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Causal role of prefrontal cortex in the threshold for access to consciousness

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What neural mechanisms support our conscious perception of briefly presented stimuli? Some theories of conscious access postulate a key role of top–down amplification loops involving prefrontal cortex (PFC). To test this issue, we measured the visual backward masking threshold in patients with focal prefrontal lesions, using both objective and subjective measures while controlling for putative attention deficits. In all conditions of temporal or spatial attention cueing, the threshold for access to consciousness was systematically shifted in patients, particular after a lesion of the left anterior PFC. The deficit affected subjective reports more than objective performance, and objective performance conditioned on subjective visibility was essentially normal. We conclude that PFC makes a causal contribution to conscious visual perception of masked stimuli, and outline a dual-route signal detection theory of objective and subjective decision making.

Introduction

In spite of recent progress on the neural correlates of consciousness, the brain structures that are necessary and sufficient to become aware of the external world remain a controversial topic. Following up on the seminal proposal of Crick and Koch (1995), many theoretical models and neuroimaging experiments argue for an essential role of distributed long-distance brain networks linking higher visual areas to prefrontal cortex (PFC) and parietal cortex (Lumer *et al*., 1998; Di Lollo *et al*., 2000; Beck *et al*., 2001; Dehaene and Naccache, 2001; Dehaene *et al*., 2001, 2003, 2006; Marois *et al*., 2004). Alternative theories, however, associate conscious perception either to the early activation of specialized visual areas (Pins and Ffytche, 2003; Tong, 2003; Zeki, 2003) or to the reverberating loops linking occipital and temporal regions (Super *et al*., 2001; Lamme *et al*., 2002; Lamme, 2006). Advocates of the latter theories emphasize that frontal lesions typically do not yield impairments in conscious perception (Pollen, 1999), and that the PFC activation during conscious perception tasks may reflect additional reporting or working memory processes unneeded for conscious experience.

Unfortunately, very few experimental studies have directly probed conscious perception in patients with frontal lesions. Frontal lesions lead to neuropsychological deficits that can

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arguably be related to impaired conscious access and control, such as hemineglect, abulia, akinetic mutism, anosognosia, impaired autonoetic memory, loss of intentional control and a surge of automatic activities such as utilization and imitation behaviours (Laplane *et al*., 1981; Lhermitte, 1983; Passingham, 1993; Husain and Kennard, 1996). Some PFC and anterior cingulate patients show a preserved behavioural adjustment to motor or cognitive conflict, but a drastic impairment in their awareness of the conflict (Slachevsky *et al*., 2001, 2003; Naccache *et al*., 2005). These findings are compatible with an intervention of prefrontal areas at a level of cognitive architecture concerned with conscious executive monitoring. Yet whether such high-level processing is necessary for conscious perception itself remains controversial, especially in the light of recent evidence that these executive processes can be partially triggered by non-conscious masked stimuli (Lau and Passingham, 2007; van Gaal *et al*., 2007).

Our aim was to test a more basic prediction of prefrontal theories of conscious perception: the mere ability to become aware of brief visual stimuli, which we term 'access to consciousness' (Dehaene *et al*., 2006), should be impaired in patients with frontal lesions. We used a visual backward masking paradigm which provides quantitative measures of conscious visual perception, as assessed by both objective and subjective measures (Del Cul *et al*., 2006, 2007; Reuter *et al*., 2007). A parafoveal target digit is briefly flashed and, after a variable stimulus onset asynchrony (SOA), is followed by a mask of surrounding letters. At short delays (SOA < 50 ms), the target is generally not consciously perceived, but its visibility increases non-linearly with SOA, thus defining a sharp, all-or-none threshold for access to consciousness. Only targets that cross this threshold induce a late activation of anterior and inferior frontal cortex, together with other focal parietal, temporal and occipital sites (Del Cul *et al*., 2007).

Based on these data, we predicted that focal prefrontal lesions, while unable to entirely abolish the large-scale distributed 'ignition' that underlies conscious access (Del Cul *et al*., 2007), would lead to an elevated threshold for conscious access. On each trial, we therefore asked subjects to report subjective visibility ('Did you see the digit?') and to name the masked digit under forced-choice instructions ('Whether or not you saw a digit, please attempt to name it'). A double staircase procedure was used to continuously adapt the target-mask SOA in order to maintain subjective visibility at threshold. Because PFC is thought to participate in a conscious global workspace that supports the brain-scale sharing of visual information (Baars, 1989; Dehaene and Naccache, 2001; Dehaene *et al*., 2001, 2003; Dehaene *et al*., 2006), we expected both subjective reports and objective performance to exhibit a shifted threshold. Theoretical models that attribute masking (Macknik and Livingstone, 1998; Breitmeyer, 2006) and conscious access (Zeki, 2003) to early visual processing confined to posterior brain areas, on the other hand, should predict that prefrontal lesions leave the threshold unaffected.

It might be argued that frontal patients suffer from attentional deficits which, by themselves, might account for an elevated perceptual threshold (Stuss and Levine, 2002). To counter this objection, we evaluated the effects of attentional modulation on the conscious access threshold, using four different cueing conditions (Fig. 1). The first condition minimized the deployment of spatial and temporal attention by having the masked stimulus appear at a random spatial location after an unpredictable delay. A second condition introduced a temporal cue that allowed subjects to predict the time, but not the place, at which the masked stimulus would occur. The third and fourth conditions added to this temporal cueing an exogenous or an endogenous spatial cue. Given this hierarchical design, we predicted a progressive decrease in the threshold across the four cueing conditions, and examined if these attentional effects were impaired or intact in prefrontal patients.

