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Comparing stimulus-evoked and spontaneous response of the face-selective multi-units in the human posterior fusiform gyrus

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Abstract

The stimulus-evoked neural response is a widely explored phenomenon. Conscious awareness is associated in many cases with the corresponding selective stimulus-evoked response. For example, conscious awareness of a face stimulus is associated with or accompanied by stimulus-evoked activity in the fusiform face area (FFA). In addition to the stimulus-evoked response, spontaneous (i.e., task-unrelated) activity in the brain is also abundant. Notably, spontaneous activity is considered unconscious. For example, spontaneous activity in the FFA is not associated with conscious awareness of a face. The question is: what is the difference at the neural level between stimulus-evoked activity in a case that this activity is associated with conscious awareness of some content (e.g., activity in the FFA in response to fully visible face stimuli) and spontaneous activity in that same region of the brain? To answer this question, in the present study, we had a rare opportunity to record two face-selective multi-units in the vicinity of the FFA in a human patient. We compared multi-unit face-selective task-evoked activity with spontaneous prestimulus and a resting-state activity. We found that when activity was examined over relatively long temporal windows (e.g. 100–200 ms), face-selective stimulus-evoked firing in the recorded multi-units was much higher than the spontaneous activity. In contrast, when activity was examined over relatively short windows, we found many cases of high firing rates within the spontaneous activity that were comparable to stimulus-evoked activity. Our results thus indicate that the sustained activity is what might differentiate between stimulus-evoked activity that is associated with conscious awareness and spontaneous activity.

Keywords: spontaneous activity; stimulus-evoked activity; face-selective activity; conscious awareness; multi-unit recording in humans; Fusiform Face Area (FFA)

Introduction

The stimulus-evoked neural response—an increase of neural activity following stimulus presentation—is probably the most robust and well-explored phenomenon related to neural processing (Friston 2005). This phenomenon is universal and can be observed across a variety of brain regions, modalities (e.g. visual and auditory), and species. The stimulus-evoked neural response can additionally be detected using various recording and imaging methods [e.g. intracranial and scalp electrophysiological recordings, functional magnetic resonance imaging (fMRI)]. Conscious awareness is associated in many cases with a corresponding selective stimulus-evoked response. For example, conscious awareness about a face stimulus is likely always associated with activity in the fusiform face area (FFA)
An additional omnipresent phenomenon is the spontaneous (or ongoing, intrinsic, resting-state) activity—the type of neural activity that occurs constantly in the background and that is not triggered by any stimuli (Raichle et al. 2001). One of the first demonstrations of spontaneous activity was the electroencephalogram (EEG) recordings done by Hans Berger (Berger 1929). Renewed interest in spontaneous activity was sparked by the pioneering works of Arieli, Grinvald, Tsodyks and colleagues (Arieli et al. 1995, 1996, Tsodyks et al. 1999) conducted in the early visual cortex in anesthetized cats. Examination of co-variation of spontaneous activity from two or more neural sources gave rise to the resting-state functional connectivity approach—one of the most prominent research directions today (Biswal et al. 1995; Damoiseaux et al. 2006; Mantini et al. 2007; Bullmore and Sporns 2009; Yeo et al. 2011; Lurie et al. 2019; Marron et al. 2020). The relationship between spontaneous activity and conscious awareness is complex. In certain scenarios, spontaneous activity has been shown to modulate cognitive behavior in domains such as visual perception (HesseLMann et al. 2008b; Hahamy et al. 2020), creative thinking (Broday-Dvir and Malach 2021), and volitional decision-making (Schurger et al. 2012). Spontaneous activity has also been suggested to play a role in consciousness (Northoff and Lamme 2020), for example, by integrating information across brain regions (He and Raichle 2009) or across brain regions (i.e. space) and time (Northoff 2013; Northoff and Huang 2017). However, the spontaneous neural activity per se is unconscious because a person does not know when the spontaneous wave is at its minimum or maximum in a given brain region. For example, while the spontaneous activity fluctuates several times per minute in the FFA and the parahippocampal place area (PPA) high-level visual areas (Nir et al. 2006), we do not have a constantly alternating experience of a face and a scene.

