Chem. Senses 37: 681–688, 2012

doi:10.1093/chemse/bjs046
Advance Access publication April 4, 2012

Multimodal Cross-Talk of Olfactory and Gustatory Information in the Endopiriform Nucleus in Rats

T. Sugai[1], R. Yamamoto[1], H. Yoshimura[2] and N. Kato[1]

[1]Department of Physiology, Kanazawa Medical University, Uchinada, Ishikawa 920-0293, Japan and [2]Department of Oral and Maxillofacial Surgery, Kanazawa Medical University, Uchinada, Ishikawa 920-0293 Japan

Correspondence to be sent to: Tokio Sugai, Department of Physiology, Kanazawa Medical University, Uchinada, Ishikawa 920-0293, Japan. e-mail: tokio@kanazawa-med.ac.jp

Accepted March 5, 2012

Abstract

The endopiriform nucleus (EPN) is a large group of multipolar cells located in the depth of the piriform cortex (PC). Although many studies have suggested that the EPN plays a role in temporal lobe epilepsy, the normal function of the EPN remains to be elucidated. By using optical imaging of coronal brain slice preparations with voltage-sensitive dye, we found signal propagation from the PC or gustatory cortex (GC) to the EPN in normal medium. In our previous research, we failed to elicit a reliable signal reproducibly in the EPN by single stimulation either to the PC or GC. In our current research, we found that a double-pulse stimulation to either the PC or GC (interpulse interval: 20−100 ms) induced robust signal propagation to the EPN through excitation in the agranular division of the insular cortex (AI), with further extension to the claustrum. Finally, double site paired-pulse stimulation to the PC and GC also evoked excitation in the AI, claustrum, and EPN.
These results suggest that the EPN has dual roles: 1) further processing of modality-specific olfactory and gustatory information from the PC and GC, respectively and 2) synergistic integration of PC-derived olfactory information and GC-derived gustatory information.

Key words: agranular division of the insular cortex, claustrum, multisensory information processing, optical imaging, paired-pulse facilitation, voltage-sensitive dye

Introduction

The endopiriform nucleus (EPN), situated beneath the piriform cortex (PC), contains multipolar cells with long axons that form a network of intrinsic connections and project extensively over long distances to extended areas in the forebrain, including the PC, entorhinal cortex, insular cortex, and amygdala (Haberly and Price 1978; Luskin and Price 1983; Behan and Haberly 1999). From a functional point of view, the importance of the EPN is believed to be in both olfactory processing and epileptogenesis (Hoffman and Haberly 1993, 1996; Demir et al. 1998). A number of studies suggest that the EPN serves as an origin of epileptic waves (Piredda and Gale 1985; Stevens et al. 1988; Hoffman and Haberly 1991, 1996; Demir et al. 1998, 2001). We also extended this line of investigation by showing that EPN responses reliably follow stimulation to the PC in a highly excitable condition with an Mg^{2+}-free medium (Fu et al. 2004). Thus, the role of this nucleus in epileptogenesis has been considerably supported. However, the normal functional role of the EPN remains unknown.

Recently, it has been increasingly recognized that the multimodal nature of the cerebral cortex is critical in perception (Ghazanfar and Schroeder 2006). Multimodal interactions are also characteristic of chemosensory systems (Kats et al. 2001), and it has been proposed that taste and smell depend on each other (Small and Prescott 2005). Indeed, Fortis-Santiago et al. (2010) demonstrated that inactivating the primary gustatory cortex (GC) influences olfactory perception. A number of studies suggested that the EPN might be a critical structure for reciprocal interactions between gustatory and olfactory cortices (Yamamoto et al. 1984; McDonald and Jackson 1987; Fu et al. 2004). In a highly excitable epileptogenic condition, we have found that EPN responses were elicited not only by PC stimulation but also sometimes by stimulation to the GC (Fu et al. 2004); this is a preliminary

result suggesting that a possible convergence of PC and GC afferents occurs in the EPN. However, it remains unknown whether olfactory and gustatory signals merge in the EPN, resulting in a multimodal integration. Thus, the aim of the present experiments is to study, by electrophysiological and optical recordings, whether gustatory and olfactory inputs to the EPN have mutual interactions.

Materials and methods

Animal protocols used in this study fulfilled all the pertinent institutional regulations, and every attempt was made to minimize the number of animals and their suffering.

Materials

Young Wistar rats (n = 15, 100–120 g) were used for the experiment. Frontal slices (400 μm thick), including the piriform cortices, were prepared. The frontal slices were cut in a plane that was approximately 10° off the frontal plane (near parallel to the middle cerebral artery [MCA]), from 2.0 mm rostral to the anterior edge of the optic chiasm or from 0.8 mm rostral to the MCA to 1.2 mm caudal to the MCA. The slices were recovered by perfusing continuously (>1 h at 30 °C) with oxygenated (95% O_2/5% CO_2) artificial cerebrospinal fluid (ACSF) containing (in millimolars): 124 NaCl, 5 KCl, 1.24 KH_2PO_4, 1.3 $MgSO_4$, 2.4 $CaCl_2$, 26 $NaHCO_3$, and 10 glucose.

