

Beyond primary visual cortex: The leading role of lateral occipital complex in early conscious visual processing

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ABSTRACT

The study of the neural substrates that serve conscious vision is one of the unsolved questions of cognitive neuroscience. So far, consciousness literature has endeavoured to disentangle which brain areas and in what order are involved in giving rise to visual awareness, but the problem of consciousness still remains unsolved. Availing of two different but complementary sources of data (i.e., Fast Optical Imaging and EEG), we sought to unravel the neural dynamics responsible for the emergence of a conscious visual experience. Our results revealed that conscious vision is characterized by a significant increase of activation in extra-striate visual areas, specifically in the Lateral Occipital Complex (LOC), and that, more interestingly, such activity occurred in the temporal window of the ERP component commonly thought to represent the electrophysiological signature of visual awareness, i.e., the Visual Awareness Negativity (VAN). Furthermore, Granger causality analysis, performed to further investigate the flow of activity occurring in the investigated areas, unveiled that neural processes relating to conscious perception mainly originated in LOC and subsequently spread towards visual and motor areas. In general, the results of the present study seem to advocate for an early contribution of LOC in conscious vision, thus suggesting that it could represent a reliable neural correlate of visual awareness. Conversely, striate visual areas, showing awareness-related activity only in later stages of stimulus processing, could be part of the cascade of neural events following awareness emergence.

1. Introduction

Most of the external information allowing the interaction with the surrounding environment comes from the visual system. For this reason, one of the most intriguing questions for cognitive neuroscience concerns the search for the neural mechanisms driving visual awareness. However, despite decades of effortful attempts, researchers are still debating about when visual awareness arises in the brain and which brain regions are directly involved in the formation of the conscious experience (Rees et al., 2002; Förster et al., 2020a).

A possible source of confounding might be due to the multifaceted nature of the concept of consciousness. Indeed, depending on how it is intended, the timing of its emergence and the brain regions engaged are found to be different. Since different subprocesses are involved in such a complex cognitive function, stressing one or another process can lead to different spatio-temporal dynamics being considered. In this respect, for instance, focusing on the entire process from the initial sensory visual

processing to the access, and report of conscious contents (Dehaene & Changeux, 2011) would result in a major role attributed to higher-order areas (mainly the prefrontal cortex) engaged at a late stage of processing as correlates of visual awareness. In EEG studies, this is exemplified by the major role attributed to a positive difference wave, the Late Positivity (LP, Sergent et al., 2005), occurring 300-500 ms after the presentation of the stimulus, i.e., in the time window of the P300 component, as a temporal correlate of awareness. Conversely, selectively focusing on the content-specific, perceptual, nature of awareness (Koch et al., 2016), also referred to as proper neural correlates of consciousness (Aru et al., 2012), would emphasize early components of the process localized in posterior brain areas and comprising temporal, occipital, and parietal cortices (Boly et al., 2017; Koivisto et al., 2018). Again, in EEG studies, this approach is documented by the main role attributed to another difference wave, the Visual Awareness Negativity (VAN), occurring earlier in the N2 temporal window (Förster et al., 2020b; Mazzi et al., 2020; Dembski et al., 2021).

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Of specific relevance to the present paper, the contribution of the different posterior brain regions remains to be elucidated, mainly for what concerns the involvement of the primary visual cortex (V1): although it is widely accepted that the primary visual cortex is necessary for normal vision, its specific role in consciousness is still unclear. On the one hand, hierarchical models (Rees et al., 2002) postulate that V1 is necessary for normal conscious vision because of its position along the flow of information. Thus, its role would be that of feeding information to higher-level areas directly involved in visual awareness (Mazzi et al., 2014; Bagattini et al., 2015). Accordingly, V1 is thought not to have a direct function in representing conscious visual information, in line with the proposal advanced by Crick & Koch in their seminal paper (1995) advocating V1 not being part of the proper correlates of awareness. On the other hand, interactive models (Lamme, 2006; Lamme & Roelfsema, 2000) postulate a central role in awareness of the interaction among visual areas. Specifically, feedback processing from higher-order areas to earlier areas, including V1, is considered crucial for awareness to emerge. According to this perspective, it is only during this recurrent processing from higher to lower brain areas that visual awareness for a stimulus can arise. By restricting our intervention to this latter debate, the experiments presented in this paper have been specifically devised to elucidate the role of striate and extra-striate visual areas in content-specific perceptual awareness.

Moreover, from the methodological point of view, another possible source of confounding comes from the techniques employed so far to investigate the NCCs, which can reach a high level of resolution only in one dimension (i.e., space or time), thus approaching the search for the neural bases of visual awareness only from the temporal or the spatial point of view, selectively. In this respect, fast optical imaging represents a very advantageous tool, as it integrates high-quality temporal and spatial information. Over recent years, a relatively novel approach known as Event-Related Optical Signal (EROS) or Fast Optical Signal (FOS) has begun to be employed to investigate brain functions (e.g. Toscano et al., 2018; Parisi et al., 2020). In contrast to the classical fNIRS methodology, which records the slow hemodynamic response occurring after the execution of a task, EROS technique allows the detection of fast changes in light scattering properties due to neuronal electrical activity (directly reflecting membrane potential changes), allowing a temporal resolution in the order of milliseconds. The main advantage of EROS technique is that it can combine this very high temporal resolution with a sub-centimeters spatial resolution (Gratton et al., 1995; Gratton & Fabiani, 2010; Baniqued et al., 2013), thus providing spatio-temporal information about brain functions (Gratton et al., 1997; Gratton & Fabiani, 1998, 2001).

In the present study, we, thus, capitalized on the advantage of EROS in resolving both the temporal and spatial dimensions of neural processing to disentangle the spatio-temporal neural dynamics underlying content-specific awareness. As our main aim was that of revealing the contribution of specific posterior brain areas to awareness emergence, EROS was recorded from occipital and left temporoparietal lobes. Moreover, as EROS connectivity analysis can also identify the predictive relationship between the different brain areas at different time-points, we sought of revealing not only which posterior brain areas are necessary for conscious content processing but also their order of activation.

2. Materials and methods

The study was composed of two identical experiments, differing only in the technique used to record brain activity: in the first experiment, we used Fast Optical Imaging to record the Event-Related Optical Signal (EROS), while in the second we recorded EEG signal.

2.1. Participants

A total of forty-one healthy adults (16 males, mean age \pm standard deviation: 23.5 ± 2.8) were recruited among the university community

and took part in EROS experiment. They all were right-handed and reported normal or corrected-to-normal vision and no history of neurological or psychiatric disorders. They gave their written informed consent before taking part in the experiment and all were naïve to the experimental hypothesis. All participants received compensation for their participation.

Data from participants reporting a proportion of awareness equal or superior to 75% were discarded in order to maintain an equal number of trials in both conditions (i.e., Aware and Unaware). Thus, the final sample for the EROS experiment was composed of twenty-four participants (10 males, mean age \pm standard deviation: 23.8 ± 3.2).

In order to test the same sample in both experiments, for the EEG experiment we recruited the same participants as EROS experiment. All but four accepted to take part in the EEG experiment, so a total of twenty participants were tested (8 males, mean age \pm standard deviation: 24.4 ± 3.5). Data from 4 participants were discarded because of behavioral reasons (awareness equal to or higher than 75%), so that the final sample was composed of sixteen participants (7 males, mean age \pm standard deviation: 24.7 ± 3.6). All of them gave new written informed consent before taking part in the experiment.

The studies were carried out according to the principles laid down in the 2013 Declaration of Helsinki and approved by the local Ethics Committee.

2.2. Stimuli

The stimuli were Gabor patches (diameter of 2°) created using a custom-made Matlab script (version R2017b; the MathWorks, Inc., Natick, MA).

As shown in Fig. 1B, Gabor patches could be horizontal (90° - catch trials) or with the right side of the stimulus tilted upwards (orientation $<90^\circ$) or downwards (orientation $>90^\circ$). Gabor patches were presented for 100 ms at an eccentricity of 3.5° from the fixation cross along the vertical meridian and 2° along the horizontal meridian, i.e., in the lower right quadrant of the screen. This was because the posterior portion of the left hemisphere is usually anatomically closer to the skull, compared to the right one, thus ensuring a better penetration of near-infrared light through brain tissues (Mullin & Steeves, 2011).

The orientation of the stimuli to be used in the experimental session for each participant was determined by means of a subjective perceptual threshold (see section 2.2.1).

2.2.1. Perceptual threshold assessment

Participants were tested in a dimly illuminated room, sitting in front of a 17 in. LCD monitor (resolution 1920×1080 , refresh rate of 144 Hz) placed at a viewing distance of 57 cm, with head laying on an adaptable chin rest with forehead support so that eyes could be aligned with the center of the screen.

