner to recent pioneering visual studies (e.g. [25,26]; see also [15,41]), except that we now applied ERP measures to study tactile rather than visual extinction. We recorded SEPs from patient ED, who had left tactile extinction as a result of unilateral right-hemisphere damage. SEPs were recorded in response to unilateral or bilateral stimulation, delivered to the left and/or right index finger. The patient had to report verbally his conscious tactile percept (“left”, “right” or “both”) on each trial.

Early sensory-specific somatosensory components (P60 and N110) were elicited contralateral to the stimulated hand on unilateral trials. These components were similar, in terms of morphology and scalp distribution, to the early SEP components observed for two age-matched neurologically unimpaired control participants, as well as for SEPs recorded in response to equivalent tactile stimuli with younger participant groups in other studies (e.g. [16,17]). More importantly, the P60 component found in patient ED was significantly reduced in amplitude over the damaged right hemisphere in response to unilateral left-hand stimulation, as compared with the left-hemisphere component found in response to right-hand stimulation (see Figs. 2 and 4). This departs from the symmetric pattern typically found for normal subjects (e.g. [16]), as observed for the age-matched control subjects here (Fig. 3).

This result adds to a growing body of evidence that although extinction is conventionally defined as a behavioural deficit arising only on bilateral trials, there may in fact be an underlying pathology even for unilateral stimulation on the contralesional side of space. Previous evidence for this has come primarily from visual rather than tactile studies (e.g. [25–27,41]; see also [3,9]). For instance, Marzi et al. [25,26] recently reported reduced visual N1 components at posterior electrodes contralateral to left unilateral visual stimuli, in right-hemisphere patients with left visual extinction. This might be considered somewhat analogous to the reduced P60 found here for left-hand tactile stimulation in patient ED.

Marzi et al. [26,27] have also reported that subtle deficits for unilateral contralesional visual stimulation may also be apparent *behaviourally* in extinction patients, in the form of increased latencies (or errors, once ceiling effects are avoided). Note that patient ED’s vocal responses to unilateral tactile stimulation of the left hand were, analogously, slower than for the right hand, to an extent that exceeds normal callosal transmission times [28]; see Table 2. Moreover, by contrast, the age-matched controls responded somewhat faster to left-hand stimuli than to stimulation of the right hand in the identical task. This behavioural slowing for patient ED may relate to the reduced amplitudes of the P60 and N110 that we found for SEPs in response to left-hand stimulation. The present tactile results, together with previous visual results, thus suggest that an underlying deficit in extinction patients may exist for stimuli on the contralesional side of space even on *unilateral* trials. Extinction may then arise on bilateral trials because the attenuated response to a contralesional stimulus must now compete with the stronger response to a simultaneous ipsilesional stimulus.

A further aim of the present study was to examine the neural fate of extinguished tactile stimuli on those bilateral trials where extinction did arise, by comparing SEPs on bilateral-extinction trials against those for unilateral right stimulation. Somatosensory P60 and N110 components were clearly elicited at lateral electrodes over the right hemisphere, on bilateral trials when an extinguished tactile stimulus was delivered to the left hand (see Fig. 5). In contrast, these components were entirely absent at right-hemisphere electrodes on trials where only the right hand was stimulated; a difference which was confirmed statistically. Although these two types of trials received the same conscious perceptual report from patient ED (i.e. that only a right touch was felt), the SEP data reveal that they differed systematically over right somatosensory cortex, with the extinguished left touch still triggering P60 and N110 components. Moreover, while these components were smaller in amplitude than for

right touch at left-hemisphere sites (Fig. 5), they were comparable to those found for consciously felt left touches over the right hemisphere (Fig. 2, right). This latter observation may suggest that the competitive processes responsible for blocking conscious perception of left-hand stimuli on bilateral trials are not located at early somatosensory processing stages, but primarily affect subsequent stimulus evaluation (see also [26] for similar suggestions with respect to visual extinction).