Electrophysiological recording

Slices were transferred to the recording chamber mounted on the stage of an inverted microscope (IMT-2; Olympus, Japan) and perfused with oxygenated ACSF. Bath temperature was maintained at 27–29 °C. For stimulation, a pair of monopolar tungsten wires were inserted into layer I/II of the PC and/or layer II/III of the GC, and single square pulses (0.02–0.2 mA, 80–100 μs) were delivered at 0.05–0.07 Hz. Glass microelectrodes containing 2% Brilliant Blue in 0.85% NaCl (4–20 MΩ, DC) were used to record extracellular field potentials with an amplifier (Intra 767, World Precision Instruments) and to mark the location of the electrode tip with dye deposit (20 μA for 5–10 min). The electrophysiological data were filtered at 1 kHz, digitized at 5 kHz, and analyzed off-line with pClamp 8 software (Axon Instruments).

Optical imaging

Frontal slices were incubated with a voltage-sensitive dye NK2761 (0.13 mg/mL; Nippon Kankoh-Sikiso Kenkyusho) for 19 min, transferred to the recording chamber, and perfused with ACSF (27–29 °C). Stimulation electrodes were inserted into layer II of the PC and/or GC. The parameters for stimulation were the same as above. The camera unit of the optical imaging system (Fujix HR-Deltaron 1700; Fujifilm Microdevices) contains a 128 × 128 photodiode array. With the 4× objective (0.20 NA, Plan Apo, Nikon), the whole array corresponded to a 2.26×2.26 mm^2 area of tissue. A narrow band interference filter of 700 ± 30 nm and a heat absorption filter were routinely placed in the light path from a halogen lamp. Sixteen responses to electrical stimulation were averaged to form a run. Neural activity was recorded optically by monitoring absorption changes ($\Delta T/T$) in transmitted light intensity in each of the elements at the rate of 1 frame per 0.6 ms, as described (Ichikawa et al. 1993; Tanifuji et al. 1994; Sugai et al. 1997; Fu et al. 2004). The optical signal obtained from each pixel was the average of signals from its own element and the 4 additional pixels surrounding it.

Histological identifications

After electrical or optical recordings, appropriate sites in the pathway of signal propagation following stimulation of the PC/GC were confirmed on a display screen, and then each site was marked on the screen with a marker. The tip of a glass pipette containing dye was superimposed on the mark after the display was replaced with the real image of the slice preparation, and then the dye was deposited. The stimulation site was also marked with the dye. The slice was then fixed with 1% paraformaldehyde in 0.1 M phosphate buffer and resectioned (40 μm), and the positions of the stimulation and recording electrodes were histologically determined.

Results

Paired-pulse facilitation in the EPN

In our previous report (Fu et al. 2004), single-pulse stimulation of layer I/II in the PC evoked a field potential with a latency of about 35 ms in the EPN. The PC-evoked EPN field potentials occurred reliably in response to initial stimulations. When stimulations were repeated, their latencies became gradually longer in ACSF containing Mg^{2+} (normal solution) and then the EPN potentials often disappeared after several stimulations. Responses reliably followed the repeated stimulations in Mg^{2+}-free medium only.

In the present study, we used paired-pulse stimulation in normal medium with Mg^{2+}. This example is shown in Figure 1. Paired-pulse PC stimulation was applied with various interpulse intervals (IPIs) with sub-threshold intensities at which the first shock alone yielded no detectable EPN response. At IPIs of 10–130 ms, paired-pulse facilitation was observed in the EPN responses. This facilitatory effect decreased gradually with increasing latencies of the EPN responses at IPI of 130 ms and disappeared at IPI of 160 ms. The occurrence of an EPN response was plotted against the different IPIs in Figure 1B. Paired-pulse facilitation reached a maximum at 10–30 ms IPIs. Thereafter, it weakened gradually and disappeared by 160 ms. Thus, unlike the previous single-pulse stimulation (Fu et al. 2004), the present paired-pulse protocol reproducibly elicited field potentials in the EPN in normal medium.

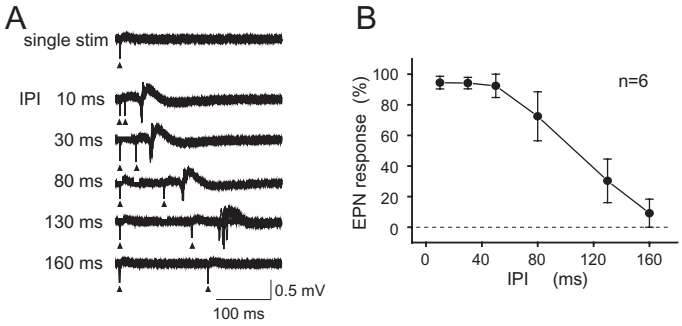

Figure 1 Field potentials evoked in the EPN. (**A**) Paired-pulse stimulation was applied to the piriform cortex (PC) with different IPIs (Bottom, IPIs). Responses obtained in 8 successive trials are superimposed. Each arrowhead indicates timing of PC stimulation. The stimulus intensity was so adjusted that a single PC stimulation failed to evoke such responses (Top, single stim). (**B**) Time course of paired-pulse facilitation. The occurrence of EPN responses in response to subthreshold intensities are plotted against IPIs. No EPN response is evoked by a single PC stimulation (dotted line).

