Neuronal synchronization during auditory emotional perception

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Abstract

The brain regions subserving the processing of emotional prosody have been investigated using functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) but few studies investigated direct electrical neuronal activity using intracranial recordings in humans. Previous studies have shown the involvement of the amygdala and the orbito-frontal cortex (OFC) in the processing of emotional prosody. In this paper we present first evidence of functional neuronal coupling between these two regions in response to different kinds of emotional prosody

1. Introduction

Several fMRI studies have shown an increase of amygdala activity in response to anger emotional prosody (Grandjean et al, 2005; Sander et al., 2005) and non linguistic emotional vocalizations (Fecteau et al., 2007). The involvement of OFC has also been demonstrated in fMRI studies in response to emotional prosody (Sander et al., 2005; Wildgruber et al., 2004). Moreover, the neuronal activity in this region was shown to correlate with inter-individual differences in sensitivity of reward-punishment; the more participants were sensitive to punishment (measured by the behavioral inhibition system; Carver & White, 1994) the more the neuronal activity of the medial part of the OFC was increased in response of anger emotional prosody when it was in the participant's attentional focus (Sander, et al., 2005). The relationship between these two regions, often reported being activated in response to emotional stimuli, is still not clear. In monkeys, anatomical connections between these two brain areas have been demonstrated (Cavada et al., 2000). Recent path analysis using a large corpus of fMRI data has confirmed the strong coupling between the OFC and the amygdala (Stein, et al., 2007). However, the functional correlates of these anatomical connections, particularly during the processing of emotional stimuli, are still not clear and require further studies to be understood.

In order to test the functional coupling between the amygdala and the different parts of the OFC in response to emotional prosody, we recorded local field potentials (LFPs) in patients prior to surgery for pharmaco-resistant epilepsy while they were instructed to listen to fearful, angry, sad or happy tone of voice, and matched control auditory stimuli.

To be able to test the neuronal dynamic coupling between the OFC and the amygdala, we systematically computed the neuronal synchronization between these two regions.

Neuronal synchronization has been conceptualized as the necessary minimal requirement, for two different neuronal assemblies, close or distant, to be able to exchange information. Fries has proposed the Communication Through Coherence (CTC) model to account for interactions between different neuronal assemblies (for a review see Fries, 2005), see Figure 1. Several studies have shown that *close* neuronal assemblies can be in a state of synchronization in the *high* frequency range, particularly for beta and gamma frequencies. Moreover, these synchronization episodes predicted the participants' performances (Womelsdorf, et al., 2006). In contrast, synchronization between *distant* neuronal assemblies has been shown for both lower (Guderian & Düzel, 2005) and higher frequency bands (Schoffelen, Oostenveld, & Fries, 2005). In the present study, the functional coupling between amygdala and OFC has been tested by computing neuronal synchronizations using phase signal information.

2. Methods

The LFP recordings were performed using depth electrode strips (8 contacts/strip) in two patients (PN and WS). The recording sites were defined only for clinical purpose and were based on previous EEG and MRI measures as well as clinical observations for each patient.

The patient PN had electrodes implanted into the left and right anterior temporal lobes including, for the medial contacts, the amygdala nuclei. Two other strips were implanted in the right and left frontal areas from the lateral to the medial part of these regions, see Figure 2A. The patient WS had electrodes implanted only in the right hemisphere in the anterior temporal lobe (including amygdala) and the OFC from the lateral to the medial part, see Figure 2B.