The goal of the threshold assessment was to identify, for each participant, two stimuli (one tilted upward and one tilted downward) that the subject reported to perceive as tilted about 50% of the time. These stimuli were then used in the experimental task, together with the horizontal one (catch). The subjective perceptual threshold was measured using the method of constant stimuli, where Gabor patches with different degrees of inclination were randomly presented: six different degrees of inclination for stimuli tilted upwards (from the easiest to the most difficult: 87° , 87.5° , 88° , 88.5° , 89° , 89.5°) and six for stimuli tilted downwards (from the easiest to the most difficult: 93.5° , 93° , 92.5° , 92° , 91.5° , 91°). This range of stimuli inclinations was selected based on the results of a previous pilot experiment in which participants were presented with a wider range of tilts, and asked to perform the same task we employed in our perceptual threshold assessment. This was done to identify a smaller range of optimal inclinations to be tested (i.e., excluding the inclinations that participants never reported as perceived and the inclinations perceived 100% of time).

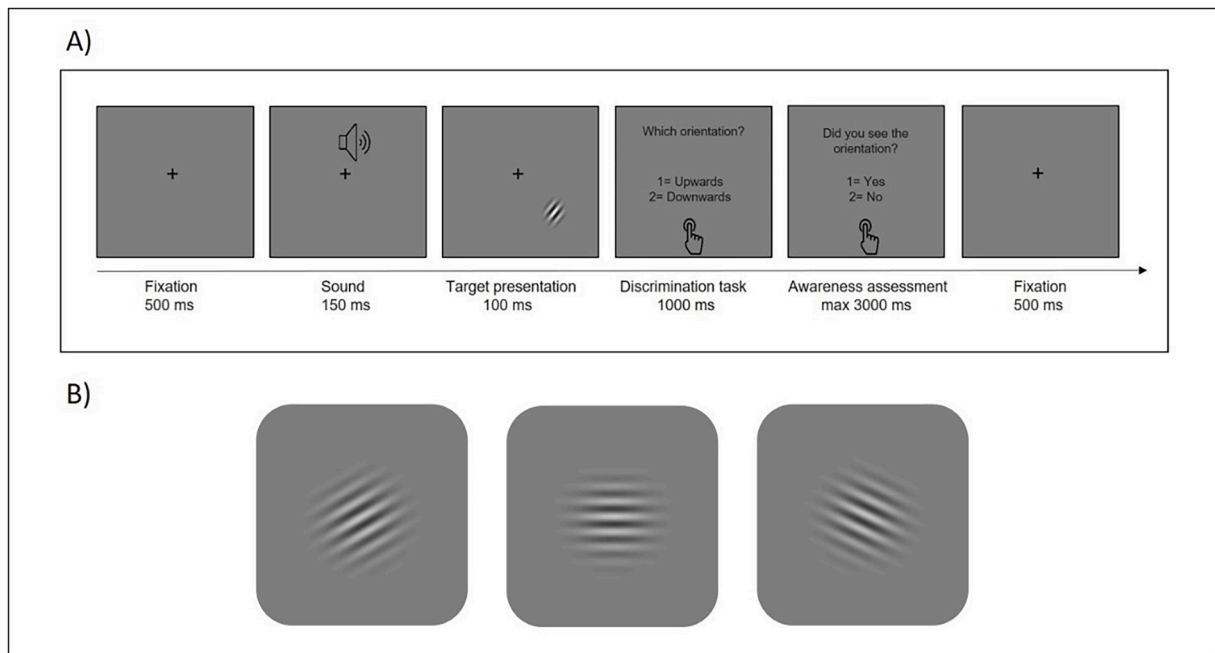


Fig. 1. Trial procedure and stimuli. A) Experimental procedure: a central fixation cross was presented for 500 ms, followed by a warning acoustic tone lasting 150 ms. Then, the stimulus was presented for 100 ms and participants were asked to discriminate its inclination (Discrimination task) and then to report whether they had seen it or not (Awareness assessment). B) Stimuli: stimuli were Gabor patches which could be slightly tilted upward or downward with respect to the horizontal plane, referring to the right side of the stimulus. Importantly, stimuli were always clearly visible, while their inclination was manipulated to result at perceptual threshold level.

Importantly, all the stimuli, as well as the catch stimulus (90°), were always clearly visible while only their tilt was manipulated. The aim of the perceptual threshold assessment, indeed, was to identify the inclination that the participant could discriminate from the horizontal one 50% of the time.

Both the tilted stimuli and the catch stimuli were presented 30 times each.

The task was the same as that of the main experiment and it consisted of a 2-alternative forced-choice inclination discrimination task, followed by the assessment of the perceptual awareness (2-alternatives “YES-NO” response).

2.3. Experimental procedure

Before taking part in the study, participants underwent magnetic resonance imaging (MRI), in order to obtain structural images of the brain to be subsequently co-registered with optical data (see below for more detailed information).

The EROS experiment was composed of two identical sessions performed on the same day, one after the other, preceded by the assessment of the subjective perceptual threshold. Each session was divided into 10 blocks of 60 trials each, thus providing a total of 1200 trials per subject. The two sessions were identical except for the EROS montages specifically devised to obtain better coverage of the brain areas of interest (see below for more detailed information).

The EEG experiment consisted of a single session (600 trials per participant), before which the subjective perceptual threshold was assessed. To verify that fixation was maintained during the task, on-line monitoring of the eye movements was performed by an infrared camera.

The experimental paradigm is shown in Fig. 1A. The task was a 2-alternative forced-choice discrimination task in which participants had to discriminate the inclination of a Gabor patch, followed by the assessment of the awareness by means of a question appearing on the screen. Each trial began with the presentation of a central black fixation cross, followed 500 ms later by a sound presented for 150 ms, notifying

participants of the onset of the stimulus. The absence of a delay between the sound and the stimulus could potentially represent a limitation, as sound-related activity could affect subsequent visual processing. However, since the sound is present in both conditions, by contrasting them one against the other, the auditory activity should not differently affect awareness-related processes.

As the stimulus appeared, participants had to discriminate as fast and as accurately as possible its inclination, by pressing one of two buttons of a response box (one if perceived upwards and another one if perceived downwards), while maintaining the gaze on the central fixation cross throughout the block (in case of catch trials, i.e., a horizontal stimulus, participants were instructed to answer by choosing randomly one of the two buttons). After that, participants were asked to report whether they had seen or not the tilt of the stimulus, by answering a question with the same response box.

The question persisted on the screen until the participant answered. Participants could rest during inter-block intervals and could initiate the next block by pressing a key.

The experiment was programmed and administered using E-Prime 2.0 software (E-Prime Psychology Software Tools Inc., Pittsburgh, PA, USA).

Experimental paradigm was the same for both EROS and EEG experiment.

2.4. Data collection

2.4.1. Optical recording

Brain activity of each participant was recorded throughout the experiment, concurrently with behavioral data acquisition, by using two synchronized Imagent frequency domain systems (ISS, Inc., Champaign, IL). Continuous fast optical data were collected using the ISS Corporation “Boxy” program. Near-infrared light (830 nm) was carried to the scalp by means of 32 light emitters (laser diodes).

Light was modulated at 110 MHz and multiplexed through the sets of sources every 25.6 ms, resulting in a sampling rate of 39.0625 Hz. Light

that scattered through the head and returned to the scalp surface was detected by eight 3-mm fiber-optic bundles connected to photomultiplier tubes. Fast Fourier transforms were applied to the current reaching the photomultiplier tubes in order to compute three measures: DC intensity (i.e., Direct Current, the mean amount of light detected), amplitude (i.e., Alternating Current, the amplitude of light modulation) and phase delay, that is changes in the transit time of light. Since in this study we were interested in the fast-optical signal, we analyzed only changes in phase delay data, converted into picoseconds delay.

Both light emitters and detectors were held in place using a custom-built helmet. To minimize interferences, before placing the optical fibers on the head, the hair was moved so that the fibers could reach the scalp. Two helmets of different sizes were available in order to better adhere to the head of the participant: one 55-56 cm large, usually used for women, and one 57-58 cm large. For each helmet, two different montages (i.e., the combination of light sources and detectors) were developed, so that to provide dense coverage of the regions of interest (Fig. 2A shows the brain regions covered by the montages). The two montages were slightly different, but they covered the same brain areas, namely the occipital and the left temporal and fronto-parietal cortices, showed in Fig. 2A.

Because of the high number of optical fibers to place, EROS montages were created using a specific program (NOMAD, Near-Infrared Optode Montage Automated Design) implemented in Matlab, useful to place sources and detectors at optimal distances (minimal distance 17.5 and maximum distance 50 mm, (Gratton et al., 2000)) while avoiding cross-talks between channels. Thus, each montage was to permit each of the 8 detectors to detect light from up to 16 sources, providing a total of 128 potential channels per session. In order to record an adequate EROS from the brain areas of interest, data from the two montages were acquired for each participant. As mentioned before, the experiment was divided into 2 sessions, that were identical except for the EROS montage. Indeed, each montage was recorded in a separate session and the order was counterbalanced across participants.

After finishing the EROS sessions, the location on the scalp of each source and detector, as well as the remaining scalp locations, in relation to the nasion and fiducial points (both crus of helix) were digitized with a neuro-navigation software (SofTactic, E.M.S., Bologna, Italy) combined with a 3D optical digitizer (Polaris Vicra, NDI, Waterloo, Canada). Successively, such digitized scalp locations were co-registered with the individual MRI of each subject using a dedicated software package (OCP, Optimized Co-registration Package, MATLAB code) developed by Chiarelli and colleagues (Chiarelli et al., 2015).