Optical imaging of signal propagation to the EPN following paired-pulse PC stimulation

Optical recordings using voltage-sensitive dye were carried out on the frontal slice preparations ($n = 6$) in normal ACSF. A representative result is shown in Figure 2. Single-pulse stimulation to the dorsal part of the PC evoked an early optical response around the stimulated sites in the PC with subthreshold intensity for the EPN response (image at 3.0 ms in Figure 2A). Subsequently, excitation propagated dorsally and disappeared around the rhinal fissure (image at 27.0 ms). Thus, no propagation to the EPN occurred. Paired-pulse stimulation of the PC with the same intensity at 20 ms IPI, by contrast, elicited excitation propagation to the EPN (Figure 2B). After the second stimulation (image at 20.6 ms), the optical signal was found to propagate 1) dorsally along layer II in the PC and vertically toward the deep layers in the PC (image at 27.0 ms), 2) further vertically toward deep layer VI in the agranular division of the insular cortex (AI) (white arrowhead in 48.6 ms), and 3) ventrally

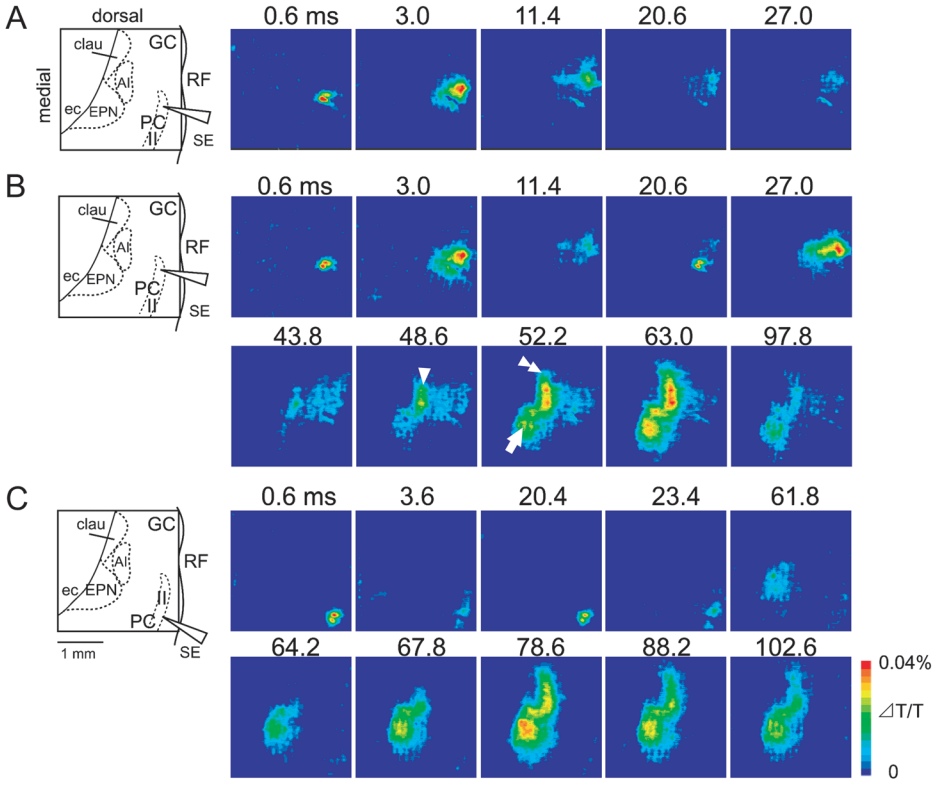

Figure 2 Time-lapse optical imaging of neural excitation evoked by single- and paired-PC stimulation in a single slice. (**A**) Single PC stimulation caused neural excitation restricted around the stimulation electrode in the PC, which lasted for less than 30 ms. The orientation of the frontal slice is indicated in the diagram (dorsal, medial), which applies also to the following figures. (**B**,**C**) Two patterns of excitation propagation to the EPN elicited by paired stimulation to 2 different PC sites at 20 ms IPI. From a 512-frame sequence, 5 or 10 frames that were selected are shown. Numerals on each image are the time (milliseconds) after stimulation. The white arrow, single- and double-arrowheads in images in (B) indicate the EPN, the AI, and the claustrum, respectively. The schematic drawings on the left show individual camera fields on the tissue (2.26 × 2.26 mm^2). Arrowheads indicate stimulating electrode (SE). In this and subsequent figures, the relative intensity change (ΔT/T, percentage) in transmitted light in each pixel was color coded according to the color calibration on the lower right. Abbreviations: AI, layer V/VI of the agranular division of the insular cortex; clau, claustrum; ec, external capsule; EPN, endopiriform nucleus; GC, gustatory cortex; PC, piriform cortex; II, layer II of PC; RF, rhinal fissure.

toward the EPN (white arrow, image at 52.2 ms) and also dorsally toward the claustrum (double white arrowhead, image at 52.2 ms). Since the responses in the AI were always detected from layers V/VI only, we hereafter refer layers V/VI of the AI just as the AI. The optical signals in the AI, claustrum, and EPN reached its maximum spatial extent by 63.0 ms and then excitation decreased gradually (image at 97.8 ms). Most of these signals disappeared by 140 ms after paired PC shocks. Thus, paired PC stimulation elicited signal propagation to both the EPN and claustrum via the AI. Next, the position of the stimulation electrode in the PC was moved ventrally in the same preparation as shown in Figure 2C. Paired PC stimulation at 20 ms IPI induced direct signal propagation to the EPN, which was not mediated by AI excitation (images at 61.8 and 64.2 ms). In this condition, AI and claustrum excitation also occurred (image at 78.6 ms) following EPN excitation. These signals faded gradually by 150 ms. The result indicates that AI excitation is not necessary for signal propagation to reach the EPN if a paired-pulse stimulation is applied to the ventral PC.

