Collins, Dawn R., J. Guillaume Pelletier, and Denis Paré. Slow and fast (gamma) neuronal oscillations in the perirhinal cortex and lateral amygdala. J Neurophysiol 85: 1661–1672, 2001. Most lesion studies emphasize the distinct contributions of the amygdala and perirhinal cortex to memory. Yet, the presence of strong reciprocal excitatory projections between these two structures suggests that they are functionally coupled. To gain some insight into this issue, the present study examined whether the close anatomical ties existing between perirhinal and lateral amygdala (LA) neurons are expressed in their spontaneous activity. To this end, multiple simultaneous recordings of single unit discharges and local field potentials were performed in the LA and perirhinal cortex in ketamine-xylazine anesthetized cats. The perirhinal cortex and LA exhibited a similar pattern of spontaneous activity. Recordings at both sites were dominated by a slow focal oscillation at 1 Hz onto which was superimposed a faster rhythm (≈30 Hz) whose amplitude fluctuated cyclically. Computing cross-correlograms between focal waves recorded simultaneously in the perirhinal cortex and LA revealed a close relationship between their spontaneous activity. Even when recording sites were separated by as much as 8 mm, the slow focal oscillation remained highly correlated ($r \geq 0.7$). In contrast, the correlation between fast oscillations was usually lower ($r \approx 0.3$). Perievent histograms of neuronal discharges revealed that the firing probability of most LA and perirhinal neurons increased during the depth-negative component of the slow oscillation. In addition, respectively, 47 and 64% of LA and perirhinal neurons exhibited a significant modulation of firing probability in relation to the fast oscillations. Finally, crosscorrelating unit discharges simultaneously recorded in the LA and perirhinal cortex confirmed the presence of phase-related oscillatory events in both structures. In summary, our results suggest that the interconnections existing between the perirhinal cortex and LA can support the genesis of coherent neuronal activities at various frequencies. These results imply that cooperative interactions must be taking place between these structures.

INTRODUCTION

In general, lesion studies emphasize the distinct role of the perirhinal (PRH) cortex and amygdala in memory. Indeed, PRH lesions were reported to interfere with recognition and associative memory in all sensory modalities tested so far (Buckley and Gaffan 1998; Buffalo et al. 1998; Eacott et al. 1994; Herzog and Otto 1997; Higuchi and Miyashita 1996; Meunier et al. 1993; Mumby and Pinel 1994; Suzuki et al. 1993; Zola-Morgan et al. 1989, 1991). Instead, these lesions were reported to interfere with classically conditioned fear responses (Davis et al. 1994; Kapp et al. 1992; LeDoux 2000), an issue that remains controversial (Cahill et al. 1999).

However, other findings suggest that the dichotomy between the role of the amygdala and PRH cortex is not absolute. For example, PRH lesions performed after classical fear conditioning reduce or abolish conditioned fear responses (Campeau and Davis 1995; Corodimas and LeDoux 1995; Kapp et al. 1992). In addition, much data suggest that the amygdala modulates the neural processes involved in the formation of declarative memory (Cahill et al. 2000; Cahill and McGaugh 1998). For instance, long-term explicit memory of emotionally arousing stories is enhanced compared with neutral ones, and this effect is abolished by amygdala lesions (Adolphs et al. 1997; Cahill et al. 1995). Moreover, brain-imaging studies have found a high correlation between long-term recall of emotionally arousing or neutral material and the amount of amygdala activation observed when these stimuli were first presented (Cahill et al. 1996; Canli et al. 1998; Hamann et al. 1999).

At present, it is unclear as to how the amygdala might modulate declarative memory. The reciprocal amygdalo-PRH connections (Krettek and Price 1977a,b; Russchen 1982) constitute an obvious possibility, but little is known about their physiology. Most amygdalocortical efferents stem from the basolateral (BL) amygdaloid complex (Krettek and Price 1977a,b), a group of nuclei including the lateral (LA), basolateral, and basomedial nuclei. Although each of these nuclei contributes a different set of cortical projections, amygdalocortical pathways always originate from spiny projection neurons (McDonald 1992a,b). These neurons have axon terminals that are glutamate-immunoreactive and form asymmetric (presumably excitatory) synaptic contacts, generally with spiny cortical cells (Paré et al. 1995; Smith and Paré 1994).