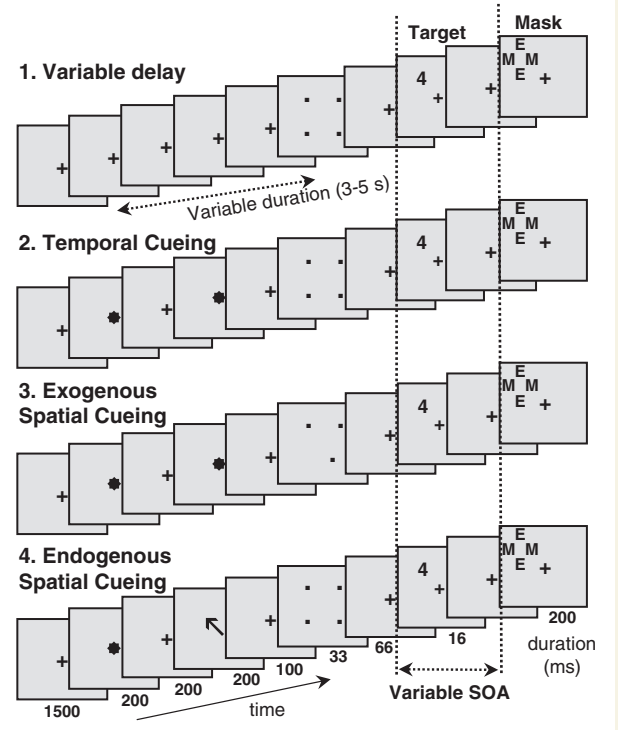

Figure 1 Stimuli used to measure the threshold for access to consciousness during masking. The target consisted of a single digit, appearing at one of four possible locations, and which was replaced after a variable delay (SOA) by a mask consisting of a blank surrounded by four letters. Four conditions of attention were used, manipulating the possible deployment of temporal and/or attention (see text for details).

Methods

Subjects

We studied 15 patients with frontal lobe lesions: 7 females and 8 males, with a mean (SD) age of 42.20 (9.68) years and educational level of 12.87 (2.99) years. All the patients had a frontal lesion on MRI (10 from an excised brain tumour, 2 a cerebral ischemic stroke and 3 a cerebral trauma). All patients were tested at least 3 months post-onset to be certain that all transient pathophysiological disturbances such as oedema have cleared. 15 control subjects (11 females and 4 males) with a mean (SD) age of 44.20 (8.31) years and educational

level of 12.87 (3.16) years were recruited by advertisement. None had a history of neurological or psychiatric disease, alcohol or drug abuse or substance dependence. They were matched for age (Mann–Whitney *U*-test, $U = 103.0$; $z = -0.395$, $P = 0.71$), and years of education (Mann–Whitney *U*-test, $U = 112.0$; $z = -0.21$, $P = 1.00$). All patients received a neuropsychological evaluation consisting in the Mattis Dementia Rating Scale (DRS), Frontal Assessment Battery (FAB), modified form of the Wisconsin Card Sorting test (MCST), letter fluency [words beginning with 'A' in 60 s, semantic fluency (animal names in 60 s) and Trail Making Test (TMT)]. The scores were (mean ± SD): DRS, 128.73 (9.82); FAB, 14.93(2.66); WCST number of criteria achieved, 4.83 (1.72); WCST number of perseverations, 4.80 (1.78); semantic fluency, 15.93 (5.23); letter fluency, 8.67 (4.91); and difference between the time taken to complete parts A and B of the TMT; 67.08 (48.17). Informed consent was obtained from all patients and control subjects after the nature of the experiment had been fully explained.

Experimental design and procedure

Stimuli and tasks

Black digits 0–9 were presented on a white background at the centre of the computer screen using E-Prime software. Presentation times of the stimuli were synchronized with the vertical refresh rate of the screen (60 Hz) and were systematically verified. The target stimulus was presented for 16 ms at one of four positions forming a virtual square ($2.8^\circ \times 2.8^\circ$) around the fixation cross. After a variable delay, a mask appeared at the target location (mask duration 250 ms). The mask was composed of four letters (two horizontally aligned M's and two vertically aligned E's) surrounding the target location without touching it. In each trial, we first recorded a subjective response (report if the masked number was seen or not) followed by an objective response (name the number that was presented). Responses were made verbally in Spanish and were recorded manually by the experimenter.

Conditions of attentional modulation

Four cueing conditions (variable delay, temporal cueing, exogenous spatial cueing and endogenous spatial cueing) were evaluated in separate blocks in randomized order. Each subject performed two sessions of the whole sequence of four blocks. Prior to each block, subjects were instructed to pay attention to the particular cue. As showed in Fig. 1, all conditions involved similar stimuli, temporal sequence, tasks and sustained attention. The 'variable delay' condition minimized the deployment of spatial and temporal attention by having the masked stimulus appear at a random spatial location after an unpredictable delay between 3000 and 5000 ms. In this condition, a central fixation cross was presented throughout this variable delay and was followed by a short slide (duration 33 ms) composed of four little red dots localized at each of the four potential target positions, 100 ms before target onset. In the 'temporal cueing' condition, a temporal cueing sequence allowed subjects to predict the time, but not the place, at which the masked stimulus would occur. After the fixation cross, two black circles (duration = 200 ms) were successively presented at a temporal interval of 400 ms, 300 ms after the onset of the second black circle, and thus 100 ms before target onset, the 'four red dots' slide was presented for 33 ms. Thus, the target digit fell 400 ms after the second black circle (and 800 ms after the first black circle) and its precise onset could be predicted. Started from this temporal cueing condition, we added either exogenous or endogenous spatial cueing. In the spatial exogenous cueing condition, aimed at inducing reflexive orienting of spatial attention, the cueing sequence only differed from temporal cueing condition by the presentation of only one red dot (instead of four) indicating the location of the upcoming masked target, 100 ms before it appeared. In the spatial endogenous cueing, allowing the voluntary deployment of spatial attention, the second black circle used in the temporal cueing (presented 400 ms before target onset) was replaced by a central arrow which indicated the quadrant where the target was presented (above or below, right or left).