The question is what is the difference at the neural level between stimulus-evoked activity in a case that this activity is associated with conscious awareness of some content and spontaneous activity? In other words, are there any properties of the neural signal that may explain whether we are consciously aware of the stimulus or not? Surprisingly, to date, there have been few studies that compared stimulus-evoked responses and spontaneous activity, and they do not provide sufficient answers. One prominent functional MRI (fMRI) study (Nir et al. 2006) demonstrated that the amplitude of spontaneous fluctuations in the FFA and the PPA was comparable to the stimulus-evoked responses. However, because fMRI measures hemodynamic activity, which is only an indirect measure of a neural response (Logothetis et al. 2001), it is challenging to extrapolate this result to neural activity.

A two additional studies compared single-unit stimulus-evoked and spontaneous activity in the cat primary visual areas (Arieli et al. 1995) and the human primary auditory cortex (Nir et al. 2008). Both of these studies showed that stimulus-evoked activity was associated with higher firing rates compared to spontaneous activity. But these studies did not focus on the question of whether periods of high firing rates can still be found in spontaneous activity. In addition, investigations in these studies have been conducted in primary cortices, regions that are unlikely to contribute directly to conscious awareness (Dehaene et al. 2006; Watanabe et al. 2011).

The present intracranial study was conducted with patients who underwent clinical monitoring for epileptic seizures. We had a rare opportunity to record multi-unit activity (MUA) of two strongly face-selective multi-units located in the posterior fusiform gyrus of one patient (Fig. 1A). As we reported previously (Axelrod et al. 2019), the multi-units were located in the vicinity of the FFA. As the control region, activity in the planum temporale (i.e. auditory cortex) was recorded in an additional patient (Fig. 1B). The present investigation included a task-based experiment with face stimuli as well as a resting-state session. This setup and design allowed us to compare electrophysiological face-selective stimulus-evoked responses, spontaneous activity that preceded face stimulus (i.e. fixation period), and spontaneous activity during resting-state session in a high-level visual area of a human brain.

### Methods

Detailed information about the patient with face-selective multi-units, recording procedures, and stimulus-evoked paradigm have been provided in detail in supplementary materials of our previous publication (Axelrod et al. 2019). Here, we provide the most essential information.

### Information about patients

The face-selective activity was recorded in a 26-year-old female subject (i.e. patient). For clinical epilepsy seizure monitoring, the patient was implanted with depth electrodes in the right occipital and temporal lobes. The experiment with the control region was conducted in a 21-year-old male patient for whom depth electrodes were implanted in the left temporal, parietal, and frontal lobes. For both patients, no epileptic activity was found in the regions of interest of the present investigation (i.e. right posterior fusiform gyrus in the patient with face-selective multi-units and left planum temporale in the control patient). Note that the location of the electrodes in such a procedure is determined solely

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**Highlights**

- Face-selective stimulus-evoked vs. spontaneous multi-unit activity in human brain is examined
- Long periods of interest: higher conscious stimulus-evoked than unconscious spontaneous activity
- Short periods of interest: comparable conscious stimulus-evoked and unconscious spontaneous activity
- Sustained activity is associated with conscious evoked but not unconscious spontaneous response

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**Figure 1.** Anatomical image of the patients with the location of the electrodes. Blue arrows point to the implanted depth electrode. Magenta arrow points to the approximate location of the microwires. (A) Anatomical image of the patient with the micro-wires implanted in the posterior fusiform gyrus. (B) Anatomical image of the control patient with the micro-wires implanted in the planum temporale.
by clinical criteria. The data were recorded during the subjects’
hospitalization in the Epilepsy ward of Pitié-Salpêtrière Hospital in
accordance with approval and guidelines of the local ethics com-
mittee (CPP Paris VI, INSERM C11-16), with the same clinical setup
as the previous intracranial studies conducted in Pitié-Salpêtrière
Hospital (El Karoui et al. 2014; Babo-Rebele et al. 2016; Corlier et al.
2016, Chammat et al. 2017).

Recording setup
Depth platinum micro-electrodes (AdTech, Wisconsin) of the
Behnke-Fried type 5 were used for stereotactic EEG recording.
The electrodes of interest for the present study were implanted
in the right posterior fusiform gyrus (Fig. 1A, the patient with
face-selective multi-units) and the left planum temporale (Fig. 1B;
the control patient). Eight platinum–iridium microwires were
located at the tip of this electrode (protruded about 5 mm beyond
the macro-electrode). Note, that there is no way to determine
the exact location of microwires in human electrophysiological
recordings (Self et al. 2016); therefore, we describe only the approx-
imate location of the microwires (Fig. 1, magenta arrow). In
our previous study (Axelrod et al. 2019), we established that the
microwires that recorded the face-selective activity were in the
vicinity of the FFA. The microwire recording (the focus of this
paper) was conducted using the Atlas recording system (Neural-
ynx Inc., Tucson, AZ). The microwire recording sampling rate was
32 kHz and the online band-pass filter was 0.1–4000 Hz.