The cerebral cortex often reciprocates these excitatory projections (Russchen 1982). The prevalent amygdaloid targets of cortical axons are the BL spiny projection cells themselves (Brinley-Reed et al. 1995; Hall 1972; Smith et al. 2000). In contrast, BL inhibitory interneurons, at least those that display parvalbumin-immunoreactivity, receive virtually no cortical inputs (Smith et al. 2000). However, cortical axons can influ-
ence them indirectly, through the intranuclear axon collaterals of projection cells (Smith et al. 2000).

Thus the available ultrastructural evidence suggests that amygdalocortical projections are mainly excitatory, leading us to predict that reciprocally connected amygdala and cortical territories, such as the LA and PRH cortex, should display correlated neuronal activity. To test this hypothesis, we examined the activity of multiple simultaneously recorded neurons of the LA and PRH cortex. Consistent with our hypothesis, similar patterns of spontaneous neuronal activity were seen in the PRH cortex and LA, with neurons at both sites exhibiting phase-related oscillations in firing probability.

**METHODS**

**Surgery**

Experiments were conducted in agreement with ethical guidelines of the Canadian Council on Animal Care. Five cats (2.5–3.5 kg) were anesthetized with a mixture of ketamine and xylazine (11 and 2 mg/kg im). This species was chosen because the large size of the cat brain facilitates the placement of multiple microelectrodes within the amygdala and PRH cortex. The level of anesthesia was determined by continuously monitoring the electroencephalogram (EEG). Supplemental doses of ketamine-xylazine (2 and 0.3 mg/kg iv, respectively) were given to maintain a synchronized EEG pattern.

In three cats, the bone overlying the left amygdala and PRH cortex was removed on one side, and the dura mater was opened. Then, an array of 25 tungsten microelectrodes (2–6 MΩ at 1 kHz; outer diameter of 80 μm; FHC, Brunswick, ME), arranged in the configuration shown in Fig. 1A, was lowered stereotaxically until the electrodes reached the LA nucleus and the dorsal aspect of the PRH cortex (for details, see Collins and Paré 1999). In two other cats, only LA electrodes were implanted.

To construct the array, small holes were drilled in a circular Teflon block, and the electrodes were inserted into them. The length and position of LA and PRH electrodes was adjusted so that simultaneous recordings could be obtained from both structures. The Teflon block was inserted in a tightly fitting Delrin sleeve, which was cemented to the bone. The microelectrodes could be lowered as a group by means of a micrometric screw.

**Recording methods**

To ensure that we did not record the same cells twice, the electrode array was lowered 100 μm between each recording. All electrodes were examined for units with a high signal-to-noise ratio (≥3). Then the spontaneous activity of neurons with the highest signal-to-noise ratio (≥8 at a time) was recorded. The spontaneous activity of selected neurons was observed on a digital oscilloscope, printed on a chart recorder, digitized, and stored on tape. Data from neurons that were not held for the duration of the recording was discarded.

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**FIG. 1.** Microelectrode configuration and histological verification of recording sites. A: scheme showing the relative position of the microelectrodes (dots) and of the intended recording sites. The length and position of the electrodes was determined using stereotaxic coordinates. Perirhinal cortex (PRH) and lateral amygdaloid nucleus (LA) electrodes were spaced at 1- and 0.5-mm intervals, respectively. B–G: photomicrographs of thionin-stained coronal sections arranged from rostral to caudal. All sections were obtained from the same cat. Arrowheads point to small electrolytic lesions performed at the end of the experiments. Curved arrows indicate electrode tracks. BL, basolateral nucleus; BM, basomedial nucleus; CE, central nucleus; ENT, entorhinal cortex; EC, external capsule; H, hippocampus; OB, olfactory bulb; ON, optic nerve; OT, optic tract; rh, rhinal sulcus.
Identification of recording sites

At the end of the experiments, selected recording sites were marked with electrolytic lesions (0.5 mA for 5 s). Following this, the animals were given an overdose of barbiturate (pentobarbital sodium, 40 mg/kg iv) and perfused with 500 ml of a cold saline solution (0.9%) followed by 1 l of fixative, containing 2% paraformaldehyde and 1% glutaraldehyde in 0.1 M phosphate buffer saline (pH 7.4). The brains were later sectioned on a vibrating microtome (at 80 μm) and stained with thionin to verify the position of the recording electrodes. The microelectrode tracks were reconstructed by combining micrometer readings with the histological controls. Knowledge of the electrodes’ relative position allowed reliable determination of recording sites.

