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Title

Odorant features differentially modulate beta/gamma oscillatory patterns in anterior versus posterior piriform cortex

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Abbreviations

OB: Olfactory bulb

aPC: anterior piriform cortex

pPC: posterior piriform cortex

LFP: local field potential

Abstract

Oscillatory activity is a prominent characteristic of the olfactory system. We previously demonstrated that beta and gamma oscillations occurrence in the olfactory bulb (OB) is modulated by the physical properties of the odorant. However, it remains unknown whether such odor-related modulation of oscillatory patterns is maintained in the piriform cortex (PC) and whether those patterns are similar between the anterior PC (aPC) and posterior PC (pPC). The present study was designed to analyze how different odorant molecular features can affect the local field potential (LFP) oscillatory signals in both the aPC and the pPC in anesthetized rats. As reported in the OB, three oscillatory patterns were observed: standard pattern (gamma + beta), gamma-only and beta-only patterns. These patterns occurred with significantly different probabilities in the two PC areas. We observed that odor identity has a strong influence on the probability of occurrence of LFP beta and gamma oscillatory activity in the aPC. Thus, some odor coding mechanisms observed in the OB are retained in the aPC. By contrast, probability of occurrence of different oscillatory patterns is homogeneous in the pPC with beta-only pattern being the most prevalent one for all the different odor families. Overall, our results confirmed the functional heterogeneity of the PC with its anterior part tightly coupled with the OB and mainly encoding odorant features whereas its posterior part activity is not correlated with odorant features but probably more involved in associative and multi-sensory encoding functions.

Keywords: piriform cortex, beta, gamma, odor, molecular features, rat

Introduction

Local field potential (LFP) oscillations are a ubiquitous brain phenomenon observed across many phyla. Oscillations are proposed to be important for cell assembly synchronization and binding as well as plasticity (Buzsáki and Draguhn, 2004).

Oscillatory activity is a prominent characteristic of the olfactory system, notably the olfactory bulb (OB) (Adrian, 1942). This oscillatory activity consists of a slow modulation related to breathing and fast oscillations, in the beta (15-35 Hz) and gamma range (40-100 Hz) (Buonviso et al., 2006; Kay et al., 2009; Martin and Ravel, 2014). In the mammalian OB, mitral/tufted cell spikes can phase-lock to LFP oscillations (Kashiwadani et al., 1999; Lagier et al., 2004; Cenier et al., 2009; David et al., 2009; Courtiol et al., 2011; Gschwend et al., 2012) and we proposed that beta and gamma oscillations could subserve the emergence of different cell assemblies (Cenier et al., 2009). Thus, LFPs could provide a temporal frame, underlying and pacing the spiking activity.

The next and largest relay of the odorant information is the piriform cortex (PC). The PC is an heterogeneous structure both from an anatomical and a functional point of view (Haberly and Price, 1978; Litaudon et al., 1997a, 1997b, 2017). Indeed, the PC could be divided in two parts, anterior (aPC) and posterior (pPC), differing in their afferent and efferent connections, spiking activity and potentiation during associative conditioning (Litaudon and Cattarelli, 1995, 1996; Mouly et al., 2001; Bouret and Sara, 2002; Litaudon et al., 2003; Sevelinges et al., 2004; Kadohisa and Wilson, 2006; Calu et al., 2007; Roesch et al., 2007). Given its strong bulbar input, the aPC receives more sensory information than the pPC. Thus, it has been proposed that aPC encodes the identity / sensory features of the odor while pPC encodes the associative value of the stimulus (Kadohisa and Wilson, 2006; Calu et al., 2007; Roesch et al., 2007; Hagiwara et al., 2012).