As mentioned above, before taking part in the experiment, participants underwent a structural MRI, which took place at the Borgo Roma Hospital in Verona, by means of a 1.5 Tesla Philips scanner with a standard 15-channel head coil. A whole brain high-resolution 3D T1-weighted image with magnetization-prepared rapid acquisition gradient echo (MPRAGE) was acquired. The acquisition parameters were the following: phase encoding direction= anterior to posterior,

voxel size= $0.5 \times 0.5 \times 1$ mm, Repetition Time= 7.7 ms, Echo Time= 3.5 ms, field of view= 250×250 mm, flip angle= 8° .

2.4.2. EEG recording

The EEG activity was continuously recorded through a BrainAmp system (Brain Products GmbH, Munich, Germany–Brain Vision Recorder) provided with 59 Ag/AgCl electrodes mounted on an elastic cap (EasyCap, GmbH, Herrshing, Germany), placed according to the 10-10 International System. Four additional electrodes placed at the left and right canthi and above and below the right eye were used for monitoring blinks and eye movements. Signal was referenced online to the right mastoid (RM), and electrode AFz served as ground. Data were recorded at a sampling rate of 1000Hz and the impedance of all the electrodes was kept below 5 K Ω .

2.5. Data analysis

2.5.1. Behavioral data

For both experiments, only tilted stimuli were included in both behavioral and functional analyses. Raw data were processed by means of scripts created on Matlab (version R2017b; the MathWorks, Inc., Natick, MA). According to the subjective awareness report, trials were sorted into the two experimental conditions (i.e., Aware and Unaware condition). For each participant, trials with no response as well as trials with reaction times lower than 150 ms and higher than 3 standard deviations were excluded from the analysis. Data were successively analyzed with IBM SPSS Statistics for Windows, version 22: paired sample t-tests (two-tailed) were applied to compare the behavioral performance (i.e., the Accuracy) and the mean reaction times (RTs) between Aware and Unaware conditions.

2.5.2. EROS data

Continuous optical data were pre-processed using a dedicated in-house software, P-POD (Pre-Processing of Optical Data, run in MATLAB, version R2013b). A full and detailed description of the pre-processing procedure is in depth described in Parisi et al. (2020). The pre-processing steps included a) normalization of data, in which data were corrected for phase wrapping, de-trended to remove low-frequency drifts and baseline corrected; b) pulse correction, i.e., heart beats artifacts removal by using a regression algorithm (Gratton & Corballis, 1995); c) filtering of data by means of a band-pass filter which allows frequencies between 0.5 Hz and 15 Hz. After that, data were segmented into epochs time-locked to the onset of the stimulus and averaged separately for each subject, condition, and channel. Each epoch comprised a period from 486 ms before the stimulus onset to 998 ms following the stimulus onset, resulting in an epoch lasting 1484 ms. Statistical analyses on functional data were then computed on averaged data with an in-house software package (Opt-3d; (Gratton et al., 2000)), which allowed to analyze and graphically display the fast optical signal.

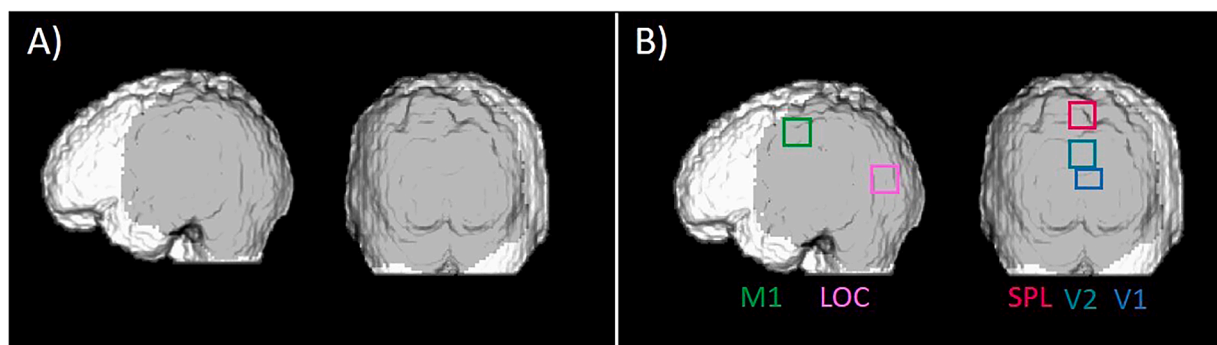


Fig. 2. Covered area and ROIs. A) The gray area represents the area covered by the montages. B) Colored squares represent the selected ROIs for EROS and Granger analyses. Their coordinates are reported in Table 1.

To compute statistics, data from channels whose diffusion paths (bananas) intersected a given voxel were combined (Wolf et al., 2014). Phase delay data were spatially filtered with an 8-mm Gaussian kernel. One-tailed paired t-tests were performed across subjects for each voxel, converted into Z-scores and corrected for multiple comparisons using random field theory (Worsley et al., 1995; Kiebel et al., 1999). Subsequently, Z-scores were weighted and orthogonally projected onto the lateral surface of a MNI template brain, according to the physical homogenous model (Arridge & Schweiger, 1995; Gratton, 2000).

Since Regions of Interest (ROIs) should be necessarily selected in order to perform statistical analyses, they are shown in Fig. 2B and their coordinates are listed in Table 1. ROIs were identified among those areas responsible for visual processing and motor execution. Thus, we selected as ROIs the primary visual cortex (V1), the secondary visual cortex (V2), the lateral occipital complex (LOC), the superior parietal lobe (SPL), and the primary motor cortex (M1). As the EROS data were projected on the surface of the brain, ROIs were defined by a 2-dimensional box-shaped structure: depending on the visualization of the data (coronal or sagittal) y or x coordinates are missing, respectively. In order to better define ROIs boundaries and to avoid the overlapping of different ROIs, we referred to the Bioimage Suite Web tool (<https://bioimagesuiteweb.github.io/webapp/mni2tal.html>). The same tool was also used to estimate the Brodmann's areas encompassed by each ROI.

2.5.3. EEG data

The analysis of EEG data was performed with MATLAB (version R2020b; the MathWorks, Inc., Natick, MA) scripts created ad-hoc based on functions from the EEGLAB toolbox (v2020.0, Delorme & Makeig, 2004). The EEG signal was first resampled to 250 Hz. Continuous raw data were filtered offline using zero-phase Hamming windowed sinc FIR high-pass and low-pass filters (cut-off frequencies: 0.1 and 90 Hz, transition bandwidth: 0.2 and 20 Hz). To remove line noise, a notch filter (cut-off frequencies: 49.5 and 50.5 Hz, transition bandwidth: 1 Hz) was applied. After that, channels with bad signal were identified and removed by means of the *clean_channels* EEGLAB function, using a correlation threshold of .5 (mean number of channels removed across participants: 1.25).

To submit a clean dataset to the independent component analysis (ICA) algorithm and to facilitate the recognition and removal of artifacts, we created a temporary dataset to which a different pre-processing had been applied (Winkler et al., 2015). Specifically, the following pre-processing steps were implemented: a) a high-pass filter at 1 Hz (cut-off frequency: 0.5 Hz, transition bandwidth: 1 Hz) was applied; b) data were segmented into epochs ranging from -1150 to 1250 ms with respect to the stimulus onset; c) artifactual epochs were detected and removed by means of improbability and kurtosis criteria ($SD > 5$ for local threshold and $SD > 3$ for global threshold).

After these steps, ICA was computed through the FastICA algorithm (Hyvärinen, 1999) on this temporary dataset, in order to correct for blinks, eye movements and muscular activity based on scalp topography, evoked time course and spectral distribution. The solution of the ICA was then applied to the original dataset (the one with the removed

bad channels and already segmented into epochs from -1150 ms to 1250 ms).

Data were subsequently low-pass filtered at 40 Hz (cut-off frequency: 45 Hz, transition bandwidth: 10 Hz) and removed channels were interpolated using a spherical spline method (Perrin et al., 1989). All scalp channels were then offline re-referenced to the linked mastoids (RM-LM) and baseline correction was applied from -450 ms to -150 ms before the stimulus onset.

Only trials with RTs > 150 ms and < 3 SD were included in further analysis. Subsequently, we applied an automatic procedure to detect artifactual epochs based on extreme values ($\pm 125 \mu\text{V}$), abnormal trend in data (maximal slope allowed = $50 \mu\text{V}/\text{epoch}$ and minimal R2 allowed = .3), and improbability and kurtosis criteria ($SD > 5$ for local threshold and $SD > 3$ for global threshold). This procedure was carried out together with the Trial by Trial (TBT) plugin of EEGLAB, that allows to automatically reject and interpolate channels on an epoch-by-epoch basis. In particular, an epoch was removed if it had more than 6 bad channels, otherwise channels were interpolated.

