Limbic Gamma Rhythms. I. Phase-Locked Oscillations in Hippocampal CA1 and Subiculum

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Colling, Simon B., Ian M. Stanford, Roger D. Traub, and John G. R. Jefferys. Limbic gamma rhythms. I. Phase-locked oscillations in hippocampal CA1 and subiculum. J. Neurophysiol. 80: 155–161, 1998. Gamma oscillations (~40 Hz) were induced in transverse hippocampal slices by tetanic stimulation of CA1 and/or subiculum. Tetanic stimulation of each site elicited population gamma oscillations in the surrounding tissue <400 μm away. Stimulation of CA1 alone could evoke activity at both CA1 and subiculum. Subicular stimulation, however, did not transmit to CA1. When the rostral end of CA1 was stimulated, gamma oscillations transmitted across ~1.5 mm of silent CA1 before reappearing in the subiculum. Tetanic stimulation of CA1 increased [K⁺]o to 8.2 ± 1.5 mM (mean ± SE). The location of the peak increase corresponded to the site of local gamma generation. Silent areas of CA1 experienced smaller [K⁺]o increases, to 4.9 ± 0.7 mM. The subiculum, which generated gamma, remained at the baseline 3.0 mM. Although fluctuations in [K⁺]o may have an impact on the generation of gamma rhythms, they are not necessary for them. Gamma oscillations had similar frequencies in CA1 and subiculum (40.4 ± 2.9 and 43.9 ± 3.1 Hz, respectively). When present in both, the oscillations typically were phase locked with the subiculum lagging by 5.4 ± 1.8 ms. When both CA1 and subiculum were stimulated the lag decreased by 28%. These delays approximate those expected for the conduction velocity of axons between the two regions, here estimated at 0.52 ± 0.07 m/s. Transmission of gamma oscillations from CA1 to subiculum was blocked by the focal addition of the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid-receptor antagonist, 6-nitro-7-sulfamoylbenzo[f]quinoloxaline-2,3-dione, to the subiculum. Oscillations induced in CA1 by local tetanic stimulation were blocked by focal application of the γ-aminobutyric acid-A (GABA₆) receptor antagonist, bicuculline, to CA1. Focal application of bicuculline to the subiculum blocked gamma due to subicular stimulation but not that due to CA1 stimulation. Bath-applied bicuculline disrupted subicular gamma evoked by subicular stimulation and led to a transient period of epileptiform responses before completely blocking responses. The further addition of the GABA₆ receptor antagonist, CGP 55845A, reversed this block, restoring the epileptic discharges evoked by tetanic stimulation. This suggests that the subiculum differs from hippocampal CA3 and neocortex, in having a powerful GABA₆ receptor-dependent mechanism to prevent epileptic discharges. The subiculum generates gamma rhythms both in response to local stimulation and to gamma rhythms evoked in CA1. Subicular gamma differs from that in CA1 in the presence of population spike doublets rather than singlets on many cycles. In both areas, generation of gamma by local stimulation depends on GABA₆ receptors, suggesting that the subiculum shares the interneuronal network mechanism we proposed for CA1.

INTRODUCTION

We have shown previously how gamma rhythms (20–80 Hz) can be induced in the hippocampal CA1 region in vitro by a mechanism dependent on networks of inhibitory neurons and how such rhythms can remain synchronized, with near zero phase lag, over distances ≤4.5 mm (Jefferys et al. 1996; Traub et al. 1996a; Whittington et al. 1995, 1997a). Our goal here is to investigate how gamma rhythms can become coupled in two separate regions, specifically CA1 and the subiculum. The subiculum occupies a strategic location in the output pathways from the hippocampus to other cortical areas and the hypothalamus (Amaral and Witter 1989). There is evidence that it operates in concert with the hippocampus proper. For instance, synchronous activity propagates from hippocampal CA3 to CA1 and subiculum during physiological sharp waves (Chrobak and Buzsáki 1994), and theta rhythms can be phase locked across these regions (Buzsáki et al. 1986; Chrobak and Buzsáki 1994).