LFP oscillatory activity (beta and gamma) has also been described in the mammalian PC (Freeman, 1959; Bressler, 1984; Kay and Freeman, 1998; Chabaud et al., 1999, 2000; Neville and Haberly, 2003; Martin et al., 2004, 2006; Hermer-Vazquez et al., 2007; Litaudon et al., 2008; Poo and Isaacson, 2009). Importantly, pyramidal cell spikes can phase-lock to LFP gamma and beta oscillations in the PC (Litaudon et al., 2008; Poo and Isaacson, 2009). The occurrence of gamma and beta oscillations as well as their pattern depend on the animal's behavior and can change across learning (Freeman, 1960; Zibrowski and Vanderwolf, 1997; Martin et al., 2006; Cohen

et al., 2015). For example, several studies showed that the amplitude of odor induced beta oscillations increases through learning in rodents (Martin and Ravel, 2014). Regarding those oscillatory activities, while most studies were performed in the aPC, very little is known about the pPC. Functionally, gamma oscillations can co-occur in both the OB and aPC during odorant stimulation and we and others have proposed that gamma oscillations can allow bulbo-cortical transfer of information (Buonviso et al., 2003; Litaudon et al., 2008; Mori et al., 2013). In the OB, we have shown that beta and gamma oscillation occurrence and features are modulated by the physical properties of the stimulus (Cenier et al., 2008). Therefore, temporal structuring of bulbar output might also reflect the molecular features of an odor, including both its chemical family and its more precise identity within the family. However, it remains unknown whether such odor related modulation of oscillatory patterns is maintained in the PC and whether those patterns are similar between the aPC and pPC.

Given the strong coupling between OB and aPC, we hypothesized that similar results could be obtained in the aPC whereas activity in the pPC would be more homogeneous regarding odor features as pPC is involved in more complex odor task learning (Litaudon et al., 1997b; Mouly and Gervais, 2002; Sevelinges et al., 2004, 2008). Thus, the present study was designed to analyze 1) the odor-evoked oscillatory patterns in aPC vs. pPC and 2) how different odorant molecular features can differentially affect the LFP signal in both the aPC and the pPC.

Experimental procedures

Animals and ethical statement

Animal care procedures were conducted in strict accordance with the European Community Council guidelines and received approval n° DSV 69387473 from veterinary services. All efforts were made to minimize pain to the animals.

Twelve Male Wistar rats weighing 250–350 g (Charles River Laboratories, L'Arbresle, France) were used. Animals were group-housed in polycarbonate cage with food and water *ad libitum* under environmental controlled conditions (temperature: $22 \pm 1^\circ\text{C}$; humidity: $55 \pm 10\%$). They were maintained under a 12 h light-dark cycle (lights on from 6:00 AM to 6:00 PM).

Preparation and recording apparatus

Experiments were performed on freely breathing, anesthetized rats. Anesthesia was performed through an intraperitoneal injection of urethane (1.5 g/kg). Supplemental doses were delivered during experimentation when necessary. Animals were immobilized with ear and teeth bars in a stereotaxic apparatus, and placed on a heating pad to maintain constant body temperature. The skull was exposed and a small bone window was drilled above the aPC and pPC. During the experiment, respiratory activity was monitored through a homemade airflow sensor placed near the entrance of the nostril (Roux et al., 2006). Neuronal activity was recorded using a 16-channel silicon neural probe (Neuronexus Technologies). Recording electrodes were lowered from the dorsal surface in the aPC ($1.5 < AP < 2.5$, $3.5 < ML < 4$ relative to Bregma) and the pPC ($-3.5 < AP < -2.5$, $5.5 < ML < 6$ relative to bregma). Placement of the deeper probe contact in layer Ia was determined according to the shape of the field potential evoked by mitral cell layer electrical stimulation (Litaudon et al., 2003, 2008). The 16 recording points were dispatched linearly along the silicone tip at 100 μm intervals. The extracellular signal was acquired in the full band (0–5000 Hz), amplified (gain = 1000) and digitalized with a high-speed 16-channels acquisition device (wavebook 512A and wavebook 10A, IOtech) at 10 kHz sampling rate. Fourteen channels, along with two channels dedicated to the continuous recording of respiratory signal and stimulus onset, were connected to the 14 lowest points on the electrode tip. Note that the two topmost recording points on the electrode were not used.

Odorant stimulation

Odors (SigmaAldrich, Fluka) were simple aliphatic compounds, varying in features such as the number of carbons in the main chain (chain length: 5, 6, 7 and 10 C) or the functional group associated with the chain (alcohol, ester, aldehyde or ketone) (Table 1). Odors were delivered in front of the animal's nose, at 18% of the saturated vapor pressure, through a dilution olfactometer (480 mL/min). Stimuli lasted 5 s and were separated from each other by at least 2 min. Stimulus onset was triggered on the respiratory cycle (at the maximum of exhalation).