Figure 3A shows optical responses obtained from 8 different sites following single (black trace) and paired (red trace) stimulation to the dorsal PC. In the PC, transient responses with durations of 10 ms occurred in response to single and paired PC stimulation (traces 1 and 2). In the deep PC layer, small responses occurred in response to paired PC stimulation (trace not shown). In the AI, excitation occurred after a latency of about 40 ms in response to paired PC stimulation (traces 3 and 4). In the EPN (traces 5, 6, and 7) and claustrum (trace 8), paired PC stimulation evoked excitation with a longer latency than in the AI. The average latencies of AI, claustrum, and EPN responses were 44.9 ± 3.9, 54.3 ± 3.8, and 50.6 ± 2.2 ms, respectively (mean ± standard error of mean, $n = 6$). The pattern of signal propagation and the propagation velocity (19.4 ± 1.4 mm/s) were similar in 6 slices. Single PC stimulation did not elicit excitation in the AI, EPN, or claustrum.

Paired stimulation was then applied to the ventral PC (Figure 3B). In this example, it is evident from the differences in response latencies that excitation in the EPN (traces 5, 6, and 7) occurred first and propagated to the AI (traces 3 and 4) and claustrum (trace 8) as well. The average of response latencies of AI, claustrum, and EPN responses were 61.4 ± 4.1, 70.4 ± 2.4, and 54.8 ± 3.8 ms, respectively ($n = 4$). The pattern of signal propagation and the propagation velocity (19.2 ± 1.3 mm/s) were similar in 4 slices. Single PC stimulation did not elicit excitation in the AI, EPN, or claustrum (data not

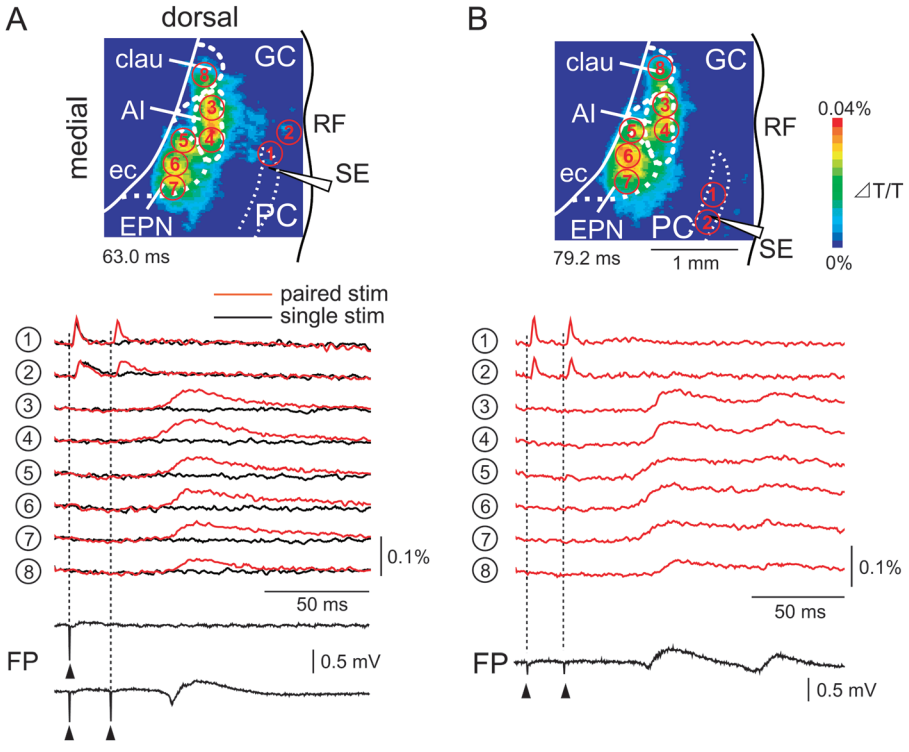

Figure 3 Optical responses to single and paired PC stimulation. Optical images at 63.0 ms (**A**) and 79.2 ms (**B**) following paired PC stimulation with different stimulation sites in the same slice as shown in Figure 2. The schematic drawings on the camera fields of the tissue are superimposed on the images in white. (A) Optical responses to single (black) and paired (red) PC stimulation at 8 pixels indicated by numbers in the image were superimposed. The locations 1 and 2 are in the PC; 3 and 4 are in the AI; 5, 6, and 7 are in the EPN; and 8 is in the claustrum. Field potentials were recorded in the EPN concurrently, and averaged over 16 responses (FP). Filled triangles are the timing of stimulation. (B) Optical responses to paired stimulation (red) of the PC site near the lateral olfactory tract at 8 pixels indicated by numbers in the image. 1 and 2 are in the PC; 3 and 4 are in the AI; 5, 6, and 7 are in the EPN; and 8 is in the claustrum. Otherwise, convention is the same as in (A).

shown). Field potentials recorded concurrently in the EPN are shown in the bottom of Figure 3A,B. Thus, the 2 propagation routes to the EPN emerged in all slices tested, depending on stimulation sites.