Analysis

Analyses were performed off-line with the software IGOR (WaveMetrics, Oregon) and home-made software running on Macintosh microcomputers. Spikes were detected using a window discriminator after digital filtering (0.3–10 kHz) of the raw waves. Focal waves were extracted by digital filtering (0–100 Hz) and analyzed by means of fast Fourier transforms (FFT), auto- and crosscorrelograms. In addition, we computed cross-correlation matrices for all sets of simultaneously recorded neurons. Perievent histograms of unit discharges were also computed with respect to particular focal events. All histograms were normalized so that the average bin value was 1. This measure ensured that the individual histograms had an equal weight when population histograms were constructed. It also facilitated comparisons between individual histograms.

RESULTS

Database

Overall, 56 groups of four to eight neurons were recorded in this study, a total of 348 cells. Histological controls (Fig. 1, B–G) revealed that 99 of these cells were recorded in the LA and 160 in the PRH cortex. These neurons constitute the basis of the present report. The spontaneous activity (0–10 kHz) of each cell group was recorded for ≥3 min. Neuronal discharges (0.3–10 kHz) and local field potentials (0–100 Hz) that were simultaneously picked up by the microelectrodes were disassociated off-line by digital filtering. Hereafter, the local field potentials will be referred to as focal waves or focal activity. Below, we will first analyze the temporal relation between the focal activity of the LA and PRH cortex and then examine coincident fluctuations in firing probability.

Relation between the focal activity of the LA and PRH cortex

Under ketamine-xylazine anesthesia, LA and PRH focal waves were dominated by a slow oscillation (0.8–1.7 Hz; Fig. 2A) as previously observed in the neocortex and thalamus (Steriade 1997). This oscillation usually occurred in trains of three to eight cycles that began and ended more or less synchronously at all sites. For example, in Fig. 2A note that epochs of high-amplitude slow oscillations seemed to occur simultaneously at all LA and PRH sites even though the distance between the most rostral (LA3) and caudal recording sites (PRH3) was 8 mm (Fig. 2B). This is in sharp contrast with the low correlation previously found between the PRH cortex and adjacent neocortical sites (see Fig. 4 in Collins et al. 1999).

FFT's of focal waves recorded in the LA (Fig. 2C1) and PRH cortex (Fig. 2C2) revealed a bimodal spectral composition: a peak at ~1 Hz, which reflects the slow oscillation and a second one, in the 20- to 35-Hz range. To determine whether there was a temporal relation between this faster activity and the slow oscillation, focal waves were filtered digitally between 20 and 35 Hz and compared with the full signal (Fig. 2D). In keeping with previous findings in the neocortex (Steriade et al. 1996), the amplitude of fast focal waves fluctuated cyclically. Epochs of high-amplitude fast activity coincided with the decaying negative component of the slow oscillation. Although this was more obvious in the PRH cortex than in the LA (Fig. 2D, compare PRH3 and LA1–2), statistical comparison of the 20- to 35-Hz power in the 0.4 s preceding versus following the negative peak of the slow oscillation (3 cats, 10 LA and 10 PRH sites each), revealed that the difference was statistically significant in both structures [Student’s paired t-test, P < 0.05; 76 ± 11.2 and 35 ± 6.3% (means ± SD) power increase in the PRH and LA, respectively].