Finally, the resulting epochs were sorted into the two experimental conditions, Aware and Unaware (average epochs included: 268.5 and 204, respectively), and statistical analyses were applied. ERP waveforms were averaged separately for the two conditions and paired-sample t-tests (two-tailed) were computed on all time points and electrodes between aware and unaware conditions.

Finally, data were thresholded using temporal clustering and only clusters of activity lasting longer than 30 ms were taken into account.

3. Results

Participants were asked to discriminate the inclination of a Gabor patch that was presented for 100 ms in the lower right quadrant of the screen and subsequently to report whether they had seen or not such inclination (Fig. 1A). The tilt of the stimulus was determined for each participant by means of a subjective perceptual threshold, so as to be visible only 50% of the times. This allowed us to manipulate the subjective awareness of participants by keeping constant the physical characteristics of the stimulus and sorting trials into Aware and Unaware.

3.1. Behavioral results

Behavioral results are depicted in Fig. 3. In both experiments, we calculated: i) the percentage of Awareness (i.e., the percentage of trials in which participants reported to see the tilt of a tilted stimulus), ii) the percentage of Accuracy (i.e., the percentage of trials in which participants could correctly discriminate the inclination of the stimulus) and iii) the mean Reaction Times at the Discrimination task (i.e., with respect to the stimulus onset). In EROS experiment, Aware trials represented on average 60.00% of the trials. Paired sample (two-tailed) t-tests revealed, as expected, that the Accuracy was significantly greater for Aware trials ($M = 90.55\%$) than Unaware trials ($M = 45.07\%$; $t(23) = 15.689$, $p < 0.001$, Cohen's $d = 3.20$, 95%, CI [2.19, 4.2]), suggesting that in the Aware condition participants could properly discriminate the tilt of the stimulus. Conversely, mean RTs for Aware (565.11 ms) and Unaware condition (568.86 ms) were not statistically different ($t(23) = -.480$, $p = .636$, Cohen's $d = .098$, 95%, CI [-.498, .304]), indicating that there was no difference in the responsiveness between the two conditions. Similarly, behavioral results of EEG experiment followed the same trend. Aware trials represented on average 57.06% of the trials. Also in this case, Accuracy for Aware trials ($M = 87.76\%$) was significantly greater than Unaware trials ($M = 55.05\%$; $t_{(15)} = 13.360$, $p < 0.001$, Cohen's $d = 3.34$, 95%, CI [2.05, 4.61]) and the paired sample (two-tailed) t-test did not reach the statistical significance ($t_{(15)} = -1.152$, $p = .267$, Cohen's $d = -.288$, 95%, CI [-.784, .217]) when comparing mean RTs of Aware trials (595.87 ms) with mean RTs of Unaware trials (603.87 ms).

Table 1
MNI coordinates of selected ROIs.

	Projection	Coordinates			Involved BA
M1	Sagittal	y =	-29	-9	4
		z =	38	58	
LOC	Sagittal	y =	-86	-66	19
		z =	4	24	
SPL	Coronal	x =	-10	10	7
		z =	46	66	
V1	Coronal	x =	-2	16	17
		z =	4	18	
V2	Coronal	x =	-10	10	18
		z =	18	35	

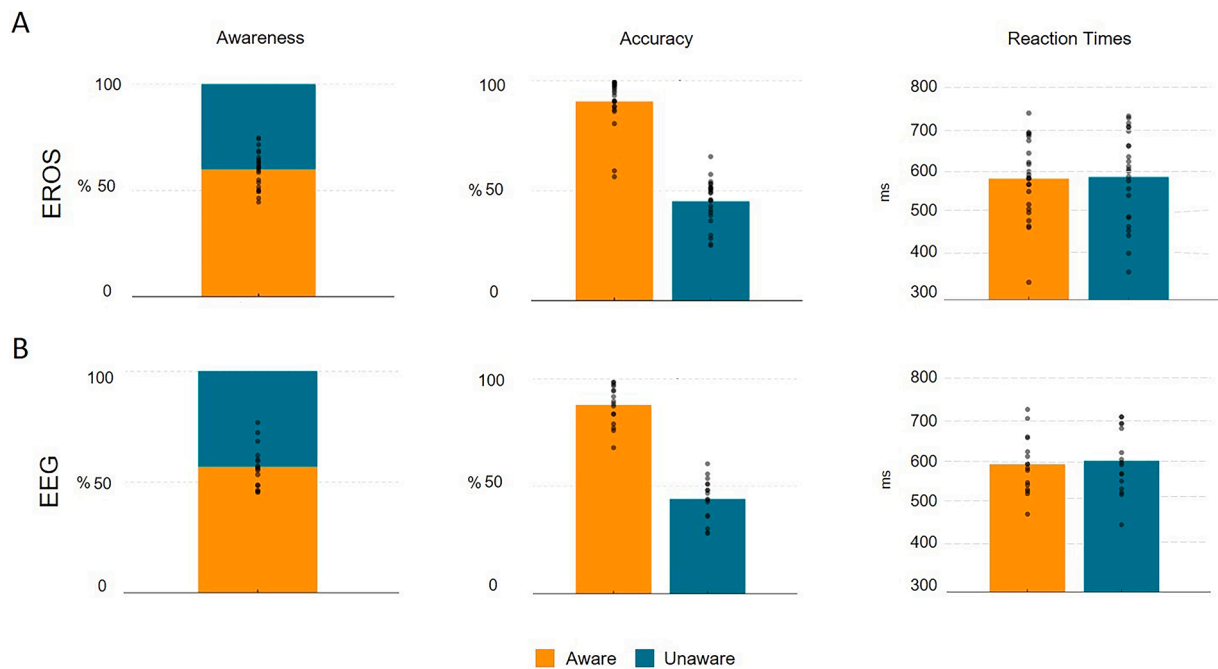


Fig. 3. Behavioral results. In both EROS (A) and EEG (B) experiments, we calculated: i) the percentage of Awareness (i.e., the percentage of trials in which participants reported to see the tilt of the stimulus), ii) the percentage of Accuracy (i.e., the percentage of trials in which participants could correctly discriminate the inclination of the stimulus) and iii) the mean Reaction Times at the discrimination task (i.e., with respect to the stimulus onset). The results refer to the participant's inclination discrimination performance under the reported awareness conditions. Black dots represent individual data.

3.2. Functional results

3.2.1. The role of extra-striate areas in visual awareness

In order to highlight the spatio-temporal dynamics underlying aware vision, neural activity occurring in Aware trials was contrasted with neural activity occurring during Unaware trials. Overall, it emerged that extra-striate visual areas seem to play a dominant role in the emergence of a conscious visual percept. Indeed, in line with previous ERPs studies, contrasting Aware and Unaware trials elicited a significant VAN occurring at posterior electrodes in a time window ranging from 156 to 424 ms after the stimulus onset (Fig. 4A). Interestingly, EROS analyses (Fig. 4B and Figure S1) revealed that in such temporal window, greater activity was observed in the Lateral Occipital Complex (LOC), an extra-striate area known to be involved in object recognition (Grill-Spector et al., 2001; Grill-Spector, 2003). Indeed, the Lateral Occipital Complex is implicated in the identification of objects with clear shapes and its damage leads to a variety of recognition deficits, such as visual object agnosia (James et al., 2003). The sustained and recurrent activity shown by this area reflects the conscious identification of the stimulus, as also suggested by the high accuracy reported by participants at the behavioral level (Fig. 3A). In addition, Granger causality analysis (Fig. 5) unveiled that neural processes relating to conscious perception principally originated in LOC and subsequently spread towards visual and motor areas.

3.2.2. The role of the primary visual cortex in visual awareness

EROS analysis revealed that the primary visual cortex seems not to be crucially involved in the early stages of conscious vision. The contrastive analysis between Aware and Unaware conditions highlighted indeed that differential activity in V1 was observed at later time windows of visual processing, specifically 460 and 486 ms after the stimulus onset. Although the advantage of contrastive analysis is precisely to dissociate the neural processing characterizing one experimental condition (i.e., the Aware condition) from confounding neural processes that take place in both conditions (Aru et al., 2012), one could argue that activity in V1 was not observed earlier because it was too

weak to be detected. Thus, in order to disentangle this ambiguity and to verify that early activity in V1 was elicited both from Aware and Unaware trials, we analyzed the evolution of the optical signal within the primary visual cortex ROI. We thus contrasted activity elicited by all trials (Aware and Unaware together) with the baseline. As shown in Fig. 6B (and Figure S2), such activity in V1 resulted to be significant at early stages of stimulus processing (i.e., 51 ms after the stimulus onset. $z = 2.68$; $z_{crit} = 2.21$) and later on (i.e., 255 ms after the presentation of the stimulus. $z = 2.46$; $z_{crit} = 2.45$). The fact that contrastive analysis between Aware and Unaware trials did not show any difference in V1 at these early stages, would imply that the primary visual cortex does not directly enable the entrance of the stimulus in consciousness, but it is rather involved in visual processing that takes place in both conditions (Hurme et al., 2017).