Experimental paradigms
The experiment was conducted in a quiet room in the hospi-
tal ward. Stimuli were projected on a Dell Precision M4600 lap-
top (15.6-inch display, 1366 × 768 resolution) using MATLAB with
Psychtoolbox-3 (Brainard 1997). The patients were sitting ~50 cm
from the monitor.

Resting-state session
The standard resting-state paradigm was used (Fox et al. 2006).
The duration of the resting-state session was 5 minutes and
50 seconds. During this time, the patients remained with their
eyes closed. They were also asked to not think about anything
specific and in particular to not imagine anything. No formal ques-
tionnaires regarding imagery were issued after the resting-state
session.

Stimulus-evoked experiment
The experiment included color images of faces (120 trials), city
views (hereinafter referred as “scenes”, 120 trials), and everyday
objects (40 trials). Two types of faces were presented, familiar
and unfamiliar. Faces familiar to patients were famous faces
(French public figures), and faces not familiar to the patient were
non-French public figures. Familiar and unfamiliar scenes were
presented as well. Familiar scenes were city views of Paris, and
unfamiliar scenes were views of cities from outside of France. The
size of the stimuli was about 11° visual angles. Each stimulus was
shown for 1 second and was preceded by a 1.2-second fixation. The
behavioral task was to indicate whether the image was familiar or
not. The main motivation behind this study was to compare the
MUA neural properties of face-selective stimulus-evoked response
and spontaneous activity. Because we were interested in the
neural response to the stimulus category, we combined familiar
and unfamiliar stimuli, resulting in two conditions: “faces” and
“scenes.” The scenes condition was only used only to inde-
dependently establish face-selectivity. Activity preceding the faces
stimuli was analyzed as well (referred to below as “prestimulus
activity”). The objects category was not included in the analysis
because an additional control condition did not contribute any
new information and because there were many fewer trials with
objects stimuli, compared to the number of trials in the faces and
scenes conditions.

Data analysis
Data analysis was done in MATLAB using FieldTrip (Oostenveld
et al. 2011), Chronux toolbox (http://chronux.org/) (Mitra 2007),
wave_clus (Quiroga et al. 2004), and Matlab Offline Spike Sort-
ing (https://github.com/JoaquinMansilla/Spike-Sorter) toolboxes
as well as custom code (Axelrod 2014). Spike detection and sort-
ing were executed using a standard procedure for analyzing MUA
recordings in humans (Quiroga et al. 2005; Reddy et al. 2015;
Kornblith et al. 2017). Before performing the MUA analysis, the
Local Field Potential (LFP) signals of the microwires were inspected
to minimize the possibility of interference from local epileptic
activity. No local epileptic activity was found. Spike detection and
spike-sorting were done using wave_clus toolbox. The average of
the cluster did not exceed 50 µV in either of the units, and they
were therefore classified as MUA. To validate the results of spike-
detection and spike-sorting, we conducted two types of control
analysis. One validation approach was to use our main analy-
sis pipeline (wave_clus toolbox) to conduct spike-detection with
three different threshold values (stdmin = 4, stdmin = 4.5 and
stdmin = 5). Another validation approach was to use a different
software package for spike-detection and spike-sorting (Matlab
Offline Spike Sorting toolbox and custom procedure). The results
we obtained using both validation approaches were similar to the
results using our main analysis pipeline.

The entire stimulus-evoked experiment was 11 minutes and
23 seconds long. The recording of this session was split into two
parts. The first part of the recording had an equal duration to
that of the resting-state session (5 minutes and 50 seconds). Our
main analyses (Figs. 3–6) were conducted using the data of the first
part. The second part was comprised of the remaining data, which
was allocated to be used to establish selectivity using independent
data (Kriegeskorte et al. 2009) (Fig. 2). Additionally, this second part
of the data was used to determine the point of beginning, peak,
and end of modulation of the faces condition compared to base-
line. The data of the stimulus-evoked experiment were split into
epochs, with a baseline (i.e. prestimulus) period of 500 ms and a
trial period of 1250 ms.

