

# Temporal dynamics of amygdala and orbitofrontal responses to emotional prosody using intracerebral local field potentials in humans

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## Abstract

The purpose of this study was to investigate how emotional prosody can modulate brain responses, taken into account the temporal dynamic of this process as a key characteristic. This study involves a young woman suffering from chronic and pharmaco-resistant epilepsy as a potential candidate to brain surgery. We used a dichotic listening paradigm, in which two neutral and/or angry pseudo-words were presented simultaneously on both ears. The task, orthogonal to emotional prosody, required the patient to identify the gender of the speaker on the side where her attention was directed. By using deep brain electrodes in order to record local field potentials (LFP), intracranial evoked potentials were computed in three brain areas: the right and left amygdala, as well as the right orbitofrontal cortex. We hypothesized that angry prosody would increase both early and late brain responses compared to neutral prosody. As expected, our results show that neuronal responses to angry prosody were enhanced early in the amygdala as well as later in the orbitofrontal cortex, compared to neutral prosody. These results are compatible with an early amygdala response to emotional prosody and a later neuronal modulation within the orbitofrontal cortex, highlighting a possible functional connectivity between these two key structures in the processing of emotional prosody.

## 1. Introduction

Decoding and understanding emotional expression carried by voice allows fast behavioral adjustment as well as successful social interactions (Scherer, 2003). Modulation of speech during an emotional process, the so-called emotional prosody, refers to segmental and supra-segmental changes in voice production (Grandjean, Bänziger, & Scherer, 2006). A corpus of data has pointed out the neural architecture as well as

the pathways underlying the processing of emotion conveyed by the voice. As part of this complex network, several studies using functional neuroimaging methods indicate an increase of amygdala activities in response to emotional prosody (Sander & Scheich, 2001; Fecteau & al., 2007) and more specifically for angry prosody (for example Grandjean & al., 2005; Sander & al., 2005; Ethofer & al., 2009). Moreover, some data indicate that the amygdala is involved in both explicit as well as implicit processing of emotional prosody, as Wilgruber and collaborators (2006) suggest in their model. Furthermore, some theories in the field of emotion postulate that the amygdala constitutes a structure designed to respond *quickly* to events rising in the environment and to trigger behavioral responses (Damasio, Adolphs & Damasio, 2003; LeDoux, 2000) in order to cope with a potentially threatening (Öhman & Mineka, 2001) or relevant (Sander & al., 2003) situation. However to our knowledge, there is no empirical evidence, using direct measures of electrical brain activity, which shows *when* the amygdala is mainly involved in emotional prosody processing. In addition, neuroimaging studies identify that the medial part of the orbitofrontal cortex responds to emotionally angry prosody processed with voluntary spatial attention (Sander & al., 2005). Although the precise acoustic features of voice driving OFC responses remain largely unknown, the Schirmer and Kotz model of emotional prosody processing proposes that OFC might mediate an explicit evaluation occurring *later* in the processing of the ongoing stimulus (Schirmer & Kotz, 2006).

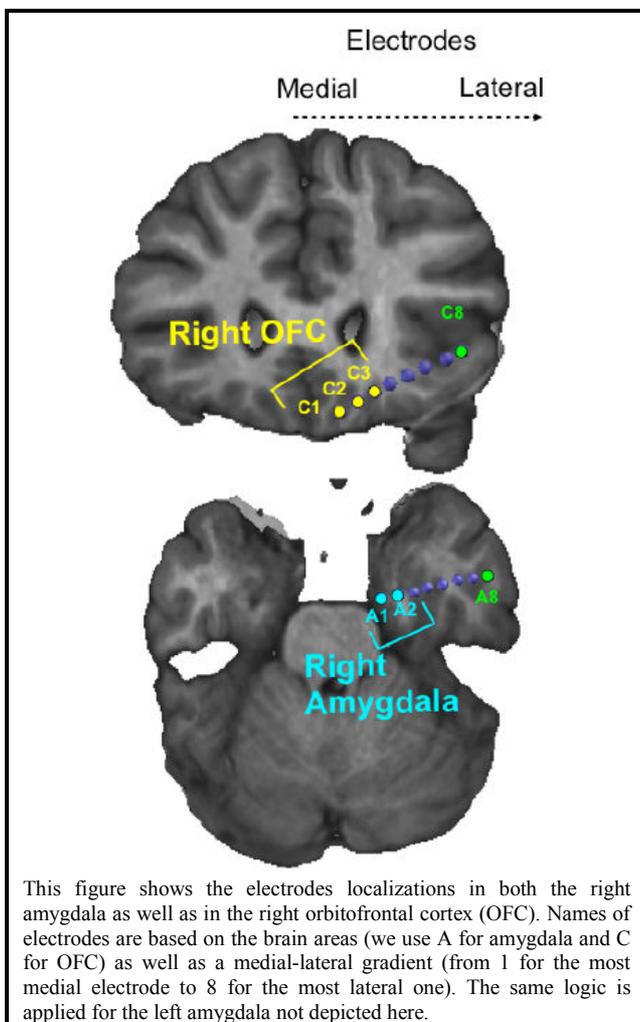
In order to investigate the implication of the amygdala *and* the OFC during emotional prosody processing, the aim of the present paper is to provide direct and temporally efficient measures of brain activity during this process, by using intracranial EEG. We hypothesize that *early* responses within the amygdala will be increased significantly for the processing of emotional