3.2.3. The involvement of motor areas in visual awareness

A result as interesting as novel concerns the involvement of motor areas when the visual stimulus enters the consciousness. As revealed by EROS analysis (Fig. 6A), greater activity in the primary motor cortex (M1) was observed 537 ms after the stimulus onset, a timing compatible with the response reaction time (RT) (i.e., mean RT for Aware trials = 565.11 ms; mean RT for Unaware trials = 568.86 ms). It is noteworthy that the motor response was required both when participants had seen the tilt of the stimulus, and in case they had not discriminated it. Thus, one should expect that the neural activity related to the preparation and the execution of the motor response should not emerge when contrasting the two conditions. Furthermore, Granger analysis revealed that such activity in motor areas was triggered by activity in LOC. Indeed, activity in LOC predicted later activity in motor and pre-motor areas (Fig. 5), probably reflecting the motor preparation and the consequent execution of the conscious response.

In the figure, each row represents a significant predictive link between the respective brain regions.

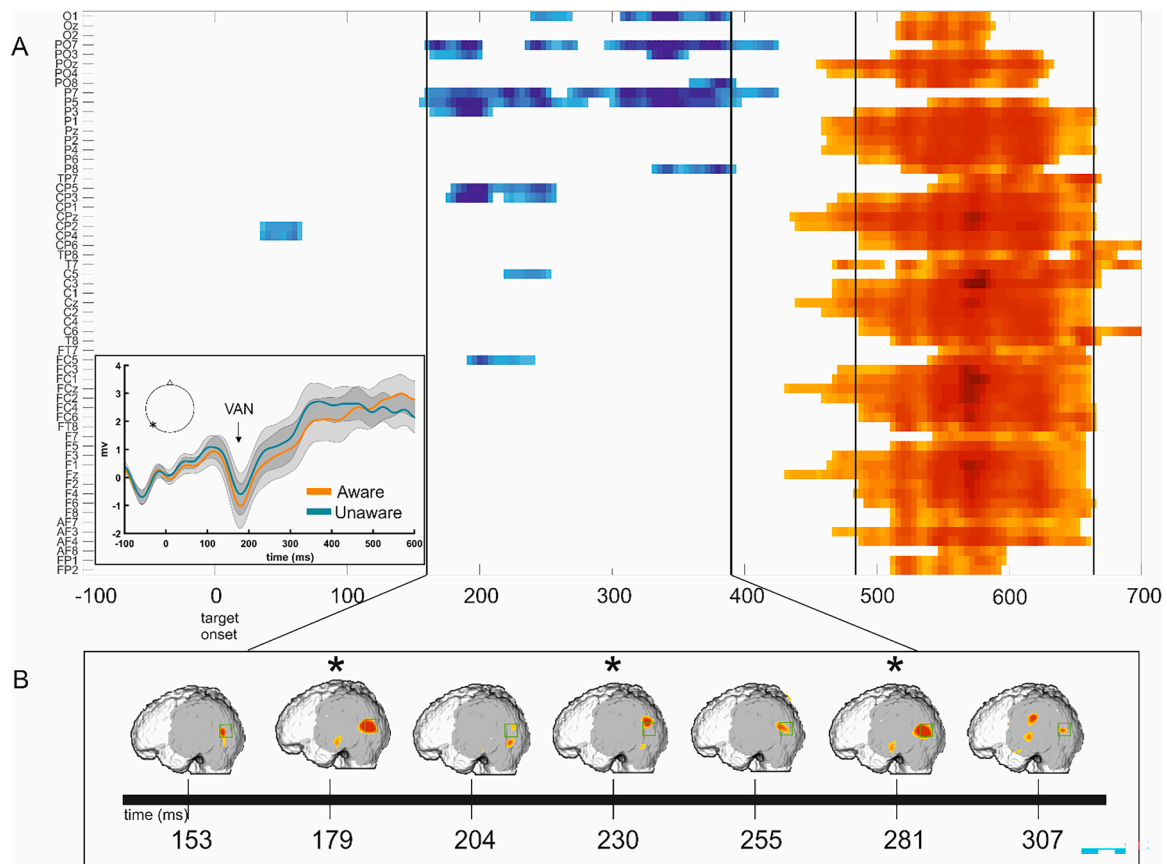


Fig. 4. EEG and EROS results. A) Raster plot representing results from a paired t-test between Aware and Unaware conditions. Data were thresholded using temporal clustering where only clusters of activity lasting longer than 30 ms were taken into account. More in detail, VAN (blue) resulted to be significant in electrode O1 between 240 and 268 ms and between 308 and 338 ms, in electrode PO7 between 160 and 200 ms, between 236 and 272 ms and between 296 and 424 ms. In electrode PO8, VAN resulted to be significant from 360 to 392 ms, in electrode P7 from 160 to 252 ms and from 268 to 424 ms, and in electrode P5 from 156 to 280 ms and from 300 to 396 ms. Moreover, electrodes P8 and CP5 showed significant VAN, respectively between 332 and 392 ms and between 180 and 256 ms. Finally, VAN was significant also in electrode CP3 between 176 and 208 ms and between 220 and 256 ms, in electrode C5 between 220 and 252 ms and in electrode FC5 between 192 and 240 ms. LP resulted to be significant in all electrodes (except for C6 electrode) in a temporal window ranging from 484 and 664 ms (represented in orange). The inset in the lower-left part of the raster plot shows the ERPs computed for Aware and Unaware conditions at channel P7 (marked with a black star) to represent the VAN. B) EROS results obtained contrasting Aware and Unaware conditions in the temporal window of VAN. Images with the star represent significant statistical parametric maps of the z-score difference computed between Aware and Unaware trials in the selected ROI (green box). Other maps represent marginally-significant effects.

4. Discussion

The present study sought to shed further light on the neural mechanisms underlying conscious visual processing by disentangling the spatio-temporal dynamics occurring when a stimulus enters the consciousness, i.e., mainly focusing on the early phases of visual processing. To do so, we adopted a combined approach in which participants' brain activity was recorded during the performance of a discrimination task by means of EEG and EROS techniques in separate sessions. The advantage of this approach was twofold: EEG allowed to investigate the electrophysiological correlates of visual awareness and to determine their exact timing, and EROS allowed to disentangle which brain regions and in what order were involved when the stimulus was reported as "seen". Importantly, EROS technique, by measuring the fast optical signal directly related to neuronal electrical activity, provided the remarkable advantage of combining both high spatial and high temporal resolution, thus making possible to investigate both the neural correlates and the timing of conscious perception.

In general, our results advocate for a pivotal role of extra-striate areas, specifically LOC, in the conscious perception of a visual stimulus, in line with previous fMRI (e.g. Tong et al., 1998; Grill-Spector et al., 2000) and intra-cranial recording studies (e.g. (Fisch et al., 2009;

Malach, 2021). Indeed, as suggested by EROS results, LOC is crucially and directly involved in the formation of a conscious visual experience since its activity resulted to be significantly greater for Aware trials when contrasted with Unaware ones. Furthermore, the fact that this significant activity was observed at an early time window, specifically that of VAN, suggests not only that LOC plays a crucial role in the conscious perception of a visual stimulus, but also that this specific area could serve as a proper correlate of visual awareness. This is consistent with previous MEG source localization studies (Vanni et al., 1996; Liu et al., 2012) that identified LOC as the cortical generator of VAN. Moreover, as highlighted by Granger causality results, it is interesting to note that the sustained activity in LOC was predictive of later activity in striate and extra-striate visual areas as well as activity in motor areas. Granger causality, when applied to EROS data, is a very powerful tool since it allows to explore the predictive interaction between different brain areas at different time-points (Roebroeck et al., 2005). However, a note of caution should be considered as far as the generalizability of the claimed prominent role of LOC in the emergence of awareness. Indeed, it could be surmised that other extra-striate areas responsible for feature integration, such as for instance FFA or PPA (Tong et al., 1998), or even single feature-selective extra-striate areas (i.e. hMT+), could also be considered as specialized hubs for the emergence of content-specific