Staircase algorithm for evaluating the masking threshold

Target-mask SOA was adapted according to target visibility using a 'double staircase' algorithm. Each trial was randomly assigned to one of the two staircases, one starting with the shortest SOA (16 ms) and the other with the highest SOA (133 ms). Independently for each staircase, the stimulus-mask SOA was decreased by one frame (16 ms) whenever the subject reported seeing the stimulus on the previous trial and was correct in the naming task. Otherwise, the SOA was increased by one frame. Once SOA reached the approximate value of the subject's conscious perception threshold, SOA progression often reversed from one trial to the next. The algorithm stopped the experimental block once the number of reversals reached an arbitrary value ($n = 18$).

MRI and statistical parameter mapping

Lesions were manually traced by a neurologist on individual axial slices of a high-resolution T_1-weighted MRI of the patients' brains. The brains were then normalized to the standard MNI space using SPM5 software, resampled at 2 mm × 2 mm × 2 mm, and the lesions converted to a 3D volume with 1 indicating the presence of the lesion, 0 the presence of normal tissue. These images were then smoothed (8 mm Gaussian isotropic) for better intersubject averaging, and entered into an SPM regression model with the conscious access threshold as a covariate. We report the results with a voxelwise threshold of $P < 0.01$ and a cluster extent threshold $P < 0.001$, corrected for multiple comparisons across the brain volume.

Results

Threshold for conscious access and effect of attentional modulations

The double staircase algorithm, which constantly modified the target-mask SOA, converged to a stable asymptote after about 15 trials (Fig. 2A). The threshold for conscious access was thus estimated as the mean SOA over trials 15–50. As predicted, this threshold was significantly higher in patients than in controls (69 ms versus 51 ms, $P < 0.01$). This difference was observed in all conditions of attention (Fig. 2B; $P < 0.001$ for spatial exogenous cueing and temporal cueing, $P < 0.05$ for endogenous spatial cueing and variable delay). An analysis of variance (ANOVA) with factors of group (two levels) and attentional modulation (four levels) showed a significant effect of the four attention conditions, both globally [$F(3,84) = 8.851$, $P < 0.001$] and within each group [patients: $F(3,42) = 6.164$, $P < 0.01$; controls: $F(3,42) = 4.348$, $P < 0.01$]. Importantly, there was no significant group × attention interaction [$F(3,84) = 0.972$, $P = 0.41$], indicating

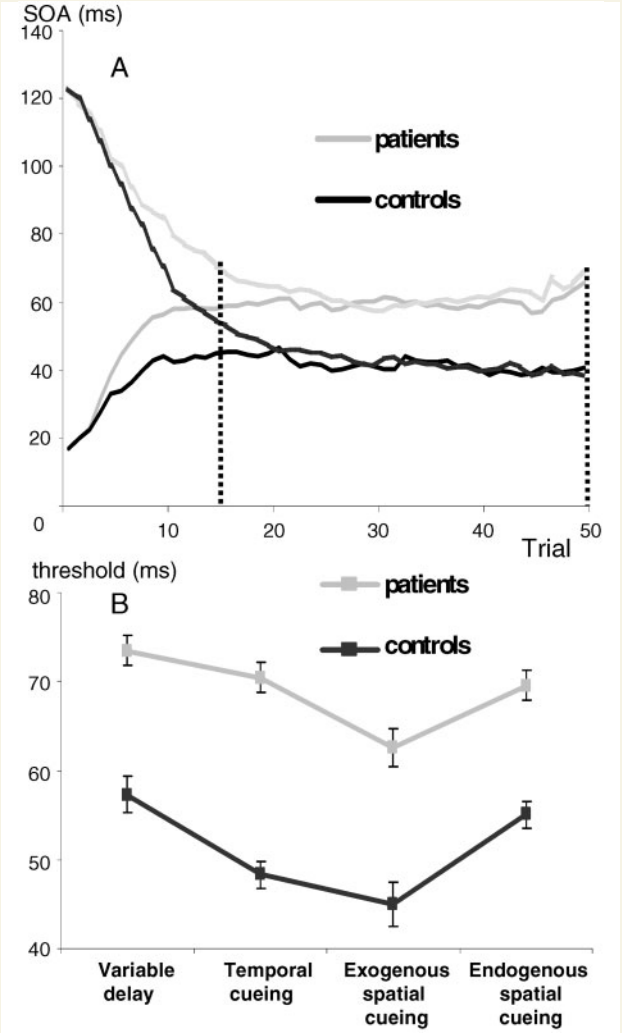

Figure 2 Threshold for conscious access in normal subjects and in patients with prefrontal lesions. (**A**) Evolution of mean SOA across trials according to the double staircase algorithm. Regardless of starting point, the algorithm quickly converges to a stable SOA which clearly differs between patients and controls. The threshold was estimated as the mean SOA from trials 15 to 50. (**B**) Mean threshold in the four attention conditions (error bars = 1 standard error).