Optical imaging of signal propagation to the EPN following paired-pulse GC stimulation

Paired-pulse stimulation of the GC also evoked excitation propagation to the EPN (Figure 4). Single GC stimulation evoked early optical response around the stimulated sites in the GC (image at 4.8 ms in Figure 4A). Subsequently, excitation gradually disappeared (image at 28.8 ms) and did not induce EPN excitation. Paired GC stimulation with the same intensity at 20 ms IPI, however, elicited excitation propagation to the EPN in 4 of the 7 slices tested (Figure 4B). After the second stimulation (at 21.0 ms), the optical signal propagated 1) vertically toward deep layers in the GC (images at 28.8 and 49.2 ms), 2) ventrally toward the AI (white arrow head) and claustrum (double white arrow head, images at 58.2 and 67.8 ms), and 3) obliquely toward the EPN (white arrow, image at 77.4 ms). Figure 4C indicates optical responses obtained from 8 different sites following single (black trace) and paired (red trace) GC stimulation. In the GC, transient

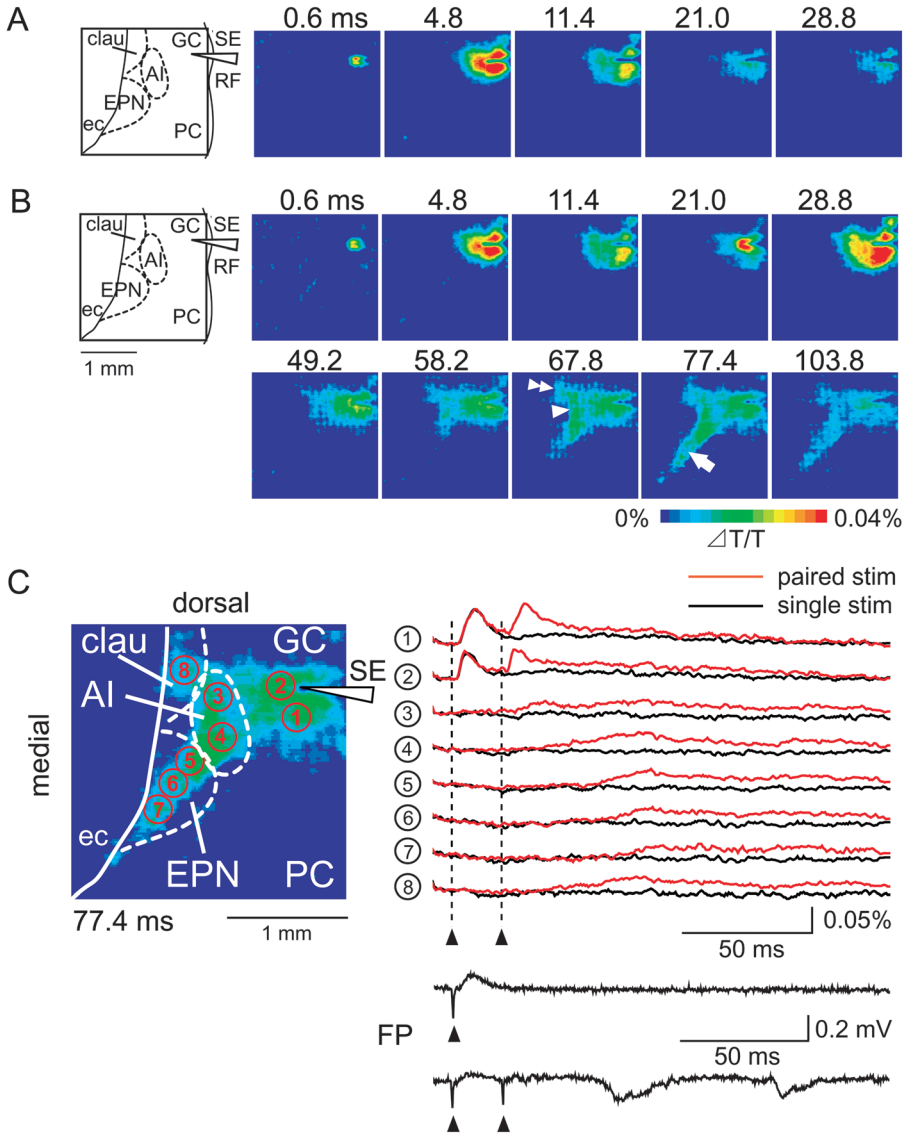

Figure 4 The time-lapse optical imaging of neural excitation evoked by single and paired GC stimulation. (**A**,**B**) Single (A) and paired stimulation (B) was given to the GC. From a 512-frame sequence, 5 or 10 frames selected are shown. Convention is the same as in Figure 2. (**C**) Time courses of optical responses to single and paired GC stimulation, recorded from representative points in a slice. (left) Optical images at 77.4 ms in response to paired GC stimulation in the same slice shown in (A). (right) Optical responses to single (black) and paired (red) GC stimulation. Field potentials were recorded in the AI concurrently and averaged over 16 responses (FP). Filled triangles are the timing of stimulation. Convention is the same as in Figure 3. The locations 1 and 2 are in the GC; 3 and 4 are in the AI; 5, 6, and 7 are in the EPN; and 8 is in the claustrum.

responses with durations of 10–20 ms occurred in response to single and paired GC stimulation (traces 1 and 2). In the AI and claustrum, excitation occurred after a delay of about 40–50 ms in response to paired GC stimulation (traces 3, 4, and 8). In the EPN, the paired stimulation to the GC elicited responses as well, albeit at longer latencies than those evoked in the AI (traces 5, 6, and 7). The average latencies of AI, claustrum, and EPN responses were 44.3 ± 2.8, 53.3 ± 3.1, and 62.9 ± 3.8 ms, respectively (n = 4). The pattern of signal propagation and the propagation velocity (19.7 ± 1.4 mm/s) were similar in 4 slices. Field potentials recorded concurrently in the AI are also shown in the bottom of Figure 4C.