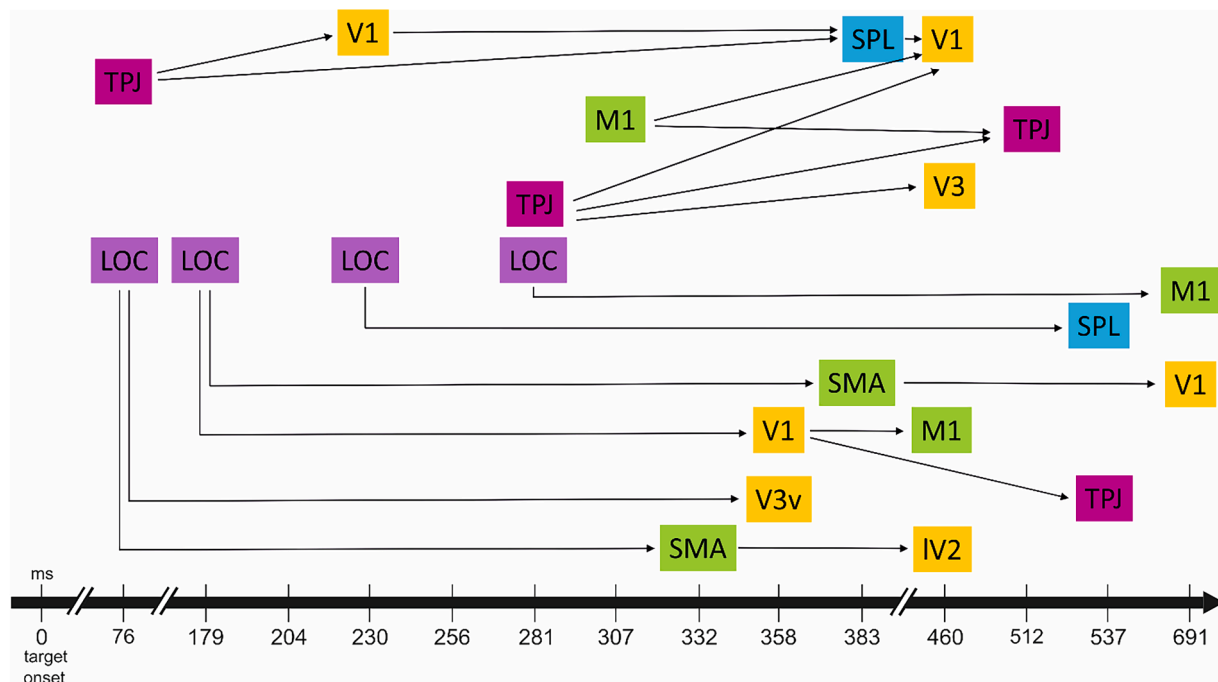


Fig. 5. Granger causality results in Aware versus Unaware contrast. G-causality allows to unveil the predictive interaction between activity in different brain areas at different time-points, thus revealing patterns of activation not highlighted by conventional EROS analyses. For this analysis, ROIs whose activity resulted significant in EROS analysis (see Table 1 in Methods) were used as seeds, as well as ROIs whose activity was predicted by G-causality analysis, specifically: TPJ: temporoparietal junction; SMA: supplementary motor area; V3: third visual cortex; V3v: ventral third visual cortex; IV2: left secondary visual cortex. The coordinates of ROIs employed for Granger analysis are listed in Table S1 and ROIs location are visualized in Figures 2B and S3.

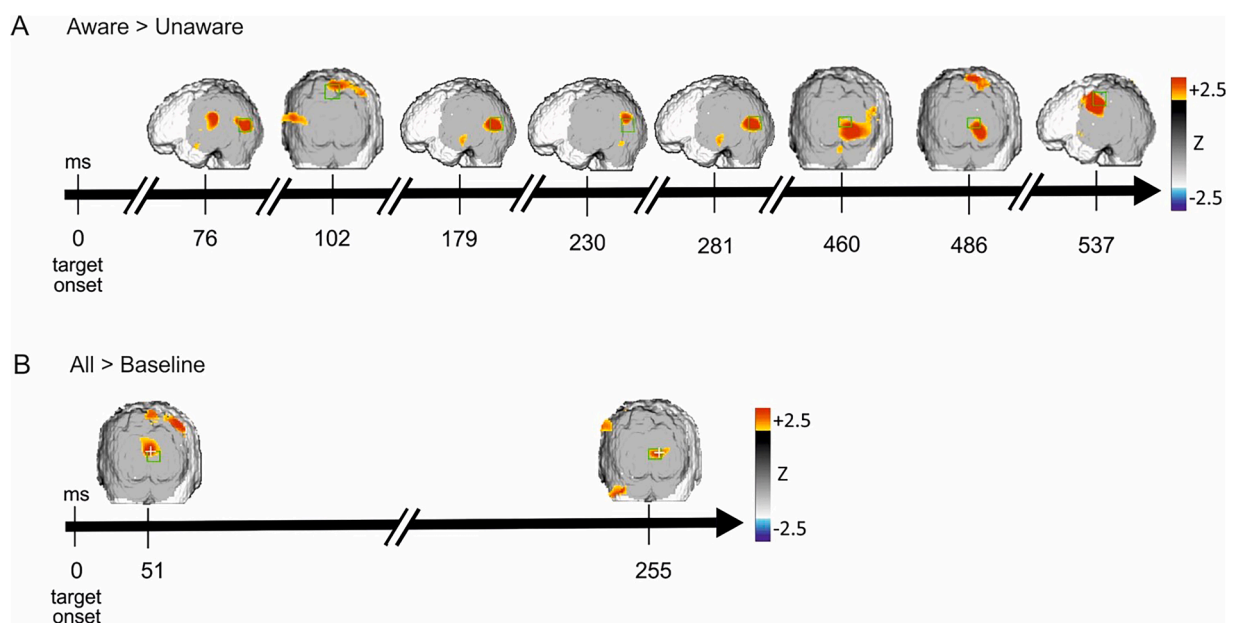


Fig. 6. EROS results. A) Aware > Unaware contrast: EROS results obtained contrasting Aware and Unaware conditions within the selected ROIs (green boxes). Each map represents a 25.6 ms interval. Aware vs Unaware contrast showed a significant increase of activation 76 ms after the presentation of the stimulus in the lateral occipital complex (LOC) ($z = 3.05$; z crit = 2.71), followed by increased activity in the superior parietal lobule (SPL) at 102 ms ($z = 2.60$; z crit = 2.22) probably reflecting top-down processes of allocation of attention towards the attended stimulus. Subsequently, LOC revealed greater activation in a time window ranging from 153 to 307 ms. Specifically, activity reached the statistical significance at 179 ms ($z = 2.54$; z crit = 2.53), 230 ms ($z = 2.72$; z crit = 2.66) and 281 ms ($z = 3.26$; z crit = 2.50). Later on, activity in LOC was followed by significant activity in the primary visual cortex (V1) at 460 ms ($z = 2.75$; z crit = 2.32) and 486 ms ($z = 2.73$; z crit = 2.36), which in turn was followed by greater activity in the primary motor cortex ($z = 3.25$; z crit = 2.63) at 537 ms. Extra-striate area V2 did not show any significant result. B) All > Baseline contrast: EROS results obtained contrasting all trials (aware and unaware together) with the baseline within V1 ROI (green box). This contrast allows to observe that activity in V1 resulted to be significant both at early stages of stimulus processing (i.e., 51 ms after the stimulus onset. $z = 2.68$; z crit = 2.21) and later on (i.e., 255 ms after the presentation of the stimulus. $z = 2.46$; z crit = 2.45).

aware experiences. This possibility would be in line with the proposal of Zeki & Ffytche (1998) about the existence of multiple “micro-consciousnesses”, with single high-order extra-striate areas being responsible for coding content-specific aware experiences of a feature, or the integration of features into meaningful percepts. Conversely, LOC could represent an over-ordinated area (Decramer et al., 2019) being responsible for the generation of the conscious experience of meaningful percepts in general, as suggested by the present results. This hypothesis would be in accord with findings highlighting that activity in LOC correlates not only with the recognition of object categories but also with object exemplar identity (Eger et al., 2008) or location (Cichy et al., 2011). At the same time, LOC has been found to be activated by perceptual grouping of elements (Fang et al., 2008), from simple salient regions and illusory contours (Stanley & Rubin, 2003) to complex objects like faces (Nagy et al., 2012) or bodies (Solanas et al., 2024). Interestingly, in this latter study, the magnitude of the elicited activity in LOC was found to gradually increase with the increase in the clarity of the perceptual experience (Mazzi et al., 2016; Tagliabue et al., 2016), thus showing strong evidence of a link between this area and the quality of content-specific perceptual awareness. Future studies should further investigate these possibilities to disentangle the role of specific extra-striate areas in the generation of awareness.

Nevertheless, our findings can help in shedding light on the controversial issue regarding the role of the primary visual cortex in visual awareness (Tong, 2003; Ffytche & Zeki, 2011; Martinelli et al., 2020). Indeed, theories that argue for a central role of V1 in conscious vision (Lamme & Roelfsema, 2000; Lamme et al., 2000) claim that feedback activity in this area is responsible for the emergence of conscious vision. According to this perspective, during feedforward processing (around 60ms in V1), activity should be equal for seen vs. unseen stimuli, and only later in time, after feedback to V1 (around 100-200ms) differences between seen vs. unseen stimuli should appear. In contrast, our EROS results, obtained contrasting Aware and Unaware conditions, highlighted that a differential activity in V1 occurred only at later stages of visual processing (i.e., 460-486 ms after the onset of the stimulus), suggesting that this brain region is not crucially involved in the formation of a conscious visual experience. Importantly, this result is in line with previous literature, claiming that V1 per se is not sufficient to give rise to a conscious visual percept (Rees et al., 2002; Mazzi et al., 2014; Koch et al., 2016; Ffytche & Zeki et al., 2011), despite being certainly part of the neural networks supporting the flow of information associated with awareness. This idea is also corroborated by the EROS analysis computed contrasting the activity elicited by all trials, regardless of the participants' awareness (Fig. 6B), with the baseline. This analysis, indeed, revealed that V1 shows both early (51 ms) and later (255 ms) activation in response to visual stimulation. Importantly, this early activity was not observed when contrasting the two conditions (Fig. 6A), thus implying that the primary visual cortex does not contribute to the emergence of awareness, despite being involved in the visual processing in general.