In order to compare the distribution of firing rates during the
faces condition, the prestimulus activity, and the resting state
(Fig. 4), instantaneous firing rates were calculated by smoothing
the binary spike train with a Gaussian kernel with a full width
at half maximum (FWHM) of 80 ms [in accordance with previous
similar analysis (Nir et al. 2008)]. The firing rates for the faces con-
dition were calculated for the periods of significant modulation
compared to baseline. Beginning and end points of these periods
were obtained using independent data (see above). To obtain the
relative proportion of each histogram bin, the histogram was nor-
malized for each condition, based on the number of instantaneous
firing rates extracted.

Comparison of power spectral density between conditions
(Fig. 5) was conducted using Fast Fourier Transform (Matlab
fft function). Qualitatively similar results were obtained when
the power spectrum was calculated using multitaper technique
(mispectrum chronux toolbox function). The spectrum was cal-
culated for each trial of each condition and then averaged (for
similar approach, see Mazzoni et al. 2008). Segment duration for all
conditions was set to 500 ms to match the prestimulus duration.
defined percentiles of top ranked values (e.g. for the 70 windows we calculated the percentage of resting-state windows in the pre-values. Fourth, this vector was ranked in descending order. Fifth, resulted in 70 (faces stimulus-evoked) spikes for each window, resulting in a vector of firing rates. This number of resting-state windows. Third, we calculated the sum of for each of the faces stimulus-evoked trials (i.e. sum of spikes within window). We examined the percentage of the resting-state windows among the top 5%, top 20%, top 35%, and top 50% of values. For example, for the top 5%, we asked what percentage of resting-state windows were within the top 7 (140 × 5% = 7) windows with the highest firing rates. The analysis comparing faces stimulus-evoked activity and prestimulus activity was conducted in the same way but without bootstrapping.

Results

During the resting-state session (5 minutes and 50 seconds), patients were asked to keep their eyes closed, not to think about anything in particular, and to not imagine anything. The stimulus-evoked experiment included static images of familiar (i.e. famous) and unfamiliar faces. In addition, the experiment included images of familiar and unfamiliar city views (referred to below as "scenes"). The scenes condition was used only to establish face selectivity and was not used in our main analyses. Each stimulus was preceded by a fixation period (referred to below as "prestimulus activity"). The behavioral task was to indicate whether the image was familiar or not (see the "Methods" section for more details). The performance of the patient with face-selective multi-units was almost perfect for faces (familiar faces = 100%, unfamiliar faces = 95%) but worse for scenes (familiar scenes = 95%, unfamiliar scenes = 22%). The low performance for unfamiliar scenes was because the patient mistakenly thought that the scene should be indicated as "familiar" even if it only resembles a familiar scene. The performance of the control patient was high for both faces (familiar faces = 99%, unfamiliar faces = 85%) and scenes (familiar scenes = 94%, unfamiliar scenes = 93%). As we were interested in the stimulus-selective response in general, we combined familiar and unfamiliar stimuli, resulting in two conditions: "faces" and "scenes".

The averaged stimulus-evoked responses (based on the second part of the stimulus-evoked experiment) are shown in Fig. 2. In multi-units 1 and 2, we see that faces elicited strong stimulus-evoked modulation compared to baseline. Additionally, faces elicited a much higher stimulus-evoked response compared to the scenes condition (i.e. face-selectivity). Statistically, the activity in the faces condition was beyond the baseline in multi-unit 2 (the period between 84 and 751 ms after stimulus onset, P < 0.001, two-tailed nonparametric cluster-based permutations (Maris and Oostenveld 2007)) and in multi-unit 2 (the period between 91 and 768 ms after stimulus onset, P < 0.001). The peak values of the faces condition relative to baseline (i.e. the highest t-values) were at 176 ms from stimulus onset (multi-unit 1) and at 173 ms from stimulus onset (multi-unit 2). In addition to beyond baseline responses in the faces condition, in multi-unit 2, the activity increased beyond the baseline in the scenes condition (the period between 131 and 483 ms after stimulus onset,
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P < 0.001; peak value at 330 ms from stimulus onset). Comparing the faces and scenes conditions revealed a face-selective response in multi-unit 1 (99 ms: 1000 ms period, P < 0.001) and multi-unit 2 ([107 ms: 733 ms period, P < 0.001]. Overall, these results establish high face selectivity of the two recorded multi-units. In the control multi-unit (Fig. 2C), there were no periods of beyond-baseline modulation for neither the faces nor the scenes condition. In addition, there were no periods of higher activity for faces compared to scenes (i.e. no face-selectivity).