that the various forms of attentional cueing that we manipulated were not affected by the frontal lesions. As expected, the highest threshold (65 ms) was observed in the variable-delay condition, where targets occurred without spatial or temporal cueing. Relative to this condition, temporal cueing significantly lowered the conscious access threshold down to 59 ms [$F(1,28) = 6.914$, $P < 0.05$], and exogenous spatial cueing yielded an even lower threshold of 54 ms [$F(1,28) = 20.263$, $P < 0.001$]. Surprisingly, our manipulation of endogenous spatial cueing had no effect over and above the temporal cueing condition [threshold = 62 ms; $F(1,28) = 0.657$, $P = 0.424$]. This finding may perhaps be attributed either to the ineffectiveness of the central arrow in a paradigm where subjects were told to focus on peripheral stimuli, or to a partial attentional blink of the central arrow onto the target digit, which would have worked against any effect of attention. The important conclusion is that attentional effects did not differ in patients and controls, and that in all conditions the conscious threshold was higher in patients than in controls.

Objective versus subjective measures

We then tested the impact of frontal lesions on subjective visibility (percent seen trials) and objective performance (percent correct naming) as a function of SOA. For this analysis, we obtained measures for all eight SOA values ranging from 16 to 133 ms (the highest value from which the staircase started). Our statistical analysis pooled over all four conditions of attention, after ANOVAs confirmed an effect of the four attentional conditions on both variables [objective performance: $F(3,84) = 10\,389$, $P < 0.001$; subjective visibility: $F(3,84) = 6.179$, $P < 0.01$], without any significant interaction with group [$F(3,84) = 0.507$, $P = 0.678$ and $F(3,84) = 0.475$, $P = 0.7$, respectively]. The means as a function of SOA are presented in Fig. 3. Note that, given the staircase procedure, different SOAs were sampled with unequal frequencies and at different times, as the data from very long and very short SOAs, far from threshold, mostly come from a few trials at the beginning of each block.

As shown in Fig. 3, both subjective and objective measures rose quickly and non-linearly with SOA, but with a shifted threshold for patients compared to controls. ANOVAs confirmed that objective performance was higher in controls than in patients [0.7 versus 0.6; $F(1,28) = 6.734$, $P < 0.05$], as was subjective visibility [0.76 versus 0.6; $F(1,28) = 18.552$, $P < 0.001$]. For subjective visibility, the group × SOA interaction was highly significant [$F(7,196) = 6.16$, $P < 0.001$]. For objective performance, the group × SOA interaction was close to significance [$F(7,196) = 1.83$, $P = 0.083$].

Instead of a shifted consciousness threshold, an alternative explanation for the results could be that patients are simply less vigilant, attentive or careful on a fixed percentage of trials, when they would respond randomly. This hypothesis predicts that, relative to controls, the patient's curves would not be shifted horizontally, but rather scaled down vertically by some multiplier. Note that this hypothesis would need to be further elaborated, because as made clear by Fig. 3, a different scaling factor would be needed for subjective and objective measures. Nevertheless, to test this possibility formally, we first examined if the two groups differed at the slowest SOA values (100–133 ms). We found no group effect for objective performance [$F(1,28) = 2.107$, $P = 0.158$] nor for subjective reports [$F(1,28) = 2.462$, $P = 0.128$], suggesting that the patients were attentive enough to respond normally to brief but largely above-threshold stimuli. To further pursue this point, we then re-analysed the data after rescaling by the small observed difference at the highest SOA of 133 ms (similar results were obtained using SOA = 116 ms). For objective data, we used an affine rescaling formula such that the data point for SOA 133 ms was aligned to 100% correct, and the chance level of 10% was left unaffected:

$$p'_{soa} = \left[\frac{p_{soa} - 10}{p_{133} - 10}\right] \times 90 + 10$$

where p_{soa} is the measured objective performance (% correct) at a certain SOA, and p'_{soa} is the rescaled value. For subjective data, a