Neocortical gamma rhythms have been implicated in the binding problem, which concerns the mechanism for association of individual sensory features into the perception of whole objects (Singer and Gray 1995; von der Malsburg and Schneider 1986). The main evidence for their role in binding is their temporal synchronization (when recorded as units or as local field potentials) in visual areas responding to various aspects of a common object. This synchronization can be tight, with phase lags of ~1 ms over distances of 7 mm within one hemisphere of the cat or across the corpus callosum (Engel et al. 1991). Longer phase delays sometimes can be observed in the visual neocortex during the presentation of a bar; such phase delays may encode how strongly cells are excited (Konig et al. 1995; Traub et al. 1997).

The role of gamma rhythms in the limbic system is unclear. In vivo, spontaneous gamma rhythms occur during the theta state, both in hippocampus proper and in the hilus, where they are synchronized over a considerable portion of the septo-temporal extent of the hippocampus (Sik et al. 1995; Ylinen et al. 1995). In vitro, gamma oscillations tetanically induced in the CA1 region have been shown to induce long-lasting synaptic plasticity, which in turn influences the synchronization of oscillatory sites separated by a few millimeters (Whittington et al. 1997b). This finding is of particular interest as the hippocampal-subicular-entorhinal system has been implicated in learning and memory (Zola-Morgan et al. 1989). These data have motivated the present study of how gamma activity in one limbic region induces gamma in another and of the mechanisms determining phase relations between, and firing patterns within, the respective oscillating regions.
METHODS

A total of 46 adult male Sprague-Dawley rats (250–300 g) were anesthetized by intraperitoneal injection of medetomidine hydrochloride (Domitor; 1 mg/kg; SmithKline Beecham) and ketamine hydrochloride (Vetalar; 100 mg/kg; Parke-Davis Veterinary) before being killed by cervical dislocation. Their brains were removed to cooled (<3°C), oxygenated, artificial cerebrospinal fluid (ACSF) and bisected along the midline, and 400-µm sagittal slices were cut from the dorsal hippocampus using a Vibroslice (Campden Instruments, Loughborough, UK). The slices were maintained in an interface recording chamber perfused with ACSF at 32–35°C and oxygenated with 95%O2-5%CO2. The composition of the ACSF was (in mM) 135 NaCl, 16 NaHCO3, 1.25 NaH2PO4, 3 KCl, 2 CaCl2, 1 MgCl2, and 10 glucose, pH 7.4.

For our present purpose, we will not divide the subicular area into its component parts; we note that the work was performed in the subiculum proper and perhaps also in the prosubiculum, but this has not been confirmed histologically. Bipolar metal stimulating electrodes (insulated 80/20 Ni/Cr wire, 0.05-mm-diam metal) were used to evoke gamma rhythms in the pyramidal cell regions of CA1 and the subiculum by tetanic stimulation (50 µs, 70–90 V square wave pulses, at 100 Hz, for 200 ms). The CA1 stimulating electrode was placed in the stratum radiatum at the rostral (CA2 end) of CA1, within 100 µm of the pyramidal cell layer. The subiculum recording electrode was positioned at a corresponding level typically >1.5 mm away from the CA1 electrode and >0.5 mm caudal to the end of the distinctive CA1 pyramidal cell layer. Extracellular glass electrodes, filled with 3 M NaCl (4–8 Ω), were used to measure gamma rhythms from various locations along the CA1 pyramidal cell layer and at a similar laminar level within the subiculum. Extracellular potassium concentration ([K+]) was measured using single-barreled K+-sensitive electrodes (Heinemann et al. 1977). Silanized, thick-walled, glass micropipettes (1–2 MΩ) were filled with 100 mM NaCl and 5 mM KCl. The tip was then filled with the potassium ionophore I cocktail B (Fluka, Buchs, Switzerland). These electrodes had resistances of 1–10 GΩ. Electrodes were accepted if they showed a response of ≥45 mV for a 10-fold change in [K+]o. They were calibrated by measuring the voltage change for the following K+ concentrations: 3, 5, and 10 mM.

Drugs used to investigate gamma rhythms included bicuculline methiodide (BMI, 30 µM; Sigma), 6-nitro-7-sulfamoylbenzo[f]1,5-quinoxaline-2,3-dione (NBQX, 20 µM; Tocris Neuramin), and CGP 55845A (5 µM; kind gift of Ciba Geigy). For focal application, drugs were loaded into the tips of broken micropipettes at 1,000 times the dose used for bath application applied to the hippocampus by diffusion from the pipette tip placed on the surface of the slice.