LFPs analysis

LFP signals were similar across the 10 channels located in the PC and inverted in layer II. Thus LFP oscillations were analyzed using the channel located just above layer II (layer Ib) where LFP oscillation amplitude was maximal.

Wavelet transform

LFPs were obtained by band-passing the recorded signal at 0.1–200 Hz. Time and frequency information were obtained using a time-frequency representation based on continuous wavelet transform; the method has been described in detail by Roux et al. (Roux et al., 2007). Briefly, the down-sampled LFP signal was convoluted with Morlet's complex wavelets (Kronland-Martinet et al., 1987). Morlet's wavelets stretch from 5 to 100 Hz with a 0.25 Hz resolution in the frequency domain and a 5 ms resolution in the temporal domain.

Wavelet ridge extraction

The goal of this study was to analyze the occurrence of LFP oscillations, the correlation between LFP oscillations and respiration, and oscillation features. Instantaneous phase and frequency of the oscillatory episodes were obtained using an algorithmic procedure based on the wavelet ridges extraction method (Roux et al., 2007). Briefly, we computed the mean and standard deviation (STD) of the time-frequency representation and defined a threshold as the mean (5 STD) of the time-frequency energy contained in the pre-stimulus period (between 0 and 5 s). Then, the coordinates in time and frequency of all local maxima in the beta band (15-35 Hz) and the gamma band (40–90 Hz) above this threshold were extracted during the stimulus period. From each maximum, we computed a high time-resolution (0.1 ms) Morlet's complex wavelet transformation, both forward and backward, following the line of maximum energy. The computation stopped when the energy fell below the threshold. Therefore, for each maximum detected on the time frequency map, we obtained a high time-resolution wavelet ridge defined by its starting and ending times, its instantaneous frequency and instantaneous phase. Thus, each oscillatory episode was characterized by the coordinates of its maximum (amplitude, frequency, respiratory phase) and its wavelet ridge (duration, instantaneous phase and frequency).

Respiratory signal analysis

In order to take into account the respiratory modulation of odor evoked activity (Litaudon et al., 2003; Buonviso et al., 2006), data were analyzed as a function of respiratory phase. Respiratory signal processing presented here was a modified version of the analysis method described in a previous paper (Roux et al., 2006). The respiratory cycle was first divided into two periods: inspiration and expiration. Second, the mean duration of both periods was computed from all recordings. Third, inspiration and expiration periods of each recording were resized according to this mean duration, and the total length of the respiratory cycle was normalized to 1. Thus, this phase representation of the respiratory cycle was used as a normalized time basis (between 0 and 1) permitting us to analyze results in a standardized data format across different recordings.

Statistical analysis

Rayleigh test for directionality was used to determine if LFP oscillations were uniformly distributed (unsynchronized) or non-uniformly distributed (synchronized) relative to the respiratory cycle (Litaudon et al., 2008). Comparisons of phase between odors or PC subunits were performed using a Watson F test (this statistical test is specific for circular data) (Mardia, 1972; Fisher, 1993). Probability of occurrence of the different oscillatory patterns between odors and PC subunits were compared using chi-square analysis. Comparison of oscillation features and odds values between PC areas were performed using one-way Anova.

Results

As described in previous studies (Neville and Haberly, 2003; Litaudon et al., 2008), odor stimulation in the anesthetized rats evokes transient epochs of LFP fast oscillations in PC in two distinct frequency bands (Fig. 1). In this study, we analyzed oscillatory burst features and occurrence of gamma and beta oscillations according to the PC area and the odor family. A total of 210 recordings were analyzed in this study. Overall, 710 oscillatory episodes were detected.

Taking into consideration all odorant stimulations, our analysis did not reveal a difference in the oscillation's intrinsic features between PC subunits, with the exception of gamma oscillations which appeared with higher amplitude and an earlier respiratory phase in the aPC than in the pPC (Table 2).