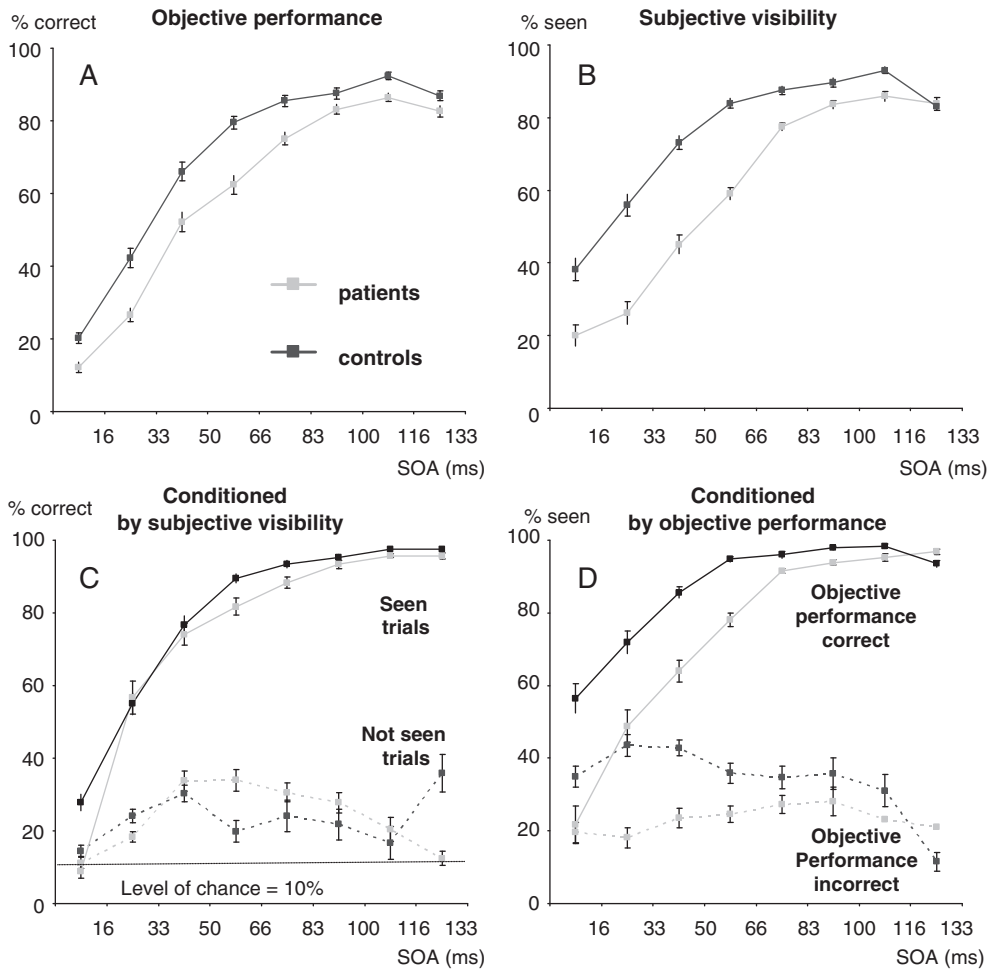

Figure 3 Evolution of objective (**A** and **C**) and subjective performance (**B** and **D**) as a function of SOA (from 16 to 133 ms) in normal subjects and in patients with prefrontal lesions. The *top graphs* show overall means (error bars = 1 standard error). The *bottom graphs* show a conditional analysis, with performance split up as a function of subjective (**C**) or objective (**D**) responding on the same trial.

simpler proportionality rule was used, since there is no chance level with subjective measures:

$$v'_{133} = \frac{v_{133}}{p_{133}} \times 100$$

where v_{soa} is the observed mean visibility rating and v'_{soa} is the rescaled value.

We then reanalysed the rescaling data from the remaining SOAs 16 to 116 ms in a group × SOA ANOVA. Consistent with the shifted-threshold view, the group × SOA interaction remained highly significant for rescaled subjective visibility [$F(6,168) = 5.067$, $P < 0.001$] and close to significance [$F(6,168) = 1.922$, $P = 0.079$] for rescaled objective performance. Thus, our results rule out the hypothesis of a mere global rescaling of performance, with a fixed percentage of inattention trials and support an elevation of the consciousness threshold.

Capitalizing on the availability on both measures on every trial, we next examined the relations between objective and subjective measures. For instance, although patients exhibit a higher visibility threshold, was their objective performance normal once they reported seeing the target? To answer this question, we examined how objective performance varied, conditioned on the fact that subjects reported seeing or not seeing the stimulus. We restricted this analysis to SOA values where data were available for each subject (SOAs 50–100 ms for 'seen' trials and SOAs 16–66 ms for 'not seen' trials; Fig. 3 shows the means for all SOAs, but with a few missing subjects for some data points). This conditional analysis revealed that, once subjective visibility was factored out, objective performance barely differed between patients and controls (Fig. 3C). When they reported 'seeing', both groups showed a high performance, still increasing with SOA [$F(3,84) = 28.73$, $P < 0.001$], but without any group difference [group effect: $F(1,28) = 0.929$, $P = 0.343$; group × SOA interaction: $F(3,84) = 0.723$; $P = 0.541$]. When they reported 'not seeing', both groups showed a low objective performance in the digit naming task, which surpassed chance level 10% ($P < 0.01$ for patients and controls) and increased with SOA [$F(3,84) = 12.48$, $P < 0.001$], indicative of a subliminal effect or 'blindsight'. There was no main effect of group [$F(1,28) = 0.174$, $P = 0.68$], but a small group × SOA interaction [$F(3,84) = 3.61$, $P < 0.05$], showed that