Next, we proceed to the main goal of the present investigation, comparing face-selective stimulus-evoked and spontaneous activity (i.e. resting-state and prestimulus activity). Note that all of the following analyses that included stimulus-evoked conditions were conducted using data that were independent from those used to establish selectivity (see above). In Fig. 3, we show representative examples of instantaneous firing rate traces of the stimulus-evoked experiment (Fig. 3A) and resting-state session (Fig. 3B), recorded from face-selective multi-unit 1. Data were smoothed with a Gaussian window of FWHM of 80 ms (Nir et al. 2008). This figure illustrates that in many cases faces elicited strong firing rate modulation at the level of single stimuli. The firing rates preceding the stimulus and during the resting state were weaker, but interestingly, there were also occasional, relatively short periods of strong firing rates comparable to those of the face-evoked activity.

To take a quantitative look at the data, we first compared the average firing rates of the segments of face-evoked activity, prestimulus activity, and the resting-state activity. The segments of stimulus-evoked activity were taken from the periods (in time) of the beyond-baseline modulation of the faces condition calculated on independent data (see above). We found that for multi-units 1 and 2, the average stimulus-evoked firing rate in the faces condition was much higher compared to resting-state activity and prestimulus activity periods: multi-unit 1 faces mean = 48.6 spikes/second, SEM = 0.15; multi-unit 1 fixation mean = 15.9 spikes/second, SEM = 0.09; multi-unit 1 resting-state mean = 14.95 spikes/second, SEM = 0.03; multi-unit 2 faces mean = 48.21 spikes/second, SEM = 0.16; multi-unit 2 fixation mean = 14.7 spikes/second, SEM = 0.09; multi-unit 2 resting-state mean = 10.38 spikes/second, SEM = 0.023. In contrast, in the control multi-unit, there was no major difference between the faces condition, the resting-state session, and the prestimulus activity: faces mean = 13.6 spikes/second, SEM = 0.06; prestimulus activity mean = 11.79 spikes/second, SEM = 0.06; resting-state mean = 12.5 spikes/second, SEM = 0.02.

Next, to explore the firing rate profile in more detail, we compared the distribution of instantaneous firing rates of the three conditions (i.e. face-selective evoked response, prestimulus activity, and the resting-state activity). The results are shown in Fig. 4. For multi-units 1 and 2, we found a reversed pattern when comparing the faces condition to the resting-state and prestimulus activities: the low firing rates were abundant in the resting-state (gray bars) and prestimulus activities (blue) but were uncommon in the faces condition (red bars); in contrast, the high firing rates were abundant in the faces condition but were almost absent in the resting-state and prestimulus activities. In contrast, in the control multi-unit, there was no major difference between the patterns of activity of the three conditions.

At the next stage, we compared the power spectral density between conditions. The power spectrum was calculated for single trials, and then, the result was averaged. In multi-units 1 and 2 (Fig. 5A and B), we can see the major differences in power spectrum across the frequencies between stimulus-evoked face condition and two spontaneous conditions. In contrast, for the control multi-unit (Fig. 5C), we do not see any differences between conditions in power spectrum.

We have already established that the selective (i.e. face-selective) stimulus-evoked response is characterized by a higher firing rate compared to resting-state activity (Fig. 4). But in the illustrative example in Fig. 3, we observed that periods with high firing rates could be also found during spontaneous activity. In the quantitative analyses that follow, we explored how probable it was that the firing rate during the resting state was higher than during face condition. In contrast to the previous analyses, the present analysis was conducted using binary spike train data (i.e., the data without Gaussian smoothing), permitting us to investigate how the length of time over which the activity is examined influences the results. In the analysis presented below, we compare stimulus-evoked face-selective responses with resting-state activity. Comparing stimulus-evoked face-selective responses and prestimulus activity produced qualitatively similar results. The analysis was conducted for a time window that varied in length from 2 to 250 ms. For each of the stimulus-evoked trials (70 trials, in the faces condition) and for an equal number of resting-state time windows, we calculated the sum of spikes over a given window. This resulted in a vector of 140 values. Then, we calculated the percentage of the resting-state values among predefined percentage of the highest values (values on Y axis in Fig. 6). Specifically, we examined the percentage of resting-state windows among the top 5%, 20%, 35% and 50% of windows with the highest firing rates. For more details, see the ‘Methods’ section.