The recording system included an Axoclamp-2A (Axon Instruments, Burlingame, CA) amplifier, Digitimer (Welwyn Garden City, UK) filters and a CED 1401-MSDOS computer system. The signal was low-pass filtered at 2 kHz, digitized at 5 kHz, and recorded and analyzed using SIGAVG and SPIKE2 software (Cambridge Electronic Design, Cambridge, UK). Data are presented as means ± SE.

RESULTS

Gamma rhythms evoked in CA1; conduction to subiculum

Gamma rhythms were evoked reliably in the CA1 pyramidal cell layer of healthy slices by trains of 20 stimuli at 100 Hz delivered to s. radiatum adjacent to the pyramidal layer as long as the repetition rate was every 80+ s. Faster repetition could cause epileptiform responses or spreading depression. Hippocampal gamma rhythms evoked in this way consisted of a train of population spikes. The peak amplitude was normally recorded within 200 µm of the CA1 stimulating electrode at a frequency of 40 ± 17 (SE) Hz (data from 38 slices). The amplitude of these oscillations decreased at increasing distances from the stimulating electrode, and the oscillations typically disappeared at ~600 µm (Fig. 1).

However, gamma oscillations reappeared in the subiculum (>1,500 µm from the stimulating electrode; Fig. 1) and had frequencies comparable with those in CA1 (43.9 ± 3.1 Hz; P > 0.05 paired t-test). Oscillations in the subiculum often consisted of double population spikes, usually after an initial 150–200 ms of single population spikes (Figs. 1 and 3A).

[Å]k at increasing distances from stimulation site

Tetanic stimulation in CA1 produced an increase in [K+]o, to a mean of 8.2 ± 1.5 mM at 200 µm from stimulating electrode (n = 6), coinciding with the induction of gamma rhythms (Fig. 2). As we have noted before, gamma rhythms occurred with very modest increases of [K+]o, to 4.1 and 5.5 mM, as well as to more significant levels of >8 mM (Whittington et al. 1997a). Within the first 600 µm from the stimulating electrode, [K+]o declined rapidly with dis-

FIG. 1. Gamma rhythms evoked in CA1 conduct to the subiculum. Tetanic stimulation in the stratum radiatum of CA1 (●) evoked gamma rhythms, recorded using an extracellular (EC) electrode placed in the CA1 pyramidal cell layer, initially 200 µm from the stimulation site. This activity decreased in amplitude between 200 and 600 µm from the stimulation site. However, gamma rhythms were recorded in the subiculum (>1,500 µm away). Note the double population spikes on the subicular field recording.
FIG. 2. Tetanic stimulation produces an increase in \([K^+]_o\). A and C: within 200 \(\mu\)m of the stimulating electrode, \([K^+]_o\) increased to 8.2 ± 1.5 mM. There was a decline in \([K^+]_o\) toward the subiculum, with a plateau phase ~600–1,600 \(\mu\)m from the stimulating electrode. (Typical traces are shown in A, and the peak \([K^+]_o\), reached is plotted in C as a function of distance from the CA1 stimulating electrode.) B: gamma rhythms were seen close to the stimulating electrode and in the subiculum but not at intervening sites; the signal recorded during the stimulus train has been omitted here and the records aligned with A.

tance to 4.9 ± 0.7 mM (Fig. 2C). \([K^+]_o\) remained at this level during the following 1,000 \(\mu\)m; this corresponded to the electrically silent region. Close to the boundary between CA1 and the subiculum \([K^+]_o\) decreased rapidly to baseline levels (3.0 ± 0.0 mM). Subicular gamma evoked by CA1 stimulation occurred caudal to this drop-off in \([K^+]_o\), showing that this distal gamma can occur without a rise in \([K^+]_o\).

Correlations of gamma rhythms between CA1 and subiculum

In slices where tetanic stimulation of CA1 alone resulted in gamma oscillations in both CA1 and subiculum, the two oscillations were phase locked with a lag of 5.42 ± 1.8 ms (5.2 ms in the case illustrated in Fig. 3A). Tetanic stimula-