As noted in Section 1, early SEP components of the type studied here are thought to relate to activity in primary and/or secondary somatosensory cortices (e.g. [19,22). If so, then the present SEP findings for patient ED imply that residual activation of primary and/or secondary somatosensory cortex, by touch on the contralesional hand, can be insufficient to generate tactile awareness in an extinction patient. In this respect, our results seem reminiscent of recent visual studies which used fMRI to show that activation of striate and extrastriate cortex can analogously be insufficient to generate corresponding visual awareness in extinction patients (e.g. [34,42]). In the tactile domain, our results may also accord with recent evidence on unconscious somatosensory processing from a different tactile disorder. Preissl et al. [33] used MEG to study two patients with tumours in right parietal cortex near the central sulcus, and consequent loss of all tactile sensation for the left hand (even for unilateral stimulation). Early neural activity attributed to primary right somatosensory cortex was found to be preserved, despite the loss of tactile awareness. Moreover, in a pioneering electrophysiological study, Vallar et al. [39] found relatively preserved SEPs for unacknowledged unilateral touch on the left hand, in right-hemisphere patients with neglect.

Considering these results together with our own suggests that significant residual activity in early areas of somatosensory cortex (or in our case, reliable components recorded at electrodes over these sites) can be insufficient to generate tactile awareness. However, this need not entail that the overall level of activity in such areas plays absolutely no role in awareness. Forss et al. [18] found with MEG that the strength of early components attributed to right S1 (in response to unilateral electric stimulation of the left median nerve) reflected the severity of conscious tactile impairment in right-hemisphere stroke patients. Moreover, in a recent PET study, Remy et al. [35] found that the activation level in right S1 was reduced during bilateral stimulation of the hands, in a group of extinction patients with primarily subcortical right-hemisphere damage.

Due to the constraints of PET methodology, the Remy et al. study [35] used a blocked design, quite unlike the intermingling of different conditions in an unpredictable sequence for the present event-related design. Accordingly, their patients could anticipate the stimulation type, unlike our own case. Moreover, their blocked method could not separate bilateral trials on which extinction arose, from those where both stimuli were perceived. Comparing these trial types for our SEP data provides initial evidence that the right-hemisphere P60 component may have been larger on those bilateral trials where patient ED successfully detected both of the concurrent tactile stimuli, rather than showing extinction (see Fig. 5, right). But because ED showed extinction on the majority (75%) of trials, we had insufficient power for formal assessment of this tendency in the present study; it, therefore, requires further corroboration. If this pattern does prove to be reliable in future studies, it could provide a tactile analogue of Marzi et al. [25] recent demonstration that contralateral visual ERP components (in their case, the N1) can be larger in amplitude for those bilateral trials on which both stimuli reach the patient's awareness. The fact that the P60 component in response to correctly detected unilateral left stimuli was numerically (although not significantly) smaller than the P60 observed on bilateral-extinction trials might initially appear inconsistent with any idea that this component is related to the conscious detection of left-side tactile stimuli. However, modulations in early tactile processing of left-hand stimuli (as reflected by contralateral P60 amplitudes) might influence stimulus detection primarily under conditions where these stimuli must compete with concurrent right tactile events, and hence could have less influence in determining whether a left-hand stimulus is detected or missed when it is presented in isolation.

6. Conclusions

The present single-case study demonstrates that an extinguished left tactile stimulus can still produce reliable P60 and N110 components at lateral right-hemisphere sites over somatosensory cortex, despite failing to reach the patient's awareness. This provides a possible neural basis for previous behavioural demonstrations of residual unconscious processing of extinguished tactile stimuli (e.g. [1,6,24]). In addition, our results show that an underlying deficit may exist even for *unilateral* tactile stimuli presented to the contralesional hand, with the early contralateral SEP components showing reduced amplitudes in comparison with those for the right hand, and with behavioural responses to unilateral left-hand stimuli being slower, in the patient only. Taken together, our results for bilateral and unilateral trials suggest that tactile extinction can arise due to an attenuation rather than elimination of somatosensory processing for the contralesional hand.