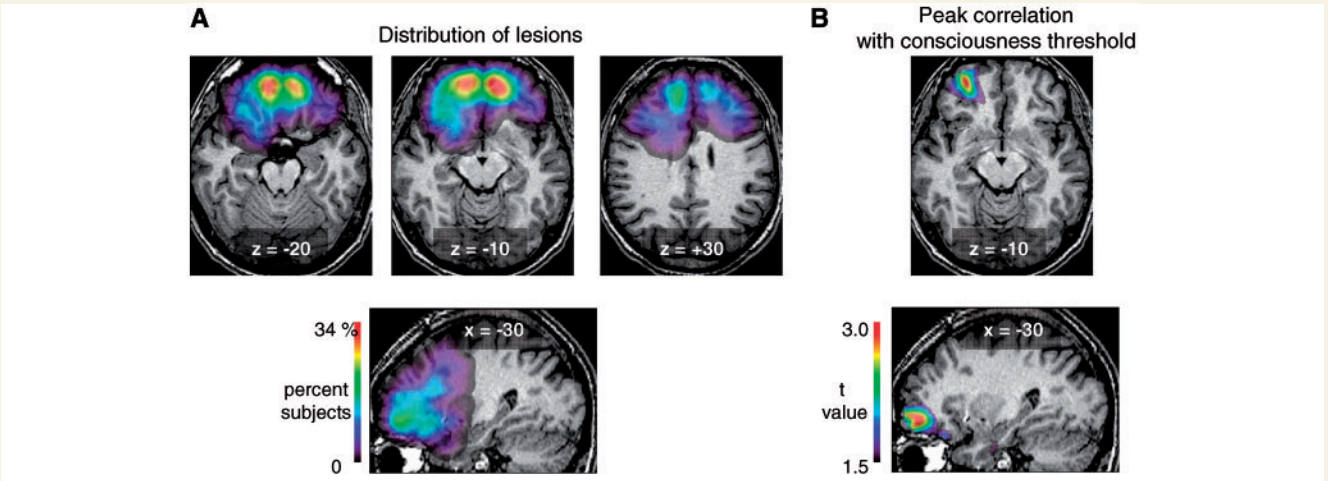

Figure 4 Relationship between prefrontal lesion site and the conscious access threshold. (**A**) Overlap of the 15 patients' lesions, showing essentially complete PFC coverage with particular concentration in bilateral anterior and inferior frontal areas. (**B**) Cluster of voxels in left anterior ventral PFC where SPM analysis suggests a significant relation between the presence of lesions and the amount of increase in the conscious access threshold.

objective performance dropped at long SOA ($\geqslant$66 ms) in normal controls, but remained high in patients (in whom such long-SOA unseen trials were much more numerous).

In summary, whether participants reported seeing or not seeing the target digit led to a large difference in objective performance. Patients reported more difficulty than controls in seeing the target, and once this difference in subjective visibility was factored out, the difference in objective performance between the two groups essentially vanished.

The converse analysis—subjective reports conditioned on objective performance—revealed that the relation between subjective and objective measures was asymmetrical (Fig. 3D; analysis restricted to SOAs 50–100 ms for correct trials, and SOAs 16–66 ms for incorrect trials). Even after factoring out differences in objective performance, subjective visibility remained strikingly different in patients and controls. When they performed correctly on the objective naming task, the patients still made fewer subjective reports of 'seeing' than the controls, especially as short SOAs [group effect: $F(1,28) = 1466$, $P < 0.001$; group $\times$ SOA interaction $F(3,84) = 7622$, $P < 0.001$]. On error trials of the objective task, a similar difference was seen: the patients again less frequently reported seeing the digit [group effect: $F(1,28) = 7.35$, $P < 0.05$], without any effect of SOA [$F(3,84) = 1.286$, $P = 0.284$] or group $\times$ SOA interaction [$F(3,84) = 1.89$, $P = 0.137$].

Correlation with neuropsychological and lesion data

We found no correlation between the conscious access threshold and performance in various neuropsychological tests [Mattis Dementia Rating Scale (DRS), Frontal Assessment Battery at bedsides (FAB), fluency test, number of criteria and perseverative errors in the Modified Version of the Wisconsin Sorting test (MCST) and time to achieve the TMT]. The threshold was correlated neither with the global volume of the lesion ($R^2 = 4.122\text{E}{-}05$, $P = 0.982$) nor with the partial volumes of white and grey matter ($R^2 = 8.2\text{E}{-}04$, $P = 0.92$ and $R^2 = 1.124\text{E}{-}04$, $P = 0.97$, respectively). Patients differed significantly from the controls regardless of the side of the lesion [left lesion: $t(21\text{d.f.}) = 3.66$, one-tailed $P < 0.001$; right: $t(17\text{d.f.}) = 1.77$, one-tailed $P = 0.045$; bilateral: $t(16\text{d.f.}) = 3.13$, $P = 0.003$]. However, within patients with unilateral lesions, there was a trend for left frontal lesions to cause a more severe increase in access threshold than right frontal lesions [$t(11\text{d.f.}) = 1.86$, two-tailed $P = 0.09$], regardless of the hemifield of presentation of the stimulus (all $P > 0.05$).

As an exploratory analysis, and since the 15 patients' lesions were distributed across the entire frontal lobe, we attempted to identify, by regression analysis, the lesion sites associated with the greatest impairment in conscious access (Fig. 4). To this aim, we entered the normalized and smoothed lesions into a linear regression model with the access threshold, determined by the double staircase procedure, as a predictor. Statistical analyses revealed a significant positive correlation with a restricted site in left frontopolar cortex (peak MNI coordinates -32, 54, -6; peak $z = 2.56$, 95 voxels with $P < 0.01$; cluster-level corrected $P = 0.001$).

Discussion

We first summarize the results. Patients with frontal lesions have an elevated masking threshold compared to controls, a deficit that seems preferentially associated with lesions to left inferior anterior PFC. The impairment appears to be characterized by a primary deficit in subjective reportability which in turn, impacts on the objective naming task. Indeed, once subjective reports are equalized, the conditional probability of succeeding in the objective task does not differ between groups. The impairment is additive with effects of attentional cueing, which are identical in patients and controls.

Using non-invasive neuroimaging, many studies have reported a correlation between conscious access and activation of frontal and parietal networks, not only in normal subjects during masking (Dehaene *et al*., 2001; Lau and Passingham, 2006; Del Cul *et al*., 2007), attentional blink (Marois *et al*., 2004; Sergent *et al*., 2005), binocular rivalry (Lumer *et al*., 1998) or change blindness (Beck *et al*., 2001), but also in pathological conditions such as hemineglect (Vuilleumier *et al*., 2002) or blindsight (Sahraie *et al*., 1997). Particularly comparable to our results is a recent fMRI study by Lau and Passingham (2006). Using a metacontrast masking paradigm, they selected a pair of stimulation conditions that led to very similar objective performance, yet with strikingly different subjective reportability of the masked stimulus. This design therefore permitted to study the fMRI correlates of subjective perception in the absence of performance confounds. Subjective reports of conscious perception were found to correlate quite specifically with activity in the mid-dorsolateral PFC. Thus, both the Lau and Passingham (2006) study and the present research parallel each other in showing that when objective performance is controlled for, PFC lesion or activation still relates to the subjective aspects of awareness.