In spite of this weak difference in their intrinsic features, oscillatory episodes in the beta and/or gamma ranges occurred with different probabilities in the two PC areas. As reported in the OB (Cenier et al., 2008), three oscillatory patterns were observed: standard pattern (gamma + beta), gamma-only pattern (only gamma oscillations) and beta-only patterns (only beta oscillations). These patterns occurred with significantly different probabilities in the two PC areas (Chi-square test, $p < 10^{-6}$). While odor stimulation evoked mainly standard patterns in the aPC, it induced more frequently beta-only patterns in the pPC (Fig. 2). In both PC areas, there were few recordings (3%) where gamma-only pattern was observed. We then wondered to what extent such differences in patterns could originate in a differential responsivity to the different odorants. Figure 3 shows the probability of occurrence for each pattern as a function of the odorant molecule. It appears clearly from this analysis that, while different odorants evoked oscillatory patterns with different probabilities in aPC, probabilities were rather similar in pPC. In order to quantify this observation, we calculated for each odor an odds value (Cenier et al., 2008) representing the ratio of the probability for the odor to elicit the standard pattern (gamma+beta) over the probability to elicit the beta-only pattern. These values are given at the top of each histogram in figure 3. On average odds value was significantly higher in the aPC compared to pPC (Anova, $p < 0.005$; Fig. 4). In addition, and as expected from the probability of occurrence of each pattern (Fig. 3), we observed a difference of variability in the odds values between aPC and pPC. In the aPC, oscillatory pattern differed between odors with odds values ranging from 0.33 to 9. For example, an alcohol with 6 carbons mostly elicits a beta only pattern, with an odds value of 0.33, while a 5 carbons ester evokes an alternation of both beta and gamma oscillations with an odds value of 9 (Fig. 3). By contrast, pPC evoked oscillatory activities across odors were much less variable ranging from 0.12 to 0.67 with most odors inducing the emergence of beta oscillations only (Fig. 3 and 4).

In our previous study (Cenier et al., 2008), we showed that, in the OB, odds values correlated well with the vapor pressure (VP) of odorants, particularly when odors were sorted into sub-groups (alcohols vs esters). We then performed the same analysis here, in the aPC and pPC. Interestingly, we observed that VP correlated with odds in aPC ($r = 0.72$, $p < 0.05$; Fig. 5A) while such a correlation was not found in the pPC ($r = 0.44$, $p = 0.196$; Fig 5B). When odors are sorted into sub-groups (alcohol and ester groups), we found that, in the aPC, VP and odds values were strongly

correlated for esters ($r=0.96$, $p<0.05$) but no correlation was found for alcohols ($r=0.58$, $p=0.42$) (Fig. 5C,D). It thus seemed that, in the aPC but not in pPC, odds values were at least partly determined by VP. Nevertheless, VP cannot account for all the odds values as for example, E07 and A06 have similar VP (124 and 91 Pa, respectively) but elicited dissimilar patterns of oscillations (odds values, 4 and 0.33 respectively) (Fig. 3). The opposite case is illustrated in Figure 3. Despite having very dissimilar VP (29 and 469 Pa) two odors (A07 and D07, respectively) elicit very similar oscillatory patterns, confirmed by their close odds values (1.25 and 1.67 respectively).

Discussion

In the olfactory system, different authors have demonstrated the importance of oscillatory LFP activity, especially in the insect (Stopfer et al., 1997; Perez-Orive et al., 2002). For example, pharmacological desynchronization in honeybees impairs fine discrimination in a behavioral paradigm (Stopfer et al., 1997), demonstrating the functional relevance of oscillatory synchronization. In mammals, a number of works describe the oscillatory activity in the first olfactory brain relay. However much less is known about the PC, especially the difference between aPC and pPC, while this structure is highly heterogeneous (Litaudon et al., 1997a; Haberly, 2001). The aim of this study was to determine the difference of oscillatory patterns in the aPC vs pPC as a function of the odorant families.