The stimuli were extracted from the Banse and Scherer database (Banse & Scherer, 1996) and were validated in several experiments (Grandjean, et al., 2005; Brosch, et al., in press). Their duration was 750 ms and they were presented binaurally. The participant had to perform a one-back task; they had to detect whether two successive stimuli were exactly the same by pressing a response button (10% of the stimuli were identical; these trials were excluded from further analysis in order to avoid the motor artifacts). For each emotional (fearful, happy, sad and angry) and neutral prosody 30 trials were presented. The trials with epileptic EEG discharges or other artifacts were excluded (mean of 26.4 valid trials by stimulus type). The LFPs have been analyzed using continuous wavelet transform (CWT); the phase shift has been computed for each frequency, for each trial and each type of prosody. The algorithm used to compute the phase synchrony has been described by Lachaux and collaborators (Lachaux et al., 1999); note that this measure is completely independent of the amplitude of the signal. The phase difference of the two signals (from the amygdala and from the OFC) has been computed at each frequency, at each time, and for each trial. Across the trials, the Phase Locking Value (PLV) was obtained for each point on the time-frequency space, see Figure 3.
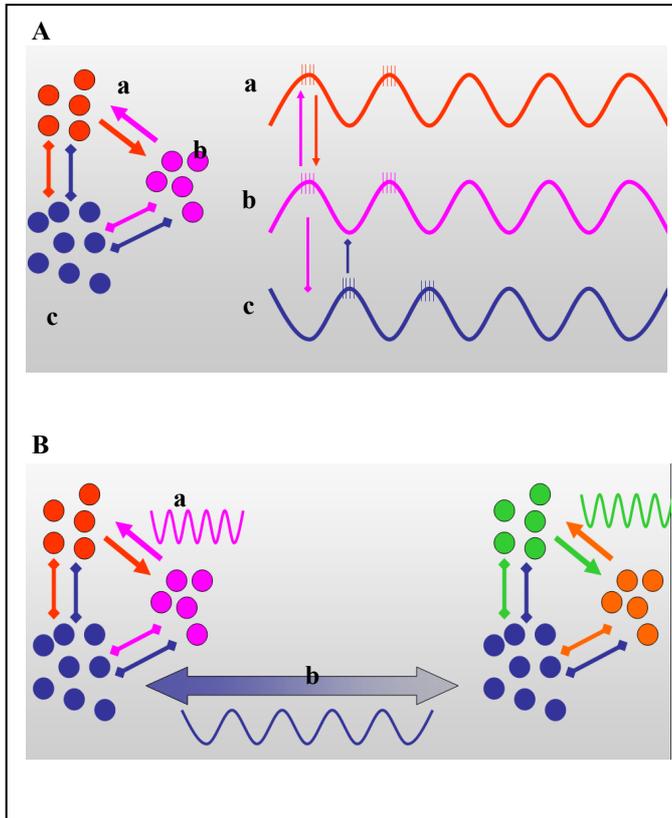
Figure 1: *The CTC model (Fries, 2005) specifies that the activity patterns of neuronal assemblies have to be in phase to be able to communicate. A) Given three groups of neurons which are anatomically interconnected; groups a) and c) are not able to communicate even though they are anatomically interconnected because their signals are not in phase, the phase shift preventing functional connectivity. Groups a) and b) are able to communicate due to a zero phase shift of their respective signals. B) Synchronization between close and distant neuronal assemblies. a) Close neuronal groups have been shown to synchronize in high frequencies (gamma and beta). b) The distant neuronal assemblies are more likely to interact in lower frequencies (Fries, 2005), for example in alpha or theta bands.*

The Phase Locking Statistics (PLS, see Lachaux et al., 1999) has been computed in order to test the significance of the neuronal synchrony at each point of the time-frequency space. Globally, the statistic tests the synchrony across trials between two regions versus the synchrony computed by shuffling the same trials (using permutations, a non parametrical statistical technique) for the different experimental conditions (e.g. neutral, anger). The second step of analysis consists of comparing the different experimental conditions (for example neutral versus anger) using permutations in order to test the significance of the differences between two experimental conditions in the different frequency bands. Synchronizations were computed also for different electrode pairs (for a given experimental condition), for example the amygdala-medial OFC contacts versus the amygdala-lateral OFC contacts. To illustrate the neuronal synchronization, the original signals were extracted and filtered in two different frequencies (6 and 11Hz) for anger and neutral prosody, see Figure 4.
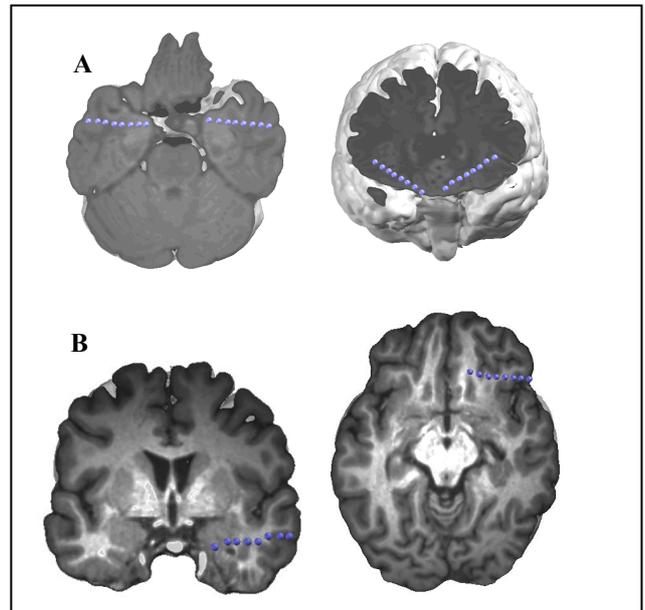