Since visual inspection of the data suggested that there was a close temporal association between focal waves in the PRH cortex and LA, the focal activity of simultaneously recorded sites was crosscorrelated in the 0- to 2- and 20- to 35-Hz bands. This analysis revealed that correlation coefficients were significantly higher for the slow (S) oscillation than the fast (F) activity (Student’s paired t-test, P < 0.05) whether the signals were recorded simultaneously within the LA (S, 0.75 ± 0.053; F, 0.62 ± 0.036; n = 22), within the PRH cortex (S, 0.81 ± 0.023; F, 0.35 ± 0.016; n = 84), or in the LA and PRH cortex (S, 0.70 ± 0.023; F, 0.33 ± 0.049; n = 101). Note that the difference was less marked for correlations among LA sites presumably because the distance between the electrodes was shorter than in the PRH cortex (Fig. 1A).

In keeping with this, the correlation of the fast oscillation decreased as the distance between PRH recording sites increased. This point is illustrated in Fig. 3A, which plots the correlation coefficient as a function of distance between the recording sites for the slow (dark circles, upper curve) and the fast (empty circles, lower curve) focal waves. Moreover, representative examples of correlograms are shown for the slow (Fig. 3B) and fast oscillations (Fig. 3C), each with superimposed short (1 mm; thick line) and long (6 mm; thin line) inter-site distances. Note that distance had a negligible effect on the correlation of the slow oscillation but significantly reduced the correlation of fast activities (Student’s t-test, P < 0.05).

In contrast, correlation of fast oscillatory activity between LA and PRH sites did not show the same trend. Correlations varied highly, irrespective of the distance (overall average, 0.33 ± 0.049).

Fluctuations in firing probability related to the slow oscillation

Since the oscillation induced by ketamine-xylazine has been observed throughout the neocortex (reviewed in Steriade 1997), as well as in several subcortical structures (Mariño et al. 2000; Wilson and Kawaguchi 1996), it is conceivable that the focal activity described above is only an artifact due to volume conduction. However, this explanation would appear unlikely if the
focal oscillations were related to rhythmic fluctuations in the firing probability of LA and PRH neurons.

As shown in Figs. 4 and 5, most LA and PRH neurons exhibited robust variations in discharge rate, phase-related to the slow oscillation. Two examples of this are shown for LA (Fig. 4A) and PRH (Fig. 4B) cells, including raw data (Fig. 4, A, I and 2, and B1) and peri-event histograms (PEH) of neuronal discharges with respect to the negative peak of the focal slow oscillation (Fig. 4, A3 and B2). In both cells, note that the firing probability peaked during the negative phase of the focal slow oscillation, reaching 2.7 (Fig. 4A3) and 2.4 (Fig. 4B2) times the average firing probability, and was lowest during the preceding positivity (0.1 and 0.5 times the average firing probability, respectively).

This trend was not only observed in neurons with high firing rates (Fig. 4, A and B, 20.2 and 5.1 Hz, respectively) but also in slow firing cells (Fig. 5A, LA1-2, PRH1-3-4). Indeed as was previously reported in naturally sleeping animals, most amygdala (Bordi et al. 1993; Gaudreau and Paré 1996; Jacobs and McGinty 1971; Paré and Gaudreau 1996) and perirhinal (Collins et al. 1999) neurons fired at low rates under ketamine-xylazine anesthesia. Nevertheless, even in such neurons, visual inspection of the data revealed a clear increase in firing probability during the negative phase of the slow oscillation (Fig. 5A, LA1-2, PRH1-3-4). However, in contrast with more active cells, they did not fire with every cycle and often remained silent for several seconds. Overall, respectively, 82 and 76% of LA and PRH
neurons displayed such clear modulations of firing probability with respect to the slow oscillation.

To further examine the temporal relation between LA and PRH unit activity and the slow focal oscillations, PEHs of neuronal discharges were computed, normalized for firing rate and averaged (LA, Fig. 5B1, n = 15; PRH, Fig. 5B2, n = 20). Because it seemed evident that most LA and PRH neurons behaved similarly with respect to the slow oscillation, only cells having a signal to noise ratio > 6 and a firing rate of ≥1 Hz were selected for this analysis. The difference between the firing probability associated to the peak positive and negative focal waves averaged 3.7 (LA, Fig. 5B1) and 3.9 (PRH, Fig. 5B2) times the respective standard deviation (SD) of bin values.