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References

[1] Aglioti S, Smania N, Moro V, Peru A. Tactile salience influences extinction. Neurology 1998;50:1010–4.
[2] Aglioti S, Smania N, Peru A. Frames of reference for mapping tactile stimuli in brain-damaged patients. Journal of Cognitive Neuroscience 1999;11:67–79.
[3] Barcelo F, Suwazono S, Knight RT. Prefrontal modulation of visual processing in humans. Nature Neuroscience 2000;3:399–403.
[4] Bender MB. Extinction and precipitation of cutaneous sensations. Archives of Neurology and Psychiatry 1945;54:1–9.
[5] Bender MB. Disorders in perception. Springfield: Thomas, 1952.
[6] Berti A, Oxbury S, Oxbury J, Affanni P, Umilta C, Orlandi L. Somatosensory extinction for meaningful objects in a patient with right-hemispheric stroke. Neuropsychologia 1999;37:333–43.
[7] Bisiach E, Vallar G. Unilateral neglect in humans. In: Boller F, Grafman J, editors. Handbook of neuropsychology. Amsterdam: Elsevier, 2000. p. 459–502.
[8] Denny-Brown D, Meyer JS, Horenstein S. The significance of perceptual rivalry resulting from parietal lesion. Brain 1952;75:433–71.
[9] Deouell LY, Hamalainen H, Bentin S. Unilateral neglect after right-hemisphere damage: contributions from event-related potentials. Audiology and Neuro-Otology 2000;5:225–34.
[10] Desimone R, Duncan J. Neural mechanisms of selective visual attention. Annual Review of Neuroscience 1995;18:193–222.
[11] Di Pellegrino G, Ladavas E, Farne A. Seeing where your hands are. Nature 1997;388:370.
[12] Driver J, Mattingley JB. Parietal neglect and visual awareness. Nature Neuroscience 1998;1:17–22.
[13] Driver J, Mattingley JB, Rorden, C, Davis G. Extinction as a paradigm measure of attentional bias and restricted capacity following brain injury. In: Thier P, Karnath HO, editors. Parietal lobe contributions to orientation in 3D space. Springer: Heidelberg, 1997. p. 401–29.
[14] Driver J, Vuilleumier P. Perceptual awareness and its loss in unilateral neglect and extinction. Cognition 2001;79:39–88.
[15] Driver J, Vuilleumier P, Eimer M, Rees G. Functional MRI and evoked potential correlates of conscious and unconscious vision in parietal extinction patients. Neuroimage 2001;14:568–75.
[16] Eimer M, Driver J. An event-related brain potential study of cross-modal links in spatial attention between vision and touch. Psychophysiology 2000;37:697–705.
[17] Eimer M, Van Velzen J, Driver J. Cross-modal interactions between audition, touch and vision in endogenous spatial attention: ERP evidence on preparatory states and sensory modulations. Journal of Cognitive Neuroscience 2002;14:254–71.
[18] Forss N, Hietanen M, Salonen O, Hari R. Modified activation of somatosensory cortical network in patients with right-hemisphere stroke. Brain 1999;122:1889–99.
[19] Frot M, Maugière F. Timing and spatial distribution of somatosensory responses recorded in the upper bank of the sylvian fissure (SII area) in humans. Cerebral Cortex 1999;9:854–63.
[20] Frot M, Rambaud L, Guénot M, Maugière F. Intracortical recordings of early pain-related CO_2 laser evoked potentials in human second somatosensory (SII) area. Clinical Neurophysiology 1999;110:133–45.
[21] Gainotti G, De Bonis C, Daniele A, Caltagirone C. Contralateral and ipsilateral tactile extinction in patients with right and left focal brain damage. International Journal of Neuroscience 1989;45:81–9.
[22] Kakigi R, Hoshiyama M, Shimojo M, Naka D, Yamasaki H, Watanabe S, et al. The somatosensory evoked magnetic fields. Progress in Neurobiology 2000;61:495–523.
[23] Libet B. Cortical activation in conscious and unconscious experience. Perspectives in Biological Medicine 1965;9:77–86.
[24] Maravita A. Implicit processing of somatosensory stimuli disclosed by a perceptual after-effect. Neuroreport 1997;8:1671–4.