prosody compared to neutral prosody. In addition, we also propose that angry prosody will enhance the later brain activity within the orbitofrontal cortex compared to neutral voices.

## 2. Methods

### 2.1. Participant

Intracranial EEG signals were recorded in a 24 years old right-handed female that suffered from chronic and pharmaco-resistant epilepsy and who was candidate for a potential brain resection of a localized epileptic focus. For this clinical purpose, deep brain electrodes had been implanted in several parts of her brain in order to find out the exact cerebral location responsible for the triggering of the epileptic crises. In this study, the electrodes of interest were located in both right and left amygdala, as well as in the right medial part of the orbitofrontal cortex (see figure 1). During the time of



**Figure 1:** Electrodes localizations

her hospitalization, the patient accepted to take part in this experimental protocol and gave her informed

consent according to the ethic rules currently in place at the University Hospital of Geneva.

### 2.2. Stimuli

The vocal stimuli were extracted and modified from a database initially developed by Banse and Scherer (1996) and have already been judged and validated in different experimental contexts (Grandjean & al., 2005; Sander & al., 2005; Brosch & al., 2008, 2009), revealing an average accuracy of anger recognition of 75 %. These stimuli consist of short segments of meaningless speech (pseudo-words), obtained by the concatenation of different syllables of several Indo-European languages, such that they are perceived across different cultures as natural utterances with emotional intonation, but without any semantic content. In our study, we only selected two categories of stimuli of interest to us; the angry and the neutral prosody ones. Each experimental condition contained 60 stimuli, equally divided into three different utterances: «Figtleich», «Goster» and «Niuvenci». Male and female speakers were counterbalanced across both conditions as well as the lateralization of the sound's occurrence. All stimuli were also matched in terms of duration (750 ms) and mean acoustic energy in order to avoid low-level effects such as loudness or intensity effects.

### 2.3. Experimental design and procedure

This experiment was initially designed to investigate how the relation between emotional prosody and spatial attention could affect brain responses. Even though the notion of attention is beyond the scope of the present paper, it is mentioned here because it explains why we chose this experimental setting. In order to manipulate voluntary attention orthogonally to emotional prosody, we used a dichotic listening paradigm, in which two sounds were delivered simultaneously (one on each ear for each trial) and appeared in a pseudorandom order. The pseudo-words were presented in both ears, being either neutral on both sides (neutral / neutral), or angry on one side and neutral on the other (anger / neutral or neutral / anger). The participant selectively attended either to the left or to the right ear during 6 successive blocks of 60 trials each (4 times to the left side and 2 times to the right side), resulting in a total of 360 trials. The initial experimental setting only included 4 blocks, but due to technical problems, the experiment was rebooted after the participant had already finished the two first blocks. The task required the patient to focus her attention on one ear in order to perform a gender-decision task on the voice heard on the target side (see Grandjean & al., 2005 for further details). She was asked to reply, as fast as possible, on the last trial before she heard a tone signal (a bip). In order to reduce the impact of motor response on EEG recordings, the participant had to give a motor response only for 10 %

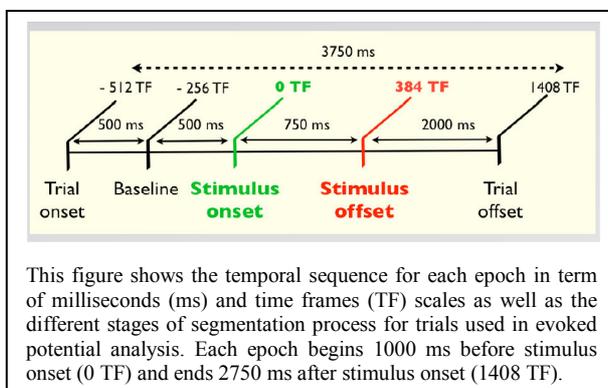
of the trials, randomly distributed during the experiment.