FIG. 3. A: stimulation of CA1 results in a consistent phase lag between gamma activity recorded in CA1 and that recorded in the subiculum (5.2 ms in this example, shown on the cross-correlation). B: stimulation of subiculum alone evokes activity in subiculum and not in CA1. C: stimulation of both CA1 and subiculum simultaneously results in phase locked oscillations, with a reduced phase lag, in this case 2.8 ms compared with the 5.2 ms in A. Traces in each case start at the end of the stimulus train; correlations were computed during the first 200 ms of the oscillations.
tion of the subiculum alone produced gamma oscillations in the subiculum, and not in CA1 (Fig. 3B). (The subicular stimulation site was slightly superficial to the recording electrode, chosen to avoid antidromic activation of CA1.) If both CA1 and subiculum received tetanic stimulation, then they again became phase locked (Fig. 3C). Stimulation of both sites could reduce the phase lag, from 5.2 to 2.8 ms in the case illustrated. In a series of eight experiments, the mean phase lag decreased from 7.83 ± 0.62 ms when only CA1 was stimulated to 5.71 ± 0.69 ms when both CA1 and subiculum were stimulated at the same time. This decrease was significant (paired t-test, \( P = 0.007 \)).

The conduction velocity of the alvear pathway from CA1 to the subiculum was estimated in other slices by measuring the latency of the antidromic spike evoked by stimulation of the caudal end of the alveus (usually in the subiculum) in two recording sites at either end of CA1, separated by 1.4–2.2 (mean 2.0) mm. The decrement in the antidromic spikes between the two ends of CA1 was of the order of 50–75%, suggesting a substantial fraction of CA1 pyramidal cell axons reached the subiculum. The mean conduction velocity was 0.52 ± 0.07 m/s. In these slices, tetanic stimulation of CA1 resulted in a phase lag of 4.6 ms between sites in CA1 and subiculum separated by 2 mm, corresponding to a propagation velocity of 0.44 m/s, i.e., close to the conduction velocity estimate. The fastest mean phase lag measured with stimulation of both CA1 and subiculum suggests a propagation velocity of 0.64 m/s, which, given the variability of the time and distance measures, is not significantly faster than the conduction velocity of the CA1 axons. This suggests that the gamma generated in CA1 can be transmitted to the subiculum by CA1 pyramidal axons in the alveus.

Pharmacology of gamma rhythms evoked in CA1 and subiculum

Figure 4, top, shows a typical CA1 tetanic stimulation, with gamma rhythms produced in CA1 and conducting to the subiculum. The focal application of the \( \gamma \)-aminobutyric acid-A (GABA\(_A\)) receptor antagonist, BMI (30 mM = 1,000 times the concentration used for bath application), within
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(our previous paper notes that partial block of AMPA receptors first disrupts the tight phase relations between gamma evoked at 2 sites within CA1). The present data show that AMPA receptors are required for the transmission of gamma rhythms from the CA1 to the subiculum.

Pharmacology of gamma rhythms evoked by stimulation of the subiculum

Gamma activity could be evoked locally in the subiculum after tetanic stimulation in the subiculum with no activity apparent in the adjacent CA1 region (Figs. 3B and 5A). Focal application of the GABA<sub>A</sub> receptor antagonist BMI (30 mM) to the subiculum abolished this local gamma activity (Fig. 5B). This shows that oscillations generated by local tetanic stimulation require activation of GABA<sub>A</sub> receptors.

BMI also was applied in the ACSF. The drug had similar effects on gamma activity evoked by stimulation of CA1 (2

A 200 µm of the subiculum recording electrode caused no change in the activity at either site (Fig. 4, middle left). However, application of BMI to within 200 µm of the CA1 electrode resulted in a reversible loss of gamma activity at both locations (Fig. 4, bottom left). This suggests that gamma oscillations in CA1 depend on activation of GABA<sub>A</sub> receptors and that this activity subsequently conducts to the subiculum.

A similar protocol was used to test the role of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors, using the antagonist, NBQX (20 mM), applied focally to the subiculum and CA1. Application of NBQX to the subiculum (Fig. 4, middle right) caused a localized loss of gamma activity at the subiculum only. When NBQX was applied to CA1, gamma activity was lost at both CA1 and the subiculum (Fig. 4, bottom right). This confirms that blocking AMPA receptors disrupts the expression of gamma rhythm involving pyramidal cell discharges in CA1 (Whittington et al. 1997a).

FIG. 6. Bicuculline disrupts and then blocks both CA1 and subicular induced 40 Hz activity. A: dual intracellular and extracellular recordings from an intrinsic bursting neuron in the subiculum in response to 200 ms/100 Hz stimulation in the CA1 layer. Control recording shows spike doublets on many cycles of the evoked 40-Hz activity. B: addition of 5 µM bicuculline to the perfusion medium disrupted the gamma activity after 3 min and induced burst firing prior to a total block of activity at 7 min (B, lower pair of traces). This effect was reversible on wash (C). Traces start at the end of the stimulus train.