In addition, Granger analysis showed that late activity in V1 was predicted by earlier activity in LOC. This finding is of particular interest since it further corroborates the idea that this extra-striate area could constitute the neural correlate that underlies the content of consciousness: according to our EROS results, LOC seems to represent the very first node of the functional circuit that underlies conscious vision.

Another interesting aspect highlighted by Granger analysis is that early activity in LOC was predictive also of later activity in motor areas. Motor areas are responsible both for the motor response and for the preparation of the response. Specifically, the supplementary motor area (SMA) and the pre-motor areas are known to play an important role in the internal preparation of the movement (Cunnington et al., 2002) while primary motor cortex is involved both in the preparation and in the execution of the motor response (Richter et al., 1997). In our study, participants were asked to respond by pressing a button on a response box even if they could not see the inclination of the stimulus, therefore

motor preparation and response were present in both the experimental conditions. For this reason, if awareness has no role in these processes, one should expect that when contrasting Aware and Unaware trials, common neural processes shared by both conditions would cancel each other out. Conversely, EROS results showed that Aware trials elicited a significant increase of activity in motor areas if compared to Unaware trials. Moreover, Granger analysis revealed that activity in motor areas was predicted by earlier activity occurring in LOC, exclusively for Aware condition. This increased activity in motor areas selectively occurring in the Aware condition could be due to the fact that when the stimulus was seen, a specific answer had to be given (i.e., a specific finger had to be moved in order to press the correct button), while when the stimulus was unseen, participants were asked to respond randomly, by pressing indifferently one of the two buttons on the response box. Thus, in the Aware condition the motor response was goal-driven and triggered by awareness, while in the Unaware condition motor response was merely an aimless movement.

Taken together, the results presented here show that when a stimulus enters the consciousness it elicits a sustained activation in LOC, if compared to when the same stimulus does not reach awareness. Granger causality results highlighted also that activity in LOC predicted activity both in striate and extra-striate areas and in motor areas. Moreover, the fact that the temporal resolution of EROS and EEG is comparable (Gratton & Fabiani, 2010), allowed us to efficiently combine EROS and EEG results, unveiling that the sustained activation in LOC occurs in the temporal window of VAN, which is considered the electrophysiological signature of visual awareness. This, along with previous literature, suggests that LOC could represent a reliable neural correlate of consciousness, endorsing the idea that visual awareness is rooted in extra-striate areas, rather than in V1.

Overall, the present study provides interesting insights into the neural correlates of conscious vision, despite presenting some limitations. The combination of EROS and Granger causality with EEG offered the possibility to achieve a comprehensive and innovative picture of the mechanisms underlying visual awareness, although a simultaneous recording of EROS and EEG would have ensured a more precise temporal overlap. Moreover, an EROS montage encompassing both anterior and posterior brain areas, and thus allowing the full coverage of the head, would have ensured a wider and more comprehensive investigation of the neural substrates that support conscious vision. In addition, despite being widely adopted in consciousness research, the use of the contrastive analysis coupled with subjective measures of awareness represents some constraints: it usually contrasts experimental conditions that may not be equal in terms of elicited neural activity (Lau, 2007), and it cannot fully allow to segregate the true NCC from prerequisites and consequences of the conscious experience (Aru et al., 2012). For these reasons, we cannot completely rule out the possibility that the sustained activity observed in LOC may be modulated by neural mechanisms elicited by enabling factors occurring before the presentation of the stimulus and, thus, influencing conscious perception.

For these reasons, future studies should try to overcome these issues by adopting an experimental paradigm suitable to isolating the true NCC from possible confounding factors and/or using objective measures of awareness, in order to shed further light on the actual footprints of visual awareness.

Ethics statement

All participants gave their written informed consent before participating in the study, which was conducted in accordance with the 2013 declaration of Helsinki and approved by the Ethics Committee of the European Research Council and of the Verona Azienda Ospedaliera Universitaria Integrata (AOUI)

CRediT authorship contribution statement

Elisabetta Colombari: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Data curation. **Giorgia Parisi:** Writing – review & editing, Software, Methodology, Investigation, Formal analysis. **Alessandra Tafuro:** Writing – review & editing, Software, Methodology, Investigation, Formal analysis. **Sonia Mele:** Writing – review & editing, Software, Methodology. **Chiara Mazzi:** Writing – review & editing, Supervision, Software, Methodology, Formal analysis. **Silvia Savazzi:** Writing – review & editing, Supervision, Software, Resources, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare no competing interests.

Data availability

The experimental data that support the findings of this study are openly available in OSF at <https://doi.org/10.17605/OSF.IO/KHW3N>

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.neuroimage.2024.120805](https://doi.org/10.1016/j.neuroimage.2024.120805).

References

- Arridge, S.R., Schweiger, M., 1995. Sensitivity to prior knowledge in optical tomographic reconstruction. In: Chance, B., Alfano, R.R. (Eds.), *Optical Tomography, Photon Migration, and Spectroscopy of Tissue and Model Media: Theory, Human Studies, and Instrumentation*. SPIE, pp. 378–388.
- Aru, J., Bachmann, T., Singer, W., Melloni, L., 2012. Distilling the neural correlates of consciousness. *Neurosci. Biobehav. Rev.* 36, 737–746.
- Bagattini, C., Mazzi, C., Savazzi, S., 2015. Waves of awareness for occipital and parietal phosphene perception. *Neuropsychologia* 70, 114–125.
- Baniqued, Pauline L., Low, Kathy A., Fabiani, Monica, Gratton, G., 2013. Frontoparietal Traffic Signals: A Fast Optical Imaging Study of Preparatory Dynamics in Response Mode Switching. *J. Cogn. Neurosci.* 25, 887–902.
- Boly, M., Massimini, M., Tsuchiya, N., Postle, B.R., Koch, C., Tononi, G., 2017. Are the neural correlates of consciousness in the front or in the back of the cerebral cortex? Clinical and neuroimaging evidence. *J. Neurosci.* 37, 9603–9613.
- Chiarelli, A.M., Maclin, E.L., Low, K.A., Fabiani, M., Gratton, G., 2015. Comparison of procedures for co-registering scalp-recording locations to anatomical magnetic resonance images. *J. Biomed. Opt.* 20, 016009.
- Cichy, R.M., Chen, Y., Haynes, J.D., 2011. Encoding the identity and location of objects in human LOC. *Neuroimage* 54, 2297–2307.
- Crick, F., Koch, C., 1995. Are we aware of neural activity in primary visual cortex? *Nature*.
- Cunnington, R., Windischberger, C., Deecke, L., Moser, E., 2002. The preparation and execution of self-initiated and externally-triggered movement: A study of event-related fMRI. *Neuroimage* 15, 373–385.
- Decramer, T., Premereur, E., Uytterhoeven, M., Van Paesschen, W., Van Loon, J., Janssen, P., Theys, T., 2019. Single-cell selectivity and functional architecture of human lateral occipital complex. *PLoS Biol.* 17, e3000280.
- Dehaene, S., Changeux, J.P., 2011. Experimental and theoretical approaches to conscious processing. *Neuron* 70, 200–227.
- Delorme, A., Makeig, S., 2004. EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J. Neurosci. Methods* 134, 9–21.
- Dembksi, C., Koch, C., Pitts, M., 2021. Perceptual awareness negativity: a physiological correlate of sensory consciousness. *Trends Cogn. Sci.* 25, 660–670.
- Eger, E., Ashburner, J., Haynes, J.D., Dolan, R.J., Rees, G., 2008. fMRI activity patterns in human LOC carry information about object exemplars within category. *J. Cogn. Neurosci.* 20, 356–370.
- Fang, F., Kersten, D., Murray, S.O., 2008. Perceptual grouping and inverse fMRI activity patterns in human visual cortex. *J. Vis.* 8, 2–9.
- Fyftche, D.H., Zeki, S., 2011. The primary visual cortex, and feedback to it, are not necessary for conscious vision. *Brain* 134, 247–257.
- Fisch, L., Privman, E., Ramot, M., Harel, M., Nir, Y., Kipervasser, S., Andelman, F., Neufeld, M.Y., Kramer, U., Fried, I., Malach, R., 2009. Neural “Ignition”: Enhanced Activation Linked to Perceptual Awareness in Human Ventral Stream Visual Cortex. *Neuron* 64, 562–574.
- Förster, J., Koivisto, M., Revonsuo, A., 2020a. ERP and MEG correlates of visual consciousness: The second decade. *Conscious. Cogn.* 80.
- Förster, J., Koivisto, M., Revonsuo, A., 2020b. ERP and MEG correlates of visual consciousness: The second decade. *Conscious. Cogn.* 80.
- Gratton, G., 2000. Opt-cont and “opt-3D”: a software suite for the analysis and 3D reconstruction of the event-related optical signal (EROS). *Psychophysiology* 37, s44.
- Gratton, G., Corballis, P.M., 1995. Removing the heart from the brain: Compensation for the pulse artifact in the photon migration signal. *Psychophysiology* 32, 292–299.
- Gratton, G., Corballis, P.M., Cho, E., Fabiani, M., Hood, D.C., 1995. Shades of gray matter: Noninvasive optical images of human brain responses during visual stimulation. *Psychophysiology*.
- Gratton, G., Fabiani, M., 1998. Dynamic brain imaging: Event-related optical signal (EROS) measures of the time course and localization of cognitive-related activity. *Psychon. Bull. Rev.* 5, 535–563.
- Gratton, G., Fabiani, M., 2001. Shedding light on brain function: The event-related optical signal. *Trends Cogn. Sci.* 5, 357–363.
- Gratton, G., Fabiani, M., 2010. Fast optical imaging of human brain function. *Front. Hum. Neurosci.* 4, 1–9.
- Gratton, G., Fabiani, M., Corballis, P.M., Hood, D.C., Goodman-Wood, M.R., Hirsch, J., Kim, K., Friedman, D., Gratton, E., 1997. Fast and localized event-related optical signals (EROS) in the human occipital cortex: Comparisons with the visual evoked potential and fMRI. *Neuroimage* 6, 168–180.
- Gratton, G., Sarno, A., Maclin, E., Corballis, P.M., Fabiani, M., 2000. Toward noninvasive 3-D imaging of the time course of cortical activity: Investigation of the depth of the event-related optical signal. *Neuroimage* 11, 491–504.
- Grill-Spector, K., 2003. The neural basis of object perception. *Curr. Opin. Neurobiol.* 13, 159–166.
- Grill-Spector, K., Kourtzi, Z., Kanwisher, N., 2001. The lateral occipital complex and its role in object recognition. *Vision. Res.* 41, 1409–1422.
- Grill-Spector, K., Kushnir, T., Hendler, T., Malach, R., 2000. The dynamics of object-selective activation correlate with recognition performance in humans. *Nat. Neurosci.* 3, 837–893.
- Hurme, M., Koivisto, M., Revonsuo, A., Railo, H., 2017. Early processing in primary visual cortex is necessary for conscious and unconscious vision while late processing is necessary only for conscious vision in neurologically healthy humans. *Neuroimage* 150, 230–238.
- Hyvärinen, A., 1999. Fast and robust fixed-point algorithms for independent component analysis. *IEEE Trans. Neural Networks* 10, 626–634.
- James, T.W., Culham, J., Humphrey, G.K., Milner, A.D., Goodale, M.A., 2003. Ventral occipital lesions impair object recognition but not object-directed grasping: An fMRI study. *Brain* 126, 2463–2475.
- Kiebel, S.J., Poline, J.B., Friston, K.J., Holmes, A.P., Worsley, K.J., 1999. Robust smoothness estimation in statistical parametric maps using standardized residuals from the general linear model. *Neuroimage* 10, 756–766.
- Koch, C., Massimini, M., Boly, M., Tononi, G., 2016. Neural correlates of consciousness: Progress and problems. *Nat. Rev. Neurosci.* 17, 307–321.
- Koivisto, M., Ruohola, M., Vahtera, A., Lehmusvuo, T., Intaitte, M., 2018. The effects of working memory load on visual awareness and its electrophysiological correlates. *Neuropsychologia* 120, 86–96.
- Lamme, V.A.F., Roelfsema, P.R., 2000. The distinct modes of vision offered by feedforward and recurrent processing. *Trends Cogn. Sci.* 23, 571–579.
- Lamme, V.A.F., 2006. Towards a true neural stance on consciousness. *Trends Cogn. Sci.* 10, 494–501.
- Lamme, V.A.F., Supér, H., Landman, R., Roelfsema, P.R., Spekreijse, H., 2000. The role of primary visual cortex (V1) in visual awareness. *Vision. Res.* 40, 1507–1521.
- Lau, H.C., 2007. A higher order Bayesian decision theory of consciousness. *Prog. Brain Res.* 168, 35–48.
- Liu, Y., Paradis, A.L., Yahia-Cherif, L., Tallon-Baudry, C., 2012. Activity in the lateral occipital cortex between 200 and 300 ms distinguishes between physically identical seen and unseen stimuli. *Front. Hum. Neurosci.* 6, 1–9.
- Malach, R., 2021. Special Issue: Consciousness science and its theories Local neuronal relational structures underlying the contents of human conscious experience. *Neurosci.* 2021, 1–13.