The results of the analysis are shown in Fig. 6. For multi-units 1 and 2, we observed the following: (i) the longer the time-window, the less likely it was to encounter firing rates from the resting-state session that were comparable to the face-selective response; (ii) proportion of resting-state time windows with a firing-rate comparable to that of the selective stimulus-evoked response depended on the percentage threshold used. Critically, with short windows,
Figure 4. Distribution of stimulus-evoked and spontaneous firing rates. The larger histogram shows the distribution of firing rates from 0 to 100 spikes per second. For better visibility, the histograms were trimmed at 100 spikes per second. The histogram in the inset zooms in on the range from 0 to 9 spikes per second. The y axis shows the relative frequency of each range of firing rates. The main finding for both multi-units was that the low firing rates were abundant in the resting state (gray bars) but were uncommon in the faces condition (red bars); in contrast, the high firing rates were abundant in the faces condition but were almost absent in the resting state. (A) Results in multi-unit 1. Beyond 100 spikes per second were 4.1% of faces, 0% of prestimulus, and 0.4% of the resting-state firing rates. (B) Results in multi-unit 2. Beyond 100 spikes per second were 5.5% of faces, 0.1% of prestimulus, and 0.1% of the resting-state firing rates. (C) Results in control multi-unit. Beyond 100 spikes per second, there were 0% of faces, 0% of prestimulus, and 0% of the resting-state firing rates.

Figure 5. Comparison of power spectral density between conditions. (A) Results in multi-unit 1. (B) Results in multi-unit 2. (C) Results in control multi-unit. Note, a major difference in power spectrum across the frequencies between stimulus-evoked face and both spontaneous conditions in multi-units 1 and 2 but not in control multi-unit. Error shadows reflect standard error of mean (SEM).

Discussion
In the present investigation, we compared multi-unit face-selective stimulus-evoked and spontaneous responses in two face-selective multi-units in the human posterior fusiform gyrus. We found that on average, face-selective stimulus-evoked firing rates were much higher than spontaneous activity. However, examining activity over varying time windows revealed a more nuanced
A potential concern that can be raised regarding our findings is that the multi-unit recording that we used is a direct measure of neural activity, in contrast to fMRI which is an indirect measure (Logothetis et al. 2001; van Gaal and Lamme 2011). Spontaneous activity happens constantly and is responsible for most of the brain’s energy consumption (Raichle 2006). From a theoretical point of view, it has been suggested that the main difference between unconscious and conscious evoked-activity might be that only the latter is reverberative and sustained (Block 2007; Boly et al. 2017).

Our results can be divided into two parts. First, in line with the results of one earlier study that recorded activity in the auditory cortex of human patients (Nir et al. 2008), we found that when activity in the FFA was examined over relatively long temporal windows (100–200 ms and longer) or large temporal Gaussian smoothing (FWHM = 80 ms) was used, stimulus-evoked activity was much higher than spontaneous activity (both resting-state and prestimulus activities). Second, most interestingly, our finding was that when the activity was examined over relatively short windows (50 ms and smaller, depending on the threshold used), resting-state activity was often high and comparable to stimulus-evoked activity (Fig. 6). Critically, this result cannot be explained by low responses during stimulus-evoked trials because (i) we used the highest level of stimulus-evoked activity as the onset of our time-windows and (ii) when the window length was 20 ms and below, the windows of the spontaneous activity could be found within even the top 5% of the windows with the highest firing rates. Also note that during the stimulus-evoked experiment the participant attended to the stimuli, as was reflected by her excellent performance in the behavioral task.