FIG. 7. High dose (30 µM) bicuculline blocked gamma rhythms evoked by subicular stimulation and failed to sustain epileptic activity (A, control; B, 6 min in bicuculline). (Intracellular recording is from an intrinsic bursting subicular neuron, which depolarized by <2 mV from a resting membrane potential of −64 mV on the addition of bicuculline.) Epileptic activity, evoked by subicular stimulation, was uncovered by the further addition of 5 µM CGP 55845A (C). Traces start at the end of the stimulus train.
cases) or of the subiculum (3 cases). The addition of 2 or 5 μM BMI gradually disrupted the gamma rhythm and resulted in epileptiform burst firing (Fig. 6). The epileptiform activity differed from the gamma rhythm in having markedly longer bursts, intracellular paroxysmal depolarization shifts with multiple action potentials (see Stanford et al. 1998), and less rhythmic bursts. Within 10–15 min, bicuculline blocked the response entirely. These effects of bicuculline all reversed on return to control solution.

It was surprising that the epileptiform activity disappeared with time in BMI. We therefore increased the dose of the GABA<sub>A</sub> receptor antagonist to 30 μM (Fig. 7). Again all responses to the tetanic stimulation were blocked, and the slow depolarization underlying the gamma rhythm was replaced by a large, slow hyperpolarization. Epileptiform activity recovered, however, when the GABA<sub>B</sub> receptor antagonist CGP 55845A (5 μM) was added. The presence of a slow, apparently bicuculline-sensitive, depolarization in the control records might suggest a role for depolarizing GABA<sub>B</sub> potentials. That this depolarization was replaced by a slow hyperpolarization in the presence of bicuculline might suggest that at least part of the effect of GABA<sub>B</sub> receptors was postsynaptic.

**DISCUSSION**

This paper shows that gamma activity induced in CA1 can transmit to the subiculum, that the subiculum can generate gamma rhythms of its own, and that oscillations in the two regions can become coupled. The area of tissue involved in the synchronous oscillation evoked by local stimulation in each area was 400–800 μm across. The transmission of gamma from CA1 to subiculum could jump silent regions ≈1.5 mm long within CA1. This transmission was blocked by focal application of the AMPA receptor antagonist NBQX to subiculum; this is consistent with activation by afferents from CA1. Focal applications of the GABA<sub>B</sub> receptor antagonist, BMI, to either CA1 or subiculum blocked the initiation of gamma rhythms by local stimulation. This observation is in keeping with our previous work on CA1 that led to the inhibitory neuronal network theory of gamma oscillations (Jefferys et al. 1996; Traub et al. 1996a; Whittington et al. 1995). However, focal BMI applications to the subiculum failed to prevent the transmission of gamma initiated in CA1. Together these observations suggest that gamma rhythms can either be generated by the local circuitry in the subiculum or they can be imposed from the CA1 region through its efferents.

Bath-applied bicuculline produced a transient period of epileptic responses before it abolished the response entirely. The epileptic activity differed from gamma in having less regular and more prolonged bursts and, intracellularly, the paroxysmal depolarization shift morphology typical of epileptic discharges (Figs. 6B and 7C). It was surprising that the epileptic discharge should disappear with time. In both CA3 and other cortical structures, bicuculline produces a consistent and stable model of epileptic activity, where we and others have shown that recurrent excitatory connections between the pyramidal cells play a key role (Gutnick et al. 1982; Traub and Wong 1982; Traub et al. 1993a,b). The observation here that GABA<sub>B</sub> receptors also need to be blocked suggests that they exert a powerful restraint on epileptic activity in the subiculum; prominent slow inhibitory postsynaptic potentials have been described in subicular neurons, both intrinsic bursting (IB) and regular spiking (RS) (Fig. 4 Taube 1993). That the addition of bicuculline blocked the slow depolarization under the gamma oscillation in the IB cells could suggest that depolarizing GABA<sub>A</sub>-receptor–mediated responses play a role in the tonic excitation of the network. This may be due to the release of an excess of GABA during the tetanic stimulus train reaching receptors that mediate depolarizing GABA responses (Alger and Nicoll 1979; Andersen et al. 1980; Michelson and Wong 1994; Wong and Watkins 1982).