**FIG. 3.** Effect of distance between recording sites on the correlation between fast and slow focal waves. A: graph plotting the correlation coefficient (y axis) as a function of distance between PRH recording sites (x axis) for slow (dark circles) and fast (empty circles) focal oscillations. B and C: 2 superimposed correlograms of slow (B) and fast (C) oscillations with inter-site distances of 1 (thick line) and 6 mm (thin line).

**FIG. 4.** Relation between unit discharges and slow focal oscillations in the LA and PRH cortex. A: unit activity and superimposed focal activity recorded in the LA displayed with a slow (A1) and a fast (A2) time base. A3: perievent histogram (PEH) of neuronal discharges for the same cell. B1: unit activity and superimposed focal waves recorded in the PRH cortex. B2: PEH of neuronal discharges for the cell shown in B1. In A3 and B2, the negative peak of digitally filtered slow oscillations was used as *time 0*. In both histograms, the binwidth is 20 ms. nS, number of spikes; nR, number of references (or peaks).
Fluctuations in firing probability related to the fast oscillation

As the relation between the fast oscillations and unit discharges seemed more variable, we computed PEHs of neuronal discharges for all available cells. To ensure that we limited our observations to epochs of high-amplitude fast activity, we considered only negative gamma peaks with an amplitude higher than 1.5 times the SD of the entire epoch after digital filtering of the data (20–35 Hz).

To determine whether the firing modulation evidenced in these histograms was statistically significant, the histograms were smoothed with a moving average of 3. The maximal peak to trough difference found within half a gamma cycle next to the origin was divided by the SD of the entire histogram. The modulation was considered significant when the peak to trough difference was >2.5 SD.

Overall, respectively 47 and 64% of LA and PRH neurons exhibited a significant modulation of firing probability with respect to the fast oscillations. Figure 6 shows examples of LA (Fig. 6A) and PRH (Fig. 6, B and C) neurons that exhibited significant firing modulations, including raw data (Fig. 6, left) and corresponding PEHs (Fig. 6, right).

Of the cells exhibiting a significant firing modulation, most increased their firing probability in relation to the negative

**FIG. 5.** The firing probability of LA and PRH neurons with low discharge rates is also modulated by the slow oscillation. A1: 6 simultaneously recorded LA and PRH neurons. There are 2 traces for each recording site: the focal waves (extracted by digital filtering) and the output of the spike window discriminator. A2: scheme showing the position of recording sites. B: population PEHs of LA (B1) and PRH (B2) neuronal discharges using the negative peak of focal slow oscillations as time 0. The binwidth is 20 ms. Calibration bars in A1 correspond to 0.5 mV and 2 s. n, number of cells.
phase of focal gamma waves (Fig. 6, A and B; histogram peak within ±45° of the origin; LA, 100%; PRH, 87%). However, in the PRH cortex, we identified a subgroup of cells (13%) whose firing probability was lowest in relation to the negative phase of focal gamma waves (Fig. 6C). This difference did not reflect dissimilarities in the depths at which these cells were recorded as neurons with the typical phase relation were recorded subsequently along the same electrode tracks.

Temporal relation between the activity of LA and PRH neurons

As the preceding analyses suggested that the PRH cortex and LA exhibit a similar pattern of spontaneous activity, we next examined temporal relations between the discharges of simultaneously recorded neurons. To this end, cross-correlation histograms were computed for all simultaneously recorded cell pairs, and the statistical significance of the firing modulation was assessed using the approach described above for the PEHs (peak to trough difference >2.5 times the corresponding SD of bin values: 5.35, 8.02, and 5.38 times the SD for A2, B2, and C2, respectively).

With a low temporal resolution (50-ms bins), respectively 61 and 29% of cell pairs simultaneously recorded in the LA (n = 141) or PRH cortex (n = 236) exhibited significantly correlated activity. As was seen with the focal waves, note that the lower proportion of significant relations observed in the PRH cortex probably reflects the longer distance between recorded neurons. Consistent with this, the proportion of significant PRH cross-correlations climbed to 47% when we considered only cells recorded within ±2 mm of each other (n = 132).