Taken together, our results indicate that the important difference between stimulus-evoked activity that is associated with a conscious percept and the spontaneous activity that is not associated with a conscious percept might be how long the activity is sustained. That being said, the present result cannot establish whether the stimulus-evoked sustained activity in the FFA directly contributes to conscious awareness (i.e. serves as a neural correlate of consciousness). Interestingly, while in the present study we tested spontaneous activity that was not associated with conscious content awareness, there has also been extensive research that examined stimulus-evoked activity that is not associated with conscious awareness about some content (Dehaene and Changeux 2011; van Gaal and Lamme 2011; Hesselmann 2013; Axelrod et al. 2011a). For example, subjectively invisible stimuli of faces elicit an evoked response in the FFA (Sterzer et al. 2008; Fahrenfort et al. 2012). From a theoretical point of view, it has been suggested that the main difference between unconscious and conscious evoked-activity might be that only the latter is reverberative and sustained (Dehaene and Naccache 2001; Dehaene et al. 2006; Lamme 2006). To this extent, our results point to potentially similar mechanisms of unconscious spontaneous and unconscious stimulus-evoked activity.
continuous session without any task (pointed out above, facial imagery was unlikely a strong factor in the spontaneous experiment. However, as we pointed out above, the fact that different facial stimuli might have resulted in different responses did not limit interpretation of the findings presented in the paper. This is because we did not focus on individual trials but rather on the facial condition as a whole. Finally, an evident limitation of the present study is that it was conducted using only two face-selective multi-units. Therefore, any potential generalization to a large neural population should be made with caution. Nevertheless, the rare setup we used gave us insight that could not be obtained in previous studies. To this extent, studies with one patient (Parvizi et al. 2012; Rosenbaum et al. 2014; Aminoff et al. 2016; Jonas et al. 2018; Liu et al. 2018; Pereira et al. 2021; Streese and Tranel 2021) or few units (Self et al. 2016) have traditionally been important in cognitive neuroscience. Thus, we believe that the present study contributes a valuable contribution to the understanding of spontaneous activity and its relationship to stimulus-evoked activity.

resting-state session. Indeed, a recent study that also recorded single- and multi-unit face-selective activity reported similarity in firing rate patterns during perception and imagery of a face (Khuvis et al. 2021). However, we think that facial imagery is unlikely a major factor that could explain our results. First, our participant got clear instructions before the resting-state session to not think about anything in particular, including to not be engaged in imagery. Second, neural activity that can be measured during imagery is by definition weaker compared to sensory stimuli (e.g. O’Craven and Kanwisher 2000). Accordingly, studies that examine neural activity for imagery of faces adopt special procedures to achieve reliable neural activity. For example, when visual stimuli are shown prior to the imagery stage, the participants are explicitly asked to remember fine facial details like unique color and facial expression (Khuvis et al. 2021). Another approach to facilitate imagery is to use only a few facial identities and to show visual stimuli immediately prior to the imagery task (Dijkstra et al. 2018). Thus, in our case, even if the participant had a brief, fleeting thought relating to a person, it is unlikely that this would have resulted in reliable neural activity in the FFA. Third, we showed that the resting-state and stimulus-evoked patterns of activity were distinct (i.e. a sustained response in the stimulus-evoked case and a brief response in the resting-state; see example in Fig. 3). Had imagery occurred during the resting-state session, the patterns of the activity during resting state would have appeared similar to the stimulus-evoked activity. Finally, according to our results (Fig. 6), for the window length of 50 ms, we found ~25% of the resting-state windows with activity comparable to stimulus-evoked activity. Even if facial imagery occurred occasionally during the resting-state session, it is highly unlikely that it occurred so frequently (i.e. many dozens of times during a 6-minute period). Note that similar to the research of mind-wandering and self-generated cognition (Smallwood and Schooler 2015), there is no straightforward solution on how to establish the extent of face imagery during the 6-minute resting-state session. One possibility is to include a formal questionnaire after the resting-state session regarding potential imagery of a face (Diaz et al. 2013; Gorgolewski et al. 2014)—the procedure that was not implemented in our study. However, reliability of the responses in such a case can be questioned because the participant might not remember at the end of the session what was going through their mind throughout the entire period. Another possibility is to include thought probes throughout the resting-state session (e.g. Robertson et al. 1997; Axelrod et al. 2015b). However, while frequent probes might disrupt the spontaneous nature of a thought, infrequent probes suffer from the limitation we discussed above with regard to the questionnaire at the end of the session. Overall, there is an inherent difficulty to establish reliable imagery phenomenology in a spontaneous experiment. However, as we pointed out above, facial imagery was unlikely a strong factor impacting our results.