[25] Marzi CA, Girelli M, Miniussi C, Smania N, Maravita A. Electrophysiological correlates of conscious vision: evidence from unilateral extinction. Journal of Cognitive Neuroscience 2000;12:869–77.
[26] Marzi CA, Girelli M, Natale E, Miniussi C. What exactly is extinguished in unilateral visual extinction? Neurophysiological evidence. Neuropsychologia 2001;39:1354–66.
[27] Marzi CA, Smania N, Martini MC, Gambina G, Tomelleri G, Palamara A, et al. Implicit redundant-target effect in visual extinction. Neuropsychologia 1997;34:9–22.
[28] Marzi CA, Bisiacchi P, Nicoletti R. Is inter-hemispheric transfer of visuomotor information asymmetric? Evidence from a meta-analysis. Neuropsychologia 1991;29:1163–77.
[29] Mattingley JB, Driver J, Beschin N, Robertson IH. Attentional competition between modalities: extinction between touch and vision after right-hemisphere damage. Neuropsychologia 1997;35:867–80.
[30] Maugière F, Gonnaud PM, Ibanez V, Schott B. Potentiels evoques somesthesiques precoces et deficits sensitifs dans les lesions thalamiques et fuxta-thalamique. Revue Neurologique (Paris) 1987;143:643–56.
[31] Maugière F, Merlet I, Forss N, Vanni S, Jousmäki V, Adelaine P, et al. Activation of distributed somatosensory cortical network in the human brain: a dipole modelling study of magnetic fields evoked by median nerve stimulation. Part I. Location and activation timing of SEF sources. Electroencephalography and Clinical Neurophysiology 1997;104:281–9.
[32] Moscovitch M, Behrmann M. Coding of spatial information in the somatosensory system: evidence from patients with neglect following parietal lobe damage. Journal of Cognitive Neuroscience 1994;6:151–5.
[33] Preissl H, Flor H, Lutzenberger W, Duffner F, Freudenstein D, Grote E, et al. Early activation of the primary somatosensory cortex without conscious awareness of somatosensory stimuli in tumour patients. Neuroscience Letters 2001;308:193–6.
[34] Rees G, Wojciulik E, Clarke K, Husain M, Frith C, Driver J. Unconscious activation of visual cortex in the damaged right hemisphere of a parietal patient with extinction. Brain 2000;123:1624–33.
[35] Remy P, Zilbovicius M, Degos JD, Bachoud-Levi AC, Rancurel G, Cesaro P, et al. Somatosensory cortical activations are suppressed in patients with tactile extinction: a PET study. Neurology 1999;52:571–7.
[36] Schwartz AS, Marchok PL, Kreinick CJ, Flynn RE. The asymmetric lateralisation of tactile extinction in patients with unilateral cerebral dysfunction. Brain 1979;102:669–84.
[37] Smania N, Aglioti S. Sensory and spatial components of somaesthetic deficits following right brain damage. Neurology 1995;45:1725–30.
[38] Vallar G, Rusconi ML, Bignamini L, Geminiani G, Perani D. Anatomical correlates of visual and tactile extinction in humans: a clinical CT scan study. Journal of Neurology, Neurosurgery and Psychiatry 1994;57:464–70.
[39] Vallar G, Sandroni P, Rusconi ML, Barbieri S. Hemianopia, hemianesthesia and spatial neglect: a study with evoked potentials. Neurology 1991;41:1918–22.
[40] Verleger R. Comment on “electrophysiological correlates of conscious vision: evidence from unilateral extinction” by Marzi, Girelli, Miniussi, Smania and Maravita. Journal of Cognitive Neuroscience 2001;13:416–7.
[41] Verleger R, Heide W, Butt C, Wascher E, Kompf D. On-line brain potential correlates of right parietal patients’ attentional deficit. Electroencephalography and Clinical Neurophysiology 1996;99:444–57.
[42] Vuilleumier P, Sagiv N, Hazeltine E, Poldrack RA, Swick D, Rafal RD, et al. Neural fate of seen and unseen faces in visuospatial neglect: a combined event-related functional MRI and event-related potential study. Proceedings of the National Academy of Science USA 2001;98:3495–500.
[43] Wilson B, Cockburn J, Halligan P. Behavioural Inattention Test. Titchfield (UK): Thames Valley, 1987.