Representative examples of significant cross-correlations are shown in Fig. 7, including ones where the peak was close to the origin (LA, Fig. 7A, I and J; PRH, Fig. 7B, I and 2) and others

![Fig. 6. Gamma-related modulation of firing probability in the LA (A) and PRH cortex (B and C). Left: unit discharges and fast focal activity recorded simultaneously by the same microelectrode. Right: PEH of neuronal discharges (1-ms bins) using the negative peak of gamma waves as time 0. In these 3 histograms, the peak-to-trough difference found closest to the origin was >2.5 times the corresponding SD of bin values (5.35, 8.02, and 5.38 times the SD for A2, B2, and C2, respectively).](image-url)
that were clearly offset (LA, Fig. 7A2; PRH, Fig. 7B3). Also, note that we illustrated pairs of neurons whose firing rates varied tremendously (see details in figure legend).

Overall, 29 and 32% of significant crosscorrelograms had peaks centered on the origin (interval ≤2 bins) in the LA and PRH cortex, respectively. Nevertheless, the average interval between the origin and the peak was less than the binwidth (−35 ± 44.7 and −42 ± 52.3 ms for pairs of LA or PRH cells, respectively). As shown in Fig. 7, many of the significant crosscorrelograms exhibited regularly spaced peaks and troughs with a period of ≈1 s (LA, 78%; PRH, 73%), as expected for neurons exhibiting a slow phase-locked oscillation in firing probability.

Cross-correlations between pairs of simultaneously recorded LA and PRH cells (n = 335; Fig. 7C) yielded results similar to those obtained with pairs of PRH cells. Thirty-eight percent of crosscorrelograms reached significance, but the proportion climbed to 49% when we considered only PRH cells located within 2 mm of the amygdala in the rostrocaudal axis (n = 101). Overall, 23% of significant correlograms had a peak centered on the origin (distance to origin ≤2 bins). Nevertheless the absolute interval between the origin and the peak averaged −32 ± 56.2 ms. Thus although there were significant variations in spike timing among LA, PRH, and LA-PRH cell couples, as a group they fired roughly in phase.

Since LA and PRH neurons have low discharge rates (LA, 0.9 ± 0.22 Hz; PRH, 1.1 ± 0.17 Hz), repeating the preceding analysis with 2-ms bins yielded histograms with very few counts. Thus cross-correlations were carried out for all cell pairs, and normalized averages were computed for each animal and as a group. In all the cases discussed below (with the exception of Fig. 8A3), the amplitude of the central peak was >2.5 times the corresponding SD (see figure legend for exact values). To quantify the importance of the firing modulation evidenced in these correlograms, the amplitude of the three central peak to trough differences was averaged. Because spike counts for each histogram had been normalized so that the bin values averaged one, the resulting modulation index (MI) allowed comparison between histograms.

In the PRH cortex, crosscorrelograms varied with the distance between recorded cells (compare Fig. 8A, 1–3). With short distances (Fig. 8A1, 1 mm), the population crosscorrelogram exhibited a peak centered on the origin flanked by regularly spaced peaks and troughs (interval ≈28–34 ms), indi-
cating a synchronized modulation of firing probability in the gamma range (MI = 0.48). However, the amplitude of this firing modulation diminished quickly as the distance between recorded cells increased to 2 (Fig. 8A2; MI = 0.25) and 3 mm (Fig. 8A3; MI = 0.18).

Because LA neurons were recorded within 1.5 mm of each other (Fig. 1A), all crosscorrelograms were averaged (Fig. 8B). However, within each pair, the most lateral and/or rostral neuron was always used as the reference cell. Note that the peak of the population crosscorrelogram is offset to the right by 8 ms (Fig. 8B), indicating that the reference cells tended to fire before the test cells. This is consistent with the lateromedial trajectory of intra-amygdaloid pathways in the cat (Krettek and Price 1978; Smith and Paré 1994). However, the rhythmicity apparent in this crosscorrelogram (Fig. 8B) was weaker (MI = 0.44) and less regular (interval between peaks ranged between 16 and 30 ms) than that observed between closely spaced PRH cells (Fig. 8A1).