Optical imaging of signal propagation to the EPN following double-site paired-pulse stimulation

Signal propagation to the EPN was observed not only by paired stimulation of the PC or GC (single-site paired stimulation) but also by double-site paired stimulation of the PC and GC (Figure 5). Paired-pulse stimulation was applied with intensities at which the single PC or GC shock alone yielded no detectable EPN excitation (data not shown). GC stimulation preceded PC stimulation at 13 ms. The first GC stimulation induced early optical response around the stimulated sites in the GC. After the second PC stimulation, excitation in the AI and claustrum occurred (image at 54.6 ms). Then, excitation in the EPN was evoked (images at 61.8 and 72.9 ms). EPN signals faded gradually by 120 ms, and almost disappeared by 150 ms.

In the GC, early responses with a short duration of about 10 ms were evoked by the first stimulation to the GC (trace 1 in Figure 5B). On the second stimulation to the PC, early small responses occurred in the PC (trace 2). Excitation in the AI was elicited after a long delay of about 50 ms by the paired stimulation to the GC and PC (traces 3 and 4). Excitation in the claustrum was also observed at a latency

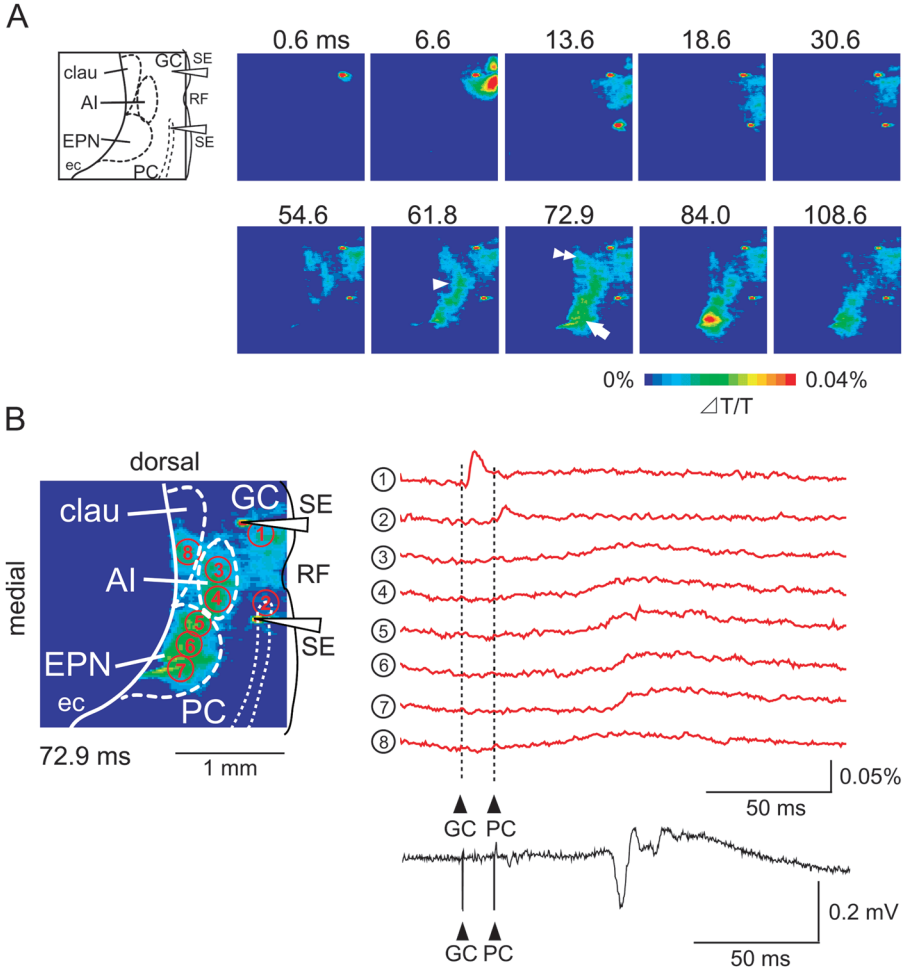

Figure 5 Time-lapse optical imaging and optical responses of neural excitation evoked by double-site paired-pulse stimulation. (**A**) GC stimulation preceded PC stimulation at 13 ms IPI. Convention is the same as in Figure 2. (**B**) Time courses of optical responses to double-site paired-pulse stimulation, recorded from representative points in a slice. (left) Optical images at 72.9 ms following double-site paired stimulation in the same slice shown in (A). (right) Optical responses at 8 pixels indicated by numbers in image. Field potentials were recorded in the EPN concurrently, and averaged over 16 responses. Convention is the same as in Figure 3. The location 1 is in the GC; 2 is in the PC; 3 and 4 are in the AI; 5, 6, and 7 are in the EPN; and 8 is in the claustrum.

similar to AI excitation (trace 8). In the EPN, excitation was evoked at a little longer latency than in the AI (traces 5, 6, and 7). The propagation to the EPN by this double-site stimulation was observed in 4 of 5 slices. The average latencies of AI, claustrum, and EPN responses were 53.9 ± 4.2, 55.4 ± 4.1, and 61.1 ± 5.8 ms, respectively (n = 4). The pattern of signal propagation and the propagation velocity (22.2 ± 1.6 mm/s) were similar in 4 slices. Field potential concurrently recorded in the EPN is shown in the bottom of Figure 5B.