There have been two main directions in the investigation of spontaneous activity. The first is the so-called resting-state—a continuous session without any task (Raichle et al. 2001). In the field of consciousness research, resting-state spontaneous activity has been linked to and is usually investigated in the context of level or state of consciousness. In particular, spontaneous activity has been shown to vary across conscious states, such as anesthesi a (Bartfeld et al. 2015; Huang et al. 2016b, sleep (Tagliazucchi and Laufs 2014), or disorder of consciousness states (Cao et al. 2019; Huang et al. 2020). Theoretically, according to the Temporospatial Theory of Consciousness (TTC), the role of spontaneous activity is to integrate across space and time, thus creating a situation of a neural predisposition of consciousness (Northoff and Huang 2017; Northoff and Lamme 2020). Note, however, that the focus of the present work was stimulus conscious awareness but not conscious state; therefore, our results are not directly related to this body of research. The second research direction has been the influence and interaction of the spontaneous prestimulus activity on the subsequent stimulus-evoked activity (Sadaghiani et al. 2010). In a seminal study conducted more than a decade ago, Hes- selmann and colleagues showed that higher prestimulus activity in the FFA increased the probability that the Rubin face-vaso illus ion stimulus is perceived as a face (Hesselmann et al. 2008b) (for related findings for other brain regions and modalities, see Hesselmann et al. 2008a; Sadaghiani et al. 2010). Since then, more studies demonstrated that prestimulus activity can shape various properties of stimulus-related activity (e.g. level of activation and trial-to-trial variability; Podvalny et al. 2019; Northoff and Lamme 2020). A major theoretical conceptualization of this phenomenon has been proposed by TTC, according to which the ongoing (spontaneous) activity and the stimulus-evoked response need to be integrated in order for the stimulus to become conscious (Northoff and Huang 2017; Northoff and Lamme 2020). In other words, if the stimulus “arrives” at the wrong phase of the ongoing wave, the stimulus might remain unconscious. To this extent, an additional important line of investigation has been to understand the interaction between spontaneous activity and stimulus-evoked activity. Specifically, it has been suggested that this interaction might be nonadditive (He 2013; Huang et al. 2015), while Huang and colleagues (Huang et al. 2015) also suggested that interaction between spontaneous and stimulus-evoked activity might depend on the phase of spontaneous activity. In our work, we compared the properties of the spontaneous (both resting-state and prestimulus activities) with stimulus-evoked activity. However, we did not address the question of interaction between prestimulus activity and stimulus activity because our experiment was not suited for that. That is, our experiment included images of 20 different facial identities (half of them familiar and half of them unfamiliar to the participant). Different facial identities might result in different neural activities in the FFA (Davidesco et al. 2013; Ghuman et al. 2014; Axelrod and Yovel 2015; Khuvis et al. 2021). In addition, familiarity of a face can also modulate the response in the FFA (Weibert and Andrews 2015; Axelrod et al. 2019). Such variability across trials in stimulus-evoked activity due to a difference in stimuli is obviously a serious confound when one investigates the interaction between prestimulus and stimulus activity. Note that the fact that different facial stimuli might have resulted in different responses did not limit interpretation of the findings presented in the paper. This is because we did not focus on individual trials but rather on the faces condition as a whole. Finally, an evident limitation of the present study is that it was conducted using only two face-selective multi-units. Therefore, any potential generalization to a large neural population should be made with caution. Nevertheless, the rare setup we used gave us insight that could not be obtained in previous studies. To this extent, studies with one patient (Parvizi et al. 2012; Rosenbaum et al. 2014; Aminoff et al. 2016; Jonas et al. 2018; Liu et al. 2018; Pereira et al. 2021; Streese and Tranel 2021) or few units (Self et al. 2016) have traditionally been important in cognitive neuroscience. Thus, we believe that the present study contributes a valuable contribution to the understanding of spontaneous activity and its relationship to stimulus-evoked activity.
Summary
In the present study, we compared task-evoked activity that was associated with conscious awareness and spontaneous activity. We found that when activity was examined for the relatively long temporal windows (e.g. 100–200 ms), stimulus-evoked firing was much higher than in the resting-state activity. However, examination of the activity for the relatively short windows (e.g. 50 ms) revealed many occurrences of resting-state activity with the firing rates comparable to stimulus-evoked activity. Thus, how sustained a response is may differentiate between stimulus-evoked activity that is associated with conscious awareness and the spontaneous activity that is not associated with conscious perception.

Data availability
Data not publicly available. The data of the paper is clinical, patient data. Therefore, it cannot be shared.

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Conflict of interest statement
None declared.

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