Figure 2: Illustration of *electrode strip placements in the patients' MRI. A) Patient PN with strips in the left and right hemispheres; in the anterior temporal lobe (panel left) and in the OFC (panel right). B) Patient WS with strips only in the right hemisphere in the temporal anterior lobe (panel left) and the OFC (panel right).*
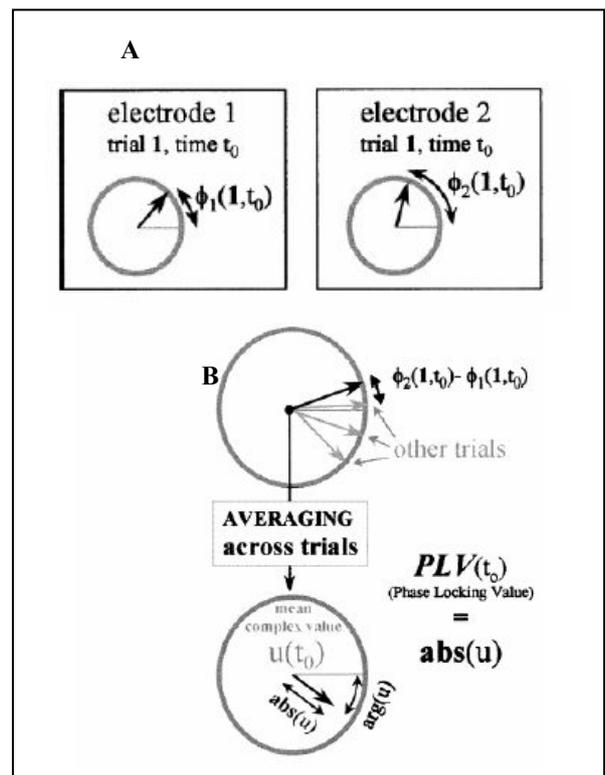

Figure 3: *Illustration of the computation of phase differences between two brain regions. A) The phase is computed for each region (e.g. amygdala[electrode 1] and OFC[electrode 2]), for each trial and at each time. B) The Phase Locking Value (PLV) is obtained by computing the differences of the phase between the region A (e.g. amygdala) and B (e.g. OFC) for all trials at each time period. Adapted from Lachaux and collaborators, 1999.*

3. Results

To summarize information in time-frequency space, the computations of neuronal synchronization between amygdala and OFC have been plotted in Figure 5. In this graph, the neuronal synchronization at low frequencies (from ~6 Hz to ~14 Hz) for anger prosody is apparent. A significant increase of neuronal synchronization in response to anger prosody compared to neutral prosody has been shown for several frequency bands.

This increase of synchronization is specific from 6.6 Hz to 9.5 Hz and from 12.4 Hz to 14 Hz for the patient PN ($p<.05$). To test the specificity of the medial part of the OFC, the neuronal synchronizations have been computed for the medial versus the lateral part of the OFC. This analysis has revealed a significant increase of synchronization for the medial part compared to the lateral part of the OFC for anger prosody.
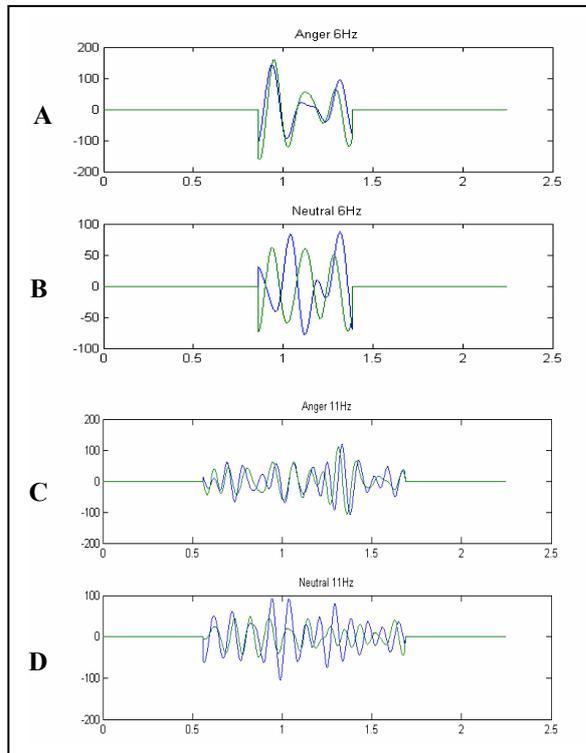