Neuroimaging studies in normal subjects, however, are only correlational. Moving closer to a causal relationship, a few TMS studies have established that interference with either parietal, frontal eye field or right dorsolateral PFC leads to impaired conscious detection in attentional blink or change blindness paradigms (Grosbras and Paus, 2002; Turatto *et al*., 2004; Beck *et al*., 2006; Babiloni *et al*., 2007; Kihara *et al*., 2007). In brain-lesioned patients, Husain *et al*. (Husain and Kennard, 1996, 1997; Husain *et al*., 2000) reported contralesional perceptual and motor neglect in patients with right frontal lesions, particularly under conditions of high distractor load. A previous study also demonstrated reduced perception of a target letter within a rapid sequential stream in small groups of patients with Huntington's disease or unspecified frontal excisions (Richer *et al*., 2002). In monkeys, lesions in frontal eye fields or Brodmann's area 8 cause an increase in the luminance threshold (Latto and Cowey, 1971), and ablation of dorsolateral PFC affects the perception of brief light flashes (Kamback, 1973).

Relative to this background literature, our study adds important elements. First, it reveals a basic and bilateral deficit of access to consciousness in a larger sample of 15 patients with lesions characterized with MRI. Second, we report quantitative objective and subjective measures of the consciousness threshold, and present several controls for attention deficits. Nevertheless, before concluding that PFC is an important player in conscious access, we must consider whether alternative explanations could account for the observed deficit. It is tempting to explain away the patients' deficit as a mere bias toward the 'not seen' response. Indeed, the conditional analysis suggests that at the same SOA and objective level of performance (whether correct or incorrect), patients with frontal lesions always categorize more trials as 'not seen' compared to normal controls. However, the detailed pattern of results seems hard to explain as a conservative bias to avoid 'seen' responses. At short SOAs, both patients and controls do not hesitate to venture an important fraction of 'seen' response even though they have a low confidence, as attested by a high proportion of 'seen' trials with incorrect naming. Furthermore, a mere bias affecting only subjective reports would predict a different profile of results. First, objective performance should be identical between patients and controls, unlike the present results. Second, if patients used a stricter criterion for visibility, objective performance conditioned by subjective visibility should significantly differ between groups, with higher objective performance in patients than in controls on 'seen' trials—again unlike our results.

In a related criticism, one could argue that the observed impairment, which was measured by a naming task and by subjective verbal report, was due to language difficulties. However, this suggestion fails to account for the details of our study, including the presence of a deficit in right-lesioned patients and of a normal naming ability at long SOAs and when conditioning by subjective reports (Fig. 3).

Might the elevated threshold be due to an attention deficit? A narrow version of this interpretation can be ruled out, since the patients showed a normal benefit of temporal and spatial cues, while the conscious threshold was constantly higher in patients in all conditions of attentional cueing. Note, however, that we did not provide exhaustive measures of attentional capacities in patients, but merely measured the effect of attentional cueing on conscious perception. Therefore, our study does not exclude the presence of additional deficits of motivation or a greater distractibility in frontal patients, which are indeed frequently reported in frontal patients. Indeed, under a broad construal of the term 'attention', an attentional origin of the deficits not only cannot be excluded, but in fact need not be seen as providing an alternative account to our hypothesis that the exchange of top–down and bottom-up signals between frontal networks and posterior visual areas plays an essential role in access to consciousness. Many PFC areas and the associated basal ganglia circuitry, including regions involved in motivational and executive attention control, play an important top–down attentional amplification role which may be a key neural mechanism simultaneously subtending selective attention, dual-task restrictions, and conscious appraisal (Dehaene and Naccache, 2001; Dehaene *et al*., 2006).

Nevertheless, the challenge for tenants of the motivation or attention hypothesis is to specify it up a sufficient level of detail to account for the present quantitative results. Analyses show that the patient's curves are not simply scaled down by a fixed multiplier relative to the controls, as would be expected if there was a percentage of trials where the patients were distracted. The fact that we observed normal performance at SOAs of 100–133 ms, which is short but above-threshold for both patients and controls, argues against any simple motivational or distraction account. Another important observation is the greater impact of PFC lesions on subjective than on objective measures. It is not immediately clear why a motivation or attention deficit should not have the exactly opposite effect, since the objective task, with 10 responses to barely visible stimuli, could be arguably described as more difficult than the subjective task of saying 'seen' or 'not-seen' without constraints. Furthermore, it could be argued that in our conditional analysis of the subset of trials in which objective performance was correct, we excluded trials in which motivation was low—and yet there remained a major difference

in subjective reports. All in all, the motivation or distraction accounts seem somewhat underspecified to explain our data.

Our findings should be considered in the light of current theoretical models of conscious access to perceptual information. A major controversy separates tenants of early-stage versus two-stage models of conscious access. According to early-stage models, masking arises solely at an early visual level, for instance as an interaction between fast and slow visual pathways (Macknik and Livingstone, 1998; Breitmeyer, 2006) or as the result of competition at many successive levels within the ventral occipito-temporal cortex (Keysers and Perrett, 2002). Conscious perception relates to the resolution of this competition, either within isolated visual areas coding for the relevant perceptual attribute (e.g. V4 for colour Zeki, 2003), or through local occipito-temporal loops linking multiple visual areas into a coherent interpretation of the visual scene (Lamme and Roelfsema, 2000; Lamme, 2006). These theories do not seem compatible with our finding of a PFC impact on the masking threshold, unless they specify in greater detail how these early posterior networks are affected by prefrontal attention systems.