As previously described in the aPC (Litaudon et al., 2008), odors evoked LFP oscillations both in the beta and gamma frequency bands. We observed that while the intrinsic characteristics (frequency, amplitude, respiratory phase) of those oscillations differed only weakly between the two PC areas, their probability of occurrence strongly differed between aPC and pPC. Notably, the most frequent pattern in the aPC was the standard one (beta + gamma) while it was mostly the beta-only pattern in the pPC. The origin of fast oscillations in the PC is not known. It has been proposed that gamma oscillations originate from the OB, are transmitted to the PC via the lateral olfactory tract (Bressler and Freeman, 1980; Neville and Haberly, 2003; Martin et al., 2004) and are maintained through local inhibitory circuits in the PC (Luna and Schoppa, 2008).

Relative to beta oscillations, their emergence requires an intact OB-PC network

(Neville and Haberly, 2003; Martin et al., 2004, 2006). In addition, a putative mechanism of oscillatory network formation is phase-lag between neuronal populations, and it has been demonstrated that two types of inhibitory interneurons in the aPC fire with a phase-lag in the range of beta oscillation frequency (Suzuki and Bekkers, 2010) Thus, the global difference of oscillatory patterns between the two PC areas may be attributed (at least in part) to the anatomical heterogeneity of the PC circuitry. Indeed, the aPC receives more afferent inputs from the OB than the pPC whereas the reverse is the case for intrinsic excitatory associational inputs (Haberly and Price, 1978; Datiche et al., 1996; Haberly, 2001; Nagayama et al., 2010; Hagiwara et al., 2012; Srinivasan and Stevens, 2018). Moreover, a gradient of inhibitory circuits has been reported with increasing pyramidal cell inhibition along the rostro-caudal axis (Löscher et al., 1998; Luna and Pettit, 2010; Franks et al., 2011; Poo and Isaacson, 2011; Large et al., 2018). Thus, there is a gradient in the balance between excitatory and inhibitory inputs along the antero-posterior axis. Interestingly, it has been shown in the medial entorhinal cortex that the expression and power of fast oscillations (30-100Hz) is determined by the amount and gradient of local inhibitory circuit along the dorsal-ventral axis (Beed et al., 2013).

Regarding how the odorant features can modulate the LFP oscillations in aPC and pPC, we observed that odor identity has a strong influence on the probability of occurrence of gamma and beta oscillations in the aPC. By contrast, probability of occurrence of different oscillatory patterns is homogeneous in the pPC with the beta-only pattern being the most prevalent one for all the different odor families. Our results in the aPC are congruent with our previous study in the OB (Cenier et al., 2008) showing that the probability of occurrence of beta and gamma oscillations seemed to vary according to the odor functional group. Moreover, odds values (the ratio between standard pattern and beta-only pattern occurrence probability) were correlated with VP which is a good estimator of airborne concentration of odor (Lowry and Kay, 2007). Thus, as previously reported in aPC (Neville and Haberly, 2003), odors at high concentrations induced both gamma and beta frequency oscillations, whereas those at lower concentrations elicited mainly beta oscillations. The relationship between VP and odds value was nearly linear within the ester family but contrary to the OB (Cenier et al., 2008) such correlation was not observed within the alcohol family. Thus, some odor coding mechanisms observed in the OB are only

partly retained in the anterior PC. The similarity of oscillatory patterns evoked by different odorant families is not surprising given the strong bulbar afferent input to aPC (Haberly, 1973; Schwob and Price, 1978) and the functional coupling observed between the OB and the aPC in both anesthetized (Fontanini and Bower, 2005; Litaudon et al., 2008) and awake rats (Kay and Freeman, 1998; Chabaud et al., 1999). This observation at the network level also agrees with the single-unit recordings. Single-unit recordings reveal that aPC neuron activity is more constrained by odor features than in the pPC (Litaudon et al., 2003; Kadohisa and Wilson, 2006; Roesch et al., 2007). The aPC can still display some associative features but to a lesser extent than the pPC (Schoenbaum and Eichenbaum, 1995; Zinyuk et al., 2001; Kadohisa and Wilson, 2006; Calu et al., 2007; Gire et al., 2013). This can be put in perspective with our LFP results showing that aPC activity was not an exact mirror of the OB activity as we did not observe correlation between alcohol VP and odds values. There are few reports on *in-vivo* pPC single-unit activity but all