No effect of distance between recording sites was noted when LA and PRH unit activities were crosscorrelated (data not shown). However, this analysis revealed inter-cat variability in the amount and frequency of the gamma rhythmicity. In one animal, crosscorrelating LA and PRH unit activity yielded a population histogram with prominent gamma rhythmicity (Fig. 8C1; MI = 1.31). In the other two cats, the rhythmicity was weaker (MI < 0.3) and irregular (interval between peaks ranged between 12 and 24 ms). Figure 8C2 illustrates the average of all histograms for the three cats (MI = 0.28).

**DISCUSSION**

The present study was undertaken to determine whether the close anatomical ties existing between the LA and PRH cortex (Krettek and Price 1977b; Russchen 1982) are expressed in their spontaneous activity. The main findings can be summarized as follows. First, the PRH cortex and LA exhibit a similar pattern of spontaneous focal activity: a slow oscillation onto which a fast (20–35 Hz) rhythm is superimposed. Second, the slow focal oscillations are highly correlated even when the recording sites are separated by as much as 8 mm. In contrast, the correlation of fast oscillations is generally lower and, in the PRH cortex, decreases steeply with distance. Fourth, LA and PRH neurons display a significant modulation of firing probability in relation to the slow and fast focal oscillations. Last, they exhibit rhythmic phase-related changes in discharge probability that are strongest for the slow rhythm.

Thus our analysis suggests that there are close functional links in this amygdalocortical circuit, consistent with the strong reciprocal connections evidenced in tract tracing studies.

**Origin of the oscillatory activity recorded in the LA and PRH cortex**

**SLOW OSCILLATION.** The slow oscillation was first described in the neocortex of anesthetized cats (Steriade et al. 1993b) and, later, during slow-wave sleep in cats (Steriade et al. 1996) and humans (Acherman and Borbély 1997). Consistent with our findings, the slow neocortical oscillation is comprised of a depth-negative phase coinciding with an increased firing rate in all classes of cortical cells, and a depth positive one associated with neuronal silence (Steriade 1997). Moreover, this oscillation also occurs in subcortical structures such as the thalamus and striatum (Mariño et al. 2000; Steriade et al. 1993a; Wilson and Kawaguchi 1996), but it is dependent on cortical inputs (Timofeev and Steriade 1996).

These findings raise the possibility that a common cortical input to the LA and PRH cortex contributes to synchronize their slow oscillatory activity. At odds with this hypothesis, however, only a weak correlation was found between the slow PRH and neocortical oscillations (Collins et al. 1999, Fig. 4), much lower than that found here between the PRH cortex and LA. This difference is unlikely to be an artifact due to volume conduction since in this earlier study (Collins et al. 1999), neocortical sites separated by as much as 20 mm (areas 4 and 22 for example) displayed phase-locked slow oscillations at various frequencies, whereas the activity of PRH and neocortical sites recorded within 6 mm of each other showed little coherence (Collins et al. 1999, Fig. 4). The lower correlation found between neocortical and PRH sites compared with LA-PRH sites is interesting because it suggests that the LA and
PRH cortex constitute a functional system, somewhat independent of the neocortex.

Thus our results are consistent with the notion that synaptic coupling within, as well as between, the LA and PRH cortex plays an important role in synchronizing their slow oscillatory activity. In this context, it should be mentioned that in addition to their reciprocal connections (Krettek and Price 1977b; Rusalchen 1982), the LA and PRH cortex are endowed with a profuse system of intrinsic connections (Krettek and Price 1978; Smith and Paré 1994; Witter et al. 1986), which probably facilitates the emergence of synchronized neuronal activity.

**FAST (GAMMA) OSCILLATIONS.** Fast oscillations have been observed in numerous cortical and subcortical sites, behavioral states, and species (Steriade 1997; Traub et al. 1998). While the fast oscillations occur spontaneously under anesthesia and during slow-wave sleep (Steriade et al. 1996), they have also been implicated in cognitive, perceptual and attentional processes (Gray 1999; Koch and Crick 1991; Llinás and Ribary 1992; Singer and Gray 1995).