- Martinelli, F., Perez, C., Caetta, F., Obadia, M., Savatovsky, J., Chokron, S., 2020. Neuroanatomic correlates of visual hallucinations in poststroke hemianopic patients. *Neurology*. 94, E1885–E1891.
- Mazzi, C., Bagattini, C., Savazzi, S., 2016. Blind-sight vs. degraded-sight: Different measures tell a different story. *Front. Psychol.* 7, 1–11.
- Mazzi, C., Mancini, F., Savazzi, S., 2014. Can IPS reach visual awareness without V1? Evidence from TMS in healthy subjects and hemianopic patients. *Neuropsychologia* 64, 134–144.
- Mazzi, C., Mazzeo, G., Savazzi, S., 2020. Late Positivity Does Not Meet the Criteria to be Considered a Proper Neural Correlate of Perceptual Awareness. *Front. Syst. Neurosci.* 14, 1–14.
- Mullin, C.R., Steeves, J.K.E., 2011. TMS to the lateral occipital cortex disrupts object processing but facilitates scene processing. *J. Cogn. Neurosci.* 23, 4174–4184.
- Nagy, K., Greenlee, M.W., Kovács, G., 2012. The lateral occipital cortex in the face perception network: An effective connectivity study. *Front. Psychol.* 3, 1–12.
- Parisi, G., Mazzi, C., Colombari, E., Chiarelli, A.M., Metzger, B.A., Marzi, C.A., Savazzi, S., 2020. Spatiotemporal dynamics of attentional orienting and reorienting revealed by fast optical imaging in occipital and parietal cortices. *Neuroimage* 222, 117244.
- Perrin, F., Pernier, J., Bertrand, O., 1989. Spherical splines for scalp potential and current density mapping 10.1016/0013-4694(89)90180-6 : *Electroencephalography and Clinical Neurophysiology* | ScienceDirect.com. *Electroencephalography Clin. Neurophysiol.* 72, 184–187.
- Rees, G., Kreiman, G., Koch, C., 2002. Neural correlates of consciousness in humans. *Nat. Rev. Neurosci.* 3, 261–270.
- Richter, W., Andersen, P.M., Georgopoulos, A.P., Kim, S.G., 1997. Sequential activity in human motor areas during a delayed cued finger movement task studied by time-resolved fMRI. *Neuroreport* 8, 1257–1261.
- Roebroek, A., Formisano, E., Goebel, R., 2005. Mapping directed influence over the brain using Granger causality and fMRI. *Neuroimage* 25, 230–242.
- Sergent, C., Baillet, S., Dehaene, S., 2005. Timing of the brain events underlying access to consciousness during the attentional blink. *Nat. Neurosci.* 8, 1391–1400.
- Solanas, M.P., Zhan, M., Gelder, B.de, 2024. Ultrahigh field fMRI reveals different roles of temporal and fronto-parietal cortices in subjective awareness. *J. Neurosci.* 44, e0425232023.
- Stanley, D.A., Rubin, N., 2003. fMRI activation in response to illusory contours and salient regions in the human Lateral Occipital Complex. *Neuron* 37, 323–331.
- Tagliabue, C.F., Mazzi, C., Bagattini, C., Savazzi, S., 2016. Early local activity in temporal areas reflects graded content of visual perception. *Front. Psychol.* 7, 1–10.
- Tong, F., 2003. Primary visual cortex and visual awareness. *Nat. Rev. Neurosci.* 4, 219–229.
- Tong, F., Nakayama, K., Vaughan, J., Kanwisher, N., 1998. Binocular rivalry and visual awareness in human extrastriate cortex. *Neuron* 21, 753–759.
- Toscano, J.C., Anderson, N.D., Fabiani, M., Gratton, G., Garnsey, S.M., 2018. The time-course of cortical responses to speech revealed by fast optical imaging. *Brain Lang.* 184, 32–42.
- Vanni, S., Revonsuo, A., Saarinen, J., Hari, R., 1996. Visual awareness of objects correlates with activity of right occipital cortex. *Neuroreport* 8, 183–186.
- Winkler, I., Debener, S., Muller, K.R., Tangermann, M., 2015. On the influence of high-pass filtering on ICA-based artifact reduction in EEG-ERP. *Proc. Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. EMBS* 4101–4105, 2015-Novem.
- Wolf, U., Wolf, M., Toronov, V., Michalos, A., Paunescu, L.A., Gratton, E., 2014. Detecting cerebral functional slow and fast signals by frequency-domain near-infrared spectroscopy using two different sensors. *Biomedical Optical Spectroscopy and Diagnostics (2000)*, Paper TuF10. The Optical Society p. TuF10.
- Worsley, K.J., Poline, J.B., Vandal, A.C., Friston, K.J., 1995. Tests for distributed, nonfocal brain activations. *Neuroimage* 2, 183–194.
- Zeki, S., Ffytche, D.H., 1998. The Riddoch syndrome: Insights into the neurobiology of conscious vision. *Brain* 121, 25–45.