Figure 4: *Illustrations of the synchronization for real neuronal signals (green=amygdala and blue=OFC) extracted and filtered for the patient PN. A) Neuronal signals at 6Hz for anger prosody, the phase synchronization is readily apparent. B) Neuronal signals at 6Hz for neutral prosody, the shift of phase compared to A is clearly visible. C) Neuronal signals at 11Hz for anger prosody; again, phase synchronization is apparent. D) Neuronal signals at 11Hz for neutral prosody, the shift of phase is visible, particularly toward the end of the signal.*

These results are compatible with recent data for monkeys showing strongest anatomical and functional connections between the medial part of the OFC compared to the lateral part (Ghashghaei, et al., 2007).
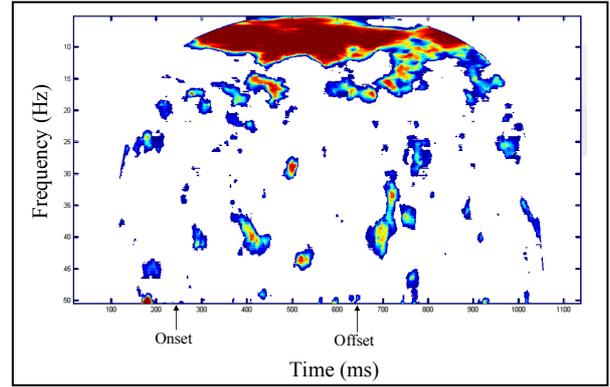

Figure 5: *Measure of synchronization (PLS) between amygdala and medial OFC for anger prosody in time-frequency space for patient PN. The significant synchronizations correspond to regions colored in red. An increase of synchronization in low frequency is apparent from the onset to the offset of the stimulus.*

In order to test the specificity of the intra-hemispheric amygdala-OFC coupling, the comparison between intra and inter-hemispheric synchronizations was computed. This analysis revealed significant differences for the intra-hemispheric comparison between anger and neutral prosody but no differences for the comparison of left amygdala and right medial OFC. Indeed, the coupling between amygdala and OFC is not only specific for the medial part of the OFC but this coupling is also specific for intra-hemispheric interactions.

The neuronal synchronization has been also tested for the unvoiced synthetic stimuli. These three different stimulus types were synthesized from the original sounds. Concretely, mean of F0, temporal dynamic of F0, and the envelope of original voiced sounds were computed and used to create the synthetic matched stimuli. Then, the neuronal synchronization was computed exactly as for the voiced stimuli. The comparison between these unvoiced stimuli, the neutral prosody, and anger prosody were computed. This analysis revealed an increase of neuronal synchronization for neutral voiced stimuli compared to the unvoiced stimuli indicating a functional coupling of these brain regions for human voices compared to synthetic stimuli, even if they are not characterized by emotional prosody.

4. Discussion

The joint involvement of the OFC and the amygdala in the processing of emotional prosody has been reported in several past fMRI studies. Moreover, anatomical connections between these two regions have been documented in monkeys and humans. However, the functional coupling of these two brain regions has never been directly investigated in humans. In the present study, using intracranial recordings, we have quantified the functional neuronal synchronization between amygdala and OFC. A significant increase of neuronal synchronization has been demonstrated between these two regions in response to anger prosody compared to neutral prosody or compared to synthetic sounds matched for different acoustical properties. This increase of neuronal synchronization has been demonstrated for two patients in the right and left hemispheres. This neuronal synchronization is

intra-hemispheric specific and restrained to the medial part of the OFC. Voiced neutral stimuli have induced an increase of neuronal synchronization compared to synthetic unvoiced stimuli. This functional coupling between amygdala and the medial part of the OFC may subserve the computation of the emotional content of the voice and the possible action tendencies which have to be selected for behavioral purposes. The synchronization increase for voiced stimuli compared to unvoiced ones would be an argument of the behavioral relevance of such stimuli for the listener. Indeed, human voices may have an appeal function and then provoke a complex computation taking into account the emotional characteristic of the voice and the possible adequate behaviors.

Further analysis and studies may investigate the neuronal synchronization for other emotional prosody types and the modulation of this functional coupling in function of the participant's task and the voluntary focus of attention.

5. References

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