The EPN signal was thus evoked by the double-site stimulation protocols, either with PC stimulation following GC stimulation, GC stimulation following PC, or simultaneous stimulation to the sites. In the single exceptional case where propagation to the EPN failed with the double-site paired stimulation, single-site paired stimulation to the GC also failed to excite the EPN.

Discussion

The present studies revealed new and intriguing physiological properties of EPN neurons that respond to single- or double-site paired stimulation to PC and/or GC. Paired-pulse facilitation around the EPN by PC stimulation has been reported in in vitro slice preparation (Tseng and Haberly 1989). The present report has extended their results by showing paired-pulse stimulation elicited excitation not only in the EPN but also in the AI and the claustrum. Furthermore, the present report is the first to show that double-site paired stimulation of the PC and GC reliably evoke a robust response in the EPN region, including the AI and the claustrum, indicating that this region is activated by subthreshold stimulation of different modalities. Thus, a large-scale multimodal integration of smell and taste information in the EPN region has been suggested.

Paired-pulse stimulation of the PC, GC, and PC/GC excited the claustrum and the AI as well as the EPN. It has been shown that the insular cortex receives dense inputs from the PC and other olfactory areas (Luskin and Price 1983), including the olfactory bulb (Shipley and Geinisman 1984). Voltage imaging in slices has revealed that paroxymal epileptiform activity can develop in the AI in synchrony with that in the EPN (Demir et al. 1998). As to the claustrum, it has been found in slice preparation that epileptiform activity in the EPN can be initiated by local activation of the claustrum with glutamate or weak electrical shocks, suggesting the presence of a projection from the claustrum to the EPN (Hoffman and Haberly 1993). In addition, the dorsal boundary of the EPN, which is adjacent rostrally to the claustrum and AI, has been found to be more epileptogenic than the remainder of the EPN. While these activities in the AI and claustrum were observed in highly epileptogenic conditions, the present study demonstrated for the first time ever that the EPN regions, including the AI and claustrum, can be activated by stimulating input fibers even in a nonepileptogenic condition. Thus, it is shown that the EPN, claustrum, and AI are intimately connected to each other and involved not only in epileptogenesis but also in multimodal information processing.

The long latency of response to paired stimulation in the EPN suggests a polysynaptic mechanism (Tseng and Haberly 1989: Fu et al. 2004). Similar long latency field potentials in the EPN have been observed in vivo in rats (Ferreyra-Moyano et al. 1988, Sugai et al. 2010). In the central representation of olfactory information, slow temporal patterns have been proposed to play important roles (Macrides 1977) and such patterns are thought to be generated, for instance, by a ''delay line'' mechanism (Tank and Hopfield 1987). The present long latency responses and similar responses reported in rats seem to fit well into this theoretical framework of olfactory coding.

Besides the role of the PC in epileptogenesis, findings have accumulated that indicate that the PC plays another important role in olfactory information processing, (Illig and Haberly 2003; Wilson 2003; Sugai et al. 2005; Rennaker et al. 2007; Poo and Isaacson 2009; Stettler and Axel 2009). Furthermore, we reported that the EPN also receives inputs from the GC, suggesting cortical integration of olfactory and gustatory information in this structure (Fu et al. 2004). The present study suggests that the activity of the EPN is closely related to the overlying PC activity. In fact, neurons in the EPN were driven by electrical stimulation to the olfactory bulb, as well as to the PC, in in vivo experiments (Sugai et al. 2010). By optical imaging of intrinsic signals, we have demonstrated a possible coding mechanism for odor concentration in the anterior PC (Sugai et al. 2005). The rostral region of the dorsal part of the anterior PC is activated with low odor concentrations, whereas odor at higher concentrations generated caudally spreading activation, suggesting a rostrocaudal gradient in the odor sensitivity within the PC. Since the EPN is one of the main targets of the PC output, it is suggested that olfactory information from the PC is at least transmitted to the EPN and integrated with gustatory information transmitted from the GC.

Funding

This work was supported by a Grant-in-aid for scientific research (22500360) from the Japan Society for Promotion of Sciences, Grants for Collaborative Research (C2006-5, C2007-2, and C2007-6), High-Tech Research (H2008-14, H2009-14 and H2010-14) and Assist KAKEN (K2010-3) from Kanazawa Medical University and a Grant from the Science Research Promotion Fund of the Promotion and Mutual Aid Corporation for Private Schools of Japan.

Acknowledgements

The authors thank Mr S. Muramoto, Mr H. Adachi, and Ms K. Yamada for technical and secretarial assistance.

References

Behan M, Haberly LB. 1999. Intrinsic and efferent connections of the endopiriform nucleus in rat. J Comp Neurol. 408:532–548.

Demir R, Haberly LB, Jackson MB. 1998. Voltage imaging of epileptiform activity in slices from rat piriform cortex: onset and propagation. J Neurophysiol. 80:2727–2742.

Demir R, Haberly LB, Jackson MB. 2001. Epileptiform discharges with in-vivo-like features in slices of rat piriform cortex with longitudinal association fibers. J Neurophysiol. 86:2445–2460.