## 2.4 Data processing

The present study includes four experimental conditions taking into account two levels of factors: two Emotions (anger and neutral) and two Attentional directions (left and right ears). The condition under which the angry prosody is delivered in the ear to which the participant is paying attention is called *Anger Attended*. All emotional messages appearing on the side on which the patient is not focusing belong to the *Anger Unattended* condition. The *Anger* condition, which included all angry prosody trials, is based on the gathering of both *Anger Attended* and *Anger Unattended* trials. Finally, the condition only composed by neutral trials appearing on both sides is called *Neutral*. For the present paper, the analyses will only focus on the contrast between *Anger* and *Neutral* conditions.

### Intracranial EEG pre-processing

Intracranial Local Fields Potentials (LFP) were continuously recorded (Ceegraph XL, Biologic System Corps.) with a sample rate of 512 Hz in both right and left amygdala, as well as in the right orbitofrontal cortex. The reference electrode was located at position Cz and the ground at position FCZ in the 10–20 international EEG system. A “Notch” filter was applied in order to suppress 50 Hz as well as 150 Hz frequencies related to electrical artifacts. Then, data were segmented into epoch for each of the three brain areas of interest, from 1000 ms before target onset to 2750 ms after the stimulus onset occurred, resulting in a length of 3750 ms for each epoch (see figure 2). A baseline correction of 500 ms before the beginning of each trial was applied on EEG epochs. Few EEG epochs affected by epileptic crisis activity were excluded from our analysis. Finally, we randomly selected the same amount of epochs for both *Anger* and *Neutral* conditions, in order to prevent an effect related to a different number of trials. Also, data analysis included 96 epochs available for the left amygdala, 88 for the right amygdala, and 71 for the right orbitofrontal cortex.



**Figure 2:** Temporal sequence for each trial

### EEG analysis: Intracranial Evoked Potentials

In order to test our hypothesis, we computed intracranial evoked potentials (iERP) by using a non-parametric statistic based on permutations. First, we calculated the difference in terms of mean amplitude of signal between our two conditions of interest (Anger and Neutral). Then, we created two new artificial conditions, made by trials randomly picked up from both Anger and Neutral conditions. We then calculated the difference between these two new values. In order to create a distribution of mean differences, we repeated this procedure 1000 times. Using this distribution and fixing a level of significance at  $\alpha = .05$ , we were able to determine if the mean amplitude difference computed between Anger and Neutral conditions was significant or not for each measure point.