The present work fits more comfortably within a second class of theories that fall under the general heading of 'two-stage' models. These theories introduce a distinction between perceptual and post-perceptual processes, and assume that both steps are needed for conscious decisions and reportability (Sperling, 1960; Neisser, 1967; Posner, 1994; Chun and Potter, 1995; Dehaene and Naccache, 2001; Kanwisher, 2001; Dehaene *et al*., 2006). The first-stage—the construction of an accurate perceptual representation of the stimulus—does not suffice for its conscious perception, since there are many experimental conditions such as the attentional blink (Vogel *et al*., 1998; Sergent *et al*., 2005), or pathologies such as hemineglect (Driver *et al*., 2001), in which perceptual processing in occipito-temporal cortices can be demonstrably intact although the stimulus evades conscious report. Two-stage theories therefore propose that a second, capacity-limited stage of processing is needed to transfer the selected percept into a more durable compartment where it can be consolidated in working memory and used for response selection. Physiologically, ERP, MEG and intracranial recordings suggest that this second stage might correspond to a late (>270 ms) phase where stimulus-induced activation expands into parietal and PFCs, and leads to a concomitant long-distance top–down amplification of visual information (Gross *et al*., 2004; Sergent *et al*., 2005; Del Cul *et al*., 2007; Gaillard *et al*., 2009).

Two-stage theories build upon the physiological distinction, arising primarily from monkey electrophysiology, between early feedforward and late feedback or re-entrant stages of visual processing (Edelman, 1993; Lamme and Roelfsema, 2000). However, while some theorists propose that the feedback information essential for conscious access arises from local visual (Lamme, 2006) or parietal cortices (Di Lollo *et al*., 2000), the present work suggests that interactions with PFC also play an important role. Our own interpretation is that the change in conscious access threshold following PFC lesions affected both subjective and objective performance because it affected the entry and/or maintenance of stimulus information into a 'conscious global workspace' (Baars, 1989; Dehaene and Naccache, 2001) needed to broadcast target identity to many brain regions, including those involved in conscious report, word selection and naming.

Interestingly, objective performance in naming digits reported as 'not seen' was better than chance in both groups, without a significant overall difference between patients and controls (Fig. 3C). This phenomenon is a form of blindsight and implies preserved non-conscious processing of masked digits in patients, compatible with the notion of a preserved first perceptual stage of feed-forward processing. A similar dissociation between impaired conscious access and preserved subliminal processing has been previously reported in several conditions that are all thought to involve, as a key clinical factor, a reduction in prefrontal connectivity, including schizophrenia and early-onset multiple sclerosis (Del Cul *et al*., 2006; Reuter *et al*., 2007). Thus, the conscious access threshold measure might be used as a simple behavioural assay of structural and/or functional abnormalities in the large neural network involved in conscious access.

The masking measure can be differentiated from another interesting psychophysical measure, the decay of iconic memory, which has been shown to constitute a potential cognitive marker for an increased risk of developing Alzheimer's disease in subjects with mild cognitive impairment (MCI) (Lu *et al*., 2005). As suggested by the authors, fast decay of iconic memory may depend critically on the functioning of the hippocampus and association cortices. In the future, it will be interesting to examine whether conscious access threshold and iconic memory decay constitute doubly dissociable measures that might reliably point to frontal versus MCI pathology.

Our results fit with the classical view (Norman and Shallice, 1980; Fuster, 1989) that PFC plays a greater role in conscious monitoring than in automatic or non-conscious evidence accumulation. In the appendix, we show how our results can be accounted for in a detailed, quantitative manner by a dual-route version of signal detection theory. This model assumes a parallel accumulation of noisy sensory evidence at two levels, each with a distinct noise level and a threshold. The higher system is 'all-or-none' and takes control of responses only if its threshold is reached (in which case a 'seen' response is recorded). Otherwise, a forced-choice 'not-seen' response is emitted from the graded evidence accumulated at the lower level. Simulations show how a mathematical formulation of these hypotheses can mimic normal subject's response curves and, with the addition of noise at the higher level, can account for the patient's displaced curves. The suggestion is that the higher level conscious route corresponds to parieto-prefrontal networks and associated higher cortical areas.

PFC itself is organized into hierarchical organized networks known to be engaged in high-level processes requiring consciousness, and particularly in top–down processes of visual perception (Bar *et al*., 2006; Summerfield *et al*., 2006) and perceptual decision (Binder *et al*., 2004; Heekeren *et al*., 2004). Our SPM analyses suggest that brain lesions encroaching on left frontopolar PFC are most crucially associated with the elevation of conscious threshold (Fig. 4). Nevertheless, this localization must be taken with caution, because all patient subgroups, with unilateral or bilateral frontal lesions, were impaired. We only studied

15 patients, and the distribution of their lesions might have affected the SPM analysis. From a theoretical standpoint, correlation of the conscious access threshold with a restricted subregion within PFC may appear unrealistic, as the theoretical arguments and neuroimaging studies cited above support the idea that conscious processes involve large networks including multiple PFC areas. Indeed, while our study indicates that PFC lesions affect the threshold for conscious access, it does not preclude a strong contribution of other cortical regions. For instance, transcranial magnetic stimulation suggests a central contribution of dorsal parietal cortex to visual perception (Beck *et al*., 2006; Babiloni *et al*., 2007; Kihara *et al*., 2007). Future work should include a greater array of cortical and subcortical lesions in order to more precisely isolate the network of regions relevant to visual awareness. The present work merely indicates that frontopolar PFC must be one of its key anterior nodes.

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