Ferreyra-Moyano H, Cinelli AR, Molina JC, Barragan E. 1988. Current generators and properties of late component evoked in rat olfactory cortex. Brain Res Bull. 20:433–446.

Fu W, Sugai T, Yoshimura H, Onoda N. 2004. Convergence of olfactory and gustatory connections onto the endopiriform nucleus in the rat. Neuroscience. 126:1033–1041.

Fortis-Santiago Y, Rodwin BA, Neseliler S, Piette CE, Katz DB. 2010. State dependence of olfactory perception as a function of taste cortical inactivation. Nat Neurosci. 13:158–159.

Ghazanfar AA, Schroeder CE. 2006. Is neocortex essentially multisensory? Trends Cogn Sci. 10:278–285.

Haberly LB, Price JL. 1978. Association and commissural fiber systems of the olfactory cortex of the rat. I. Systems originating in the piriform cortex and adjacent areas. J Comp Neurol. 178:711–740.

Hoffman WH, Haberly LB. 1991. Bursting-induced epileptiform EPSPs in slices of piriform cortex are generated by deep cells. J Neurosci. 11:2021–2031.

Hoffman WH, Haberly LB. 1993. Role of synaptic excitation in the generation of bursting-induced epileptiform potentials in the endopiriform nucleus and piriform cortex. J Neurophysiol. 70:2550–2561.

Hoffman WH, Haberly LB. 1996. Kindling-induced epileptiform potentials in piriform cortex slices originate in underlying endopiriform nucleus. J Neurophysiol. 76:1430–1438.

Ichikawa M, Iijima T, Matsumoto G. 1993. Real-time optical recording of neuronal activities in the brain. In: Ono T, Squire LR, Raichle ME, Perrett DI, Fukuda M, editors. Brain mechanisms of perception and memory. New York: Oxford University. Press. p. 638–648.

Illig KR, Haberly LB. 2003. Odor-evoked activity is spatially distributed in piriform cortex. J Comp Neurol. 457:361–373.

Kats DB, Simon SA, Nicolelis MA. 2001. Dynamic and multimodal responses of gustatory cortical neurons in awake rats. J Neurosci. 21:4478–4489.

Luskin MB, Price JL. 1983. The laminar distribution of intracortical fibers originating in the olfactory cortex of the rat. J Comp Neurol. 216:292–302.

Macrides F. 1977. Dynamic aspects of central olfactory processing. In: Muller-Schwarze D, Mozell MM, editors. Chemical signals in vertebrates. New York: Plenum. p. 499–514.

McDonald AJ, Jackson TR. 1987. Amygdaloid connections with posterior insular and temporal cortical areas in the rats. J Comp Neurol. 262:59–77.

Piredda S, Gale K. 1985. A crucial epileptic site in the deep prepiriform cortex. Nature. 317:623–625.

Poo C, Isaacson JS. 2009. Odor representations in olfactory cortex: "sparse" coding, global inhibition, and oscillations. Neuron. 62: 850–861.

Rennaker RL, Chen CF, Ruyle AM, Sloan AM, Wilson DA. 2007. Spatial and temporal distribution of odorant-evoked activity in the piriform cortex. J Neurosci. 27:1534–1542.

Shipley MT, Geinisman Y. 1984. Anatomical evidence for convergence of olfactory, gustatory, and visceral afferent pathways in mouse cerebral cortex. Brain Res Bull. 12:221–226.

Small DM, Prescott J. 2005. Odor/taste integration and the perception of flavor. Exp Brain Res. 166:345–357.

Stettler DD, Axel R. 2009. Representations of odor in the piriform cortex. Neuron. 63:854–864.

Stevens JR, Philips I, Beaurepaire R. 1988. Gamma-vinyl GABA in endopiriform area suppresses kindled amygdale seizures. Epilepsia. 29:404–411.

Sugai T, Miyazawa T, Fukuda M, Yoshimura H, Onoda N. 2005. Odor-concentration coding in the guinea-pig piriform cortex. Neuroscience. 130:769–781.

Sugai T, Sugitani M, Onoda N. 1997. Subdivisions of the guinea-pig accessory olfactory bulb revealed by the combined method with immunohistochemistry, electrophysiological and optical recordings. Neuroscience. 79:871–885.

Sugai T, Yamamoto R, Yoshimura H, Kato N. 2010. In vivo electrophysiological studies revealed the convergence of olfactory and gustatory information in the endopiriform nucleus in the rat. J Physiol Sci. 60:S143

Tanifuji M, Sugiyama T, Murase K. 1994. Horizontal propagation of excitation in rat visual cortical slices revealed by optical imaging. Science. 266:1057–1059.

Tank DW, Hopfield JJ. 1987. Neural computation by concentrating information in time. Proc Natl Acad Sci U S A. 84:1896–1900.

Tseng GF, Haberly LB. 1989. Deep neurons in piriform cortex. I. Morphology and synaptically evoked responses including a unique high-amplitude paired shock facilitation. J Neurophysiol. 62:369–385.

Wilson DA. 2003. Rapid, experience-induced enhancement in odorants by discrimination by anterior piriform cortex neurons. J Neurophysiol. 90:65–72.

Yamamoto T, Azuma S, Kawamura Y. 1984. Functional relations between the cortical gustatory area and the amygdale: electrophysiological and behavioral studies in rats. Exp Brain Res. 56:23–31.