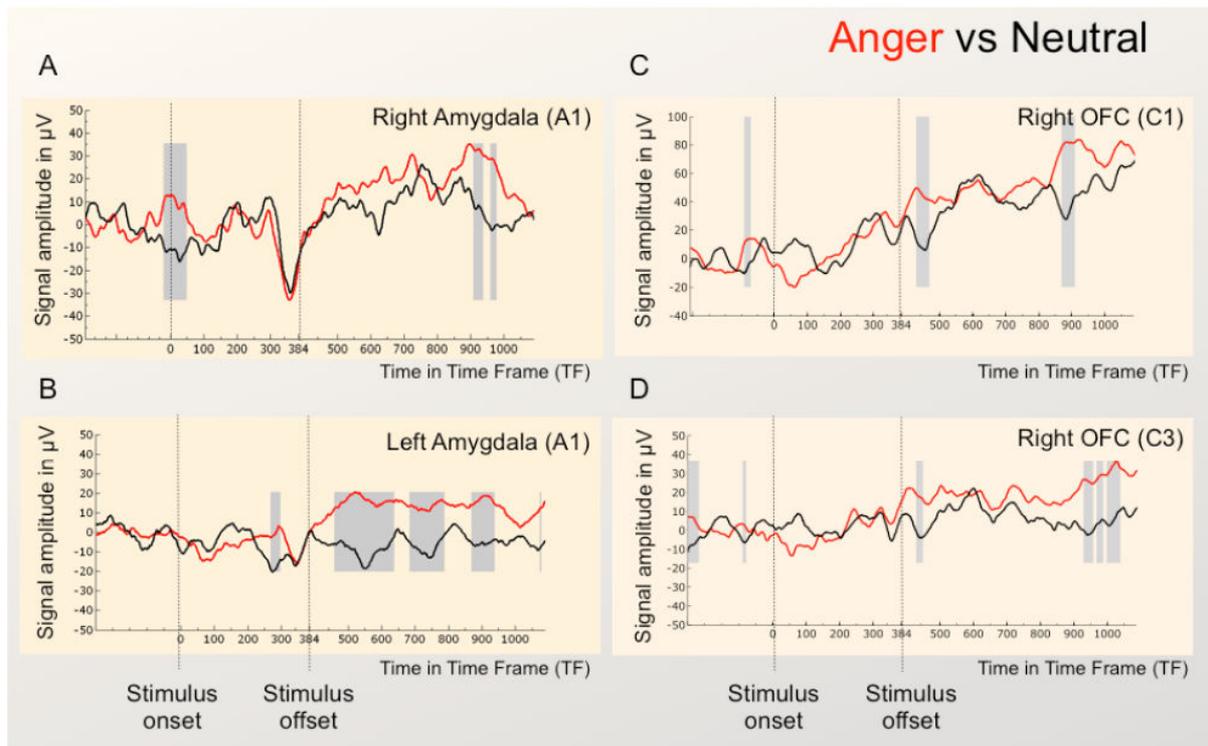
## 3. Results

### 3.1. Behavioral data processing: control analyses

In this study, we did not expect any differences in terms of reaction time between our conditions of interest, because the experimental setting only included a small amount (10 %) of behavioral responses. Descriptive analysis concerning the amount of mistakes indicates that the patient was able to identify the gender of the speaker 100 % of the times with *Neutral* trials, as well as 71 % with *Anger* trials. A chi-square test did not reach significance. This analysis reveals that the patient performed correctly the gender task.

### 3.2. Temporal dynamic of emotional processing modulates brain activity differentially

We hypothesized that angry prosody could increase early brain responses dedicated to the processing of angry prosody in both right and left amygdala compared to neutral vocal stimuli. Moreover, we expected that emotional prosody could enhance late brain activity in the right orbitofrontal cortex compared to neutral prosody. To test this couple of hypotheses, we used a method based on permutations in order to determine if the differences, in terms of mean amplitude observed between *Anger* and *Neutral* conditions, reach significance. Our results show that the processing of emotional prosody induces an early and systematic increase of ERP amplitude responses in the right amygdala ( $p < .05$ ). These results reveal that this brain area replies precociously to the emotional aspect contained in the vocal message, during a temporal window of 100 ms after the emotional stimulus onset (see figure 3, A). Furthermore, the amplitude of ERP is statistically increased in the left amygdala during the processing of angry prosody compared to neutral prosody, between 510 ms and 600 ms after the stimulus onset ( $p < .05$ ; see figure 3, B). Finally, differences were observed between these two conditions at and after the stimulus offset. In fact, late and massive responses, probably due to the emotional content of the voice, were



These four panels depicted mean differences in evoked responses amplitudes with time course in time frame (TF), for angry prosody (red line) compared to neutral prosody (black line). A: Responses of the right amygdala. B: Responses of the left amygdala. C and D: Responses of the right orbitofrontal cortex (OFC). Grey parts indicate time windows reaching significance ( $p < .05$ ) for the differences between *Anger* minus *Neutral* prosody. Dashed vertical lines indicate onset (0TF) and offset of the stimuli (384 TF).

**Figure 3:** Early and late brain modulations for the processing of emotional prosody compare to neutral prosody

found in the left amygdala ( $p < .05$ , see figure 3, B) as well as in the right medial orbitofrontal cortex ( $p < .05$ , see figure 3, C and D). These responses take place 880 ms after the onset of the stimulus. All together, these results confirm our two hypotheses concerning the presence of early modulation within the amygdala as well as a later one occurring in the right medial orbitofrontal cortex in response to emotional prosody.

#### 4. Discussion

In this study, a dichotic listening paradigm was used and local field potentials were recorded by means of deep brain electrodes in order to investigate how the temporal dynamics of emotion prosody processing can modulate brain activity in the amygdala as well as in the medial part of the OFC. Our results show that angry prosody increases brain activity early in the human left and right amygdala, and later in the medial part of OFC, compared to neutral prosody. These data provide the first evidence indicating that the processing of emotional prosody involves both amygdala and medial OFC, but that the temporal window remains a key characteristic that must be taken into account in order to understand different stages of emotional processing.

Moreover, our results support the idea that the amygdala is a structure involved in an early stage of emotional processing, contributing to detect potentially relevant (Sander & al., 2003) or threatening (Öhman & Mineka, 2001) information in the environment. The later brain activation observed in the medial OFC for angry prosody, similar to the effects reported in Sander and al. (2005) but without timing, might reflect higher processes either related to the cognitive evaluation of the stimulus (Schirmer & Kotz, 2006 ; Wilgruber & al., 2006). Further studies should be conducted in order to assess how the anatomical brain connectivity between the amygdala and the medial OFC (Ghashghaei, 2002; 2007) might underlie functional emotional prosody processing.

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