The projection of gamma rhythms from CA1 to subiculum had a phase lag that was close to that predicted from the conduction velocity of the CA1 axons in the alveus. When both CA1 and subiculum were stimulated simultaneously, the phase lag often appeared to decrease. It did not, however, decrease to values that would be incompatible with axonal conduction. These observations differ from our previous work on coupling of separate sites in CA1 where phase lags close to zero were commonly produced (Traub et al. 1996b; Whittington et al. 1997a). This difference is most likely due to the unidirectional excitatory projection from CA1 to subiculum, which contrasts with the reciprocal excitatory and inhibitory connections within CA1. The shortening of the phase lag from CA1 to subiculum after the tetanic stimulation of the latter may be due to the following mechanism: tetanic stimulation leads to a tonic depolarization of both pyramidal cells and interneurons (Whittington et al. 1997a). Such depolarization could allow afferent excitatory postsynaptic potentials to trigger firing faster than would be the case in resting neurons and so reduce the phase lag. In addition, increased [K<sup>+</sup>]i could accelerate conduction in CA1 axons by inducing a “supernormal period” (Eng and Kocsis 1987; Kocsis et al. 1983).

The anatomy of the projection from CA1 to subiculum has been studied in some detail (Amaral et al. 1991; Tamamaki and Nojyo 1990). The rostral end of CA1 projects to the distal subiculum, which corresponds to the pathways in Figs. 1–4 of this paper. The caudal end of CA1 projects to the near subiculum (Amaral et al. 1991). This presents a potential risk to the specificity of our stimulation of the subiculum directly. Our recordings from the most caudal aspect of CA1 (e.g., Fig. 5), however, suggest that this was not a problem, perhaps because the subicular electrodes were positioned >500 μm from the caudal end of CA1, and the stimuli we use here drive gamma oscillations ≤400 μm away (Fig. 1).

The data presented here also showed that [K<sup>+</sup>]i increased from 3 to 8 mM in the part of CA1 where gamma occurred. This is likely to add to the tonic excitation that arises primarily from metabotropic glutamate receptors (mGluRs) and muscarinic acetylcholine receptors (mACHRs) (Whittington et al. 1997a). Rises in [K<sup>+</sup>]i are not in themselves sufficient to induce gamma rhythms, as shown by the ability of mGluR antagonists to block both gamma rhythms (Whittington et al. 1995) and to attenuate the underlying depolarization evoked by stimulation with further attenuation by M1 muscarinic antagonists (Whittington et al. 1997a). The increase in [K<sup>+</sup>]i described here may contribute to the slow depolarization, found in our previous study, that remains after block-
ade of both mGluRs and mACHRs. The $[\mathrm{K}^+]_o$ increase was smaller and relatively uniform over the remainder of CA1 than it was close to the stimulation site. One mechanism for this more modest, long-range, change could be the release of $\mathrm{K}^+$ from glia as part of the spatial buffering mechanism. The increase in $[\mathrm{K}^+]_o$ rapidly decayed with distance in the neighborhood of the CA1-subiculum border, which suggests that fluctuations in $[\mathrm{K}^+]_o$ play no part in the gamma rhythms when they are transmitted to the subiculum. The coincidence of the CA1-subiculum border and the drop in $[\mathrm{K}^+]_o$ transients further suggests discontinuities in the spatial buffering mechanisms in the two regions.

The subiculum thus can experience gamma rhythms both transmitted through afferents and generated endogenously. The two forms of gamma can combine to reduce the phase lag between CA1 and subiculum but not to abolish the lag entirely. The persistence of a phase lag presumably is a consequence of the absence of a backwards projection in the slice from subiculum to CA1. These issues should be reexamined in vivo where other circuits may affect synchronization of CA1 and subiculum and indeed of other limbic regions. A key link in the wider circuitry is likely to be the entorhinal cortex, which can entrain gamma rhythms in the CA1 region in the anesthetized guinea pig (Charpuk et al. 1995). The maintenance of topography within the relays among subiculum, CA1, and entorhinal cortex would suggest that these structures may well combine to form and integrated functional system (Tamamaki and Noiyo 1995) The following paper addresses the generation and patterning of subicular gamma rhythms in more detail.

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