In the neocortex and hippocampus, fast oscillations represent a complex network phenomenon emerging from the intrinsic membrane properties (Gray and McCormick 1996; Llinás et al. 1991; Steriade et al. 1996; Traub et al. 1996) and connections of constitutive neurons (reviewed in Traub et al. 1998). Mounting evidence suggests that the divergent projections of inhibitory interneurons to principal cells play a critical role in synchronizing fast oscillations (Buhl et al. 1998; Buszaki and Chrobak 1995; Cobb et al. 1995; Fisahn et al. 1998; Tamás et al. 2000; Traub et al. 1996). Indeed interneurons are coupled by chemical synapses (for instance, see Cobb et al. 1997; Kisvárdy and Eysel 1993; Tamás et al. 1997, 1998) and gap junctions (Galaretta and Hestrin 1999; Gibson et al. 1999). As a result, in conditions of afferent excitation, interneurons would generate synchronized GABA\(_A\) inhibitory postsynaptic potentials (IPSPs) in thousands of pyramidal cells, thus entraining them to fire preferentially on the decaying phase of IPSPs in phase with the local field potential.

The presence of fast oscillations in the amygdala and PRH cortex (present study) adds to the wealth of data indicating that the gamma rhythm is widespread in the CNS. Moreover, as was found in the neocortex of anesthetized cats (Steriade et al. 1996), the amplitude of fast LA-PRH oscillations fluctuated cyclically, their amplitude being highest during the negative phase of the slow oscillation, when most cortical cells are depolarized (Steriade 1997).

Although fast cortical rhythms can be synchronized over large distances in some stimulation paradigms (Desmedt and Tomberg 1994; Gray et al. 1989), their coherence decreases rapidly with distance in spontaneous conditions (Bullock and McClune 1989; Murthy and Fetz 1992; Steriade et al. 1996). Our results are also consistent with this pattern; clear evidence of correlated firing in the gamma band was only seen between closely spaced PRH neurons.

However, the approach used here to compensate for low firing rates (i.e., averaging crosscorrelograms) greatly reduced the likelihood of obtaining positive results. Indeed, the gamma frequency changes from moment to moment in spontaneous conditions. Moreover, Faulkner and Brown (1999) have reported that a high proportion of perirhinal neurons are endowed with a K\(^+\) conductance that delays firing onset on depolarization, thus blurring the peaks and valleys that correlated rhythmic activity might have produced.

Since the firing probability of PRH and LA neurons fluctuated rhythmically in relation to focal gamma waves, the possibility remains that these fast oscillations transiently synchronize subsets of connected LA and PRH cells. After all, the presence of a peak to the right of the origin in the population crosscorrelogram of LA-PRH couples (Fig. 8C2) is consistent with the existence of monosynaptic links between some of these simultaneously recorded neurons.

In conclusion, the present study adds to the body of data indicating that the LA and PRH cortex engage in cooperative interactions. Indeed, the presence of phase-related neuronal oscillations in these structures suggests that they are functionally coupled. This is in agreement with anatomical data indicating that the LA and PRH cortex are reciprocally connected by excitatory glutamatergic connections. Moreover, our observations concur with behavioral data showing that LA or PRH lesions affect performance on tests of declarative and non-declarative memory. Thus, it will be important to examine the nature of LA-PRH interactions in behaving animals presented with sensory stimuli whose affective valence will be manipulated.

Recent results suggest that the conduction time from the amygdala to the PRH cortex is constant irrespective of distance (J. G. Pelletier, D. Paré, unpublished observations). Thus we hypothesize that afferent activation of the LA results in a synchronized depolarization of PRH neurons located at various rostrocaudal levels. As a result, coincident but spatially distributed inputs of the same or different sensory modalities will become suprathreshold in the PRH cortex. Moreover, because LA axons (Smith and Paré 1994) and long-range intrinsic PRH axons (Martina et al. 2000) do not contact inhibitory PRH interneurons, these events should promote N-methyl-D-aspartate-dependent synaptic plasticity (Bilkey 1996; Bliss and Collingridge 1993; Malenka and Nicoll 1993). Ultimately, the links between PRH neurons representing different aspects of coincident sensory patterns will be reinforced. In this manner, the LA could facilitate associative processes in the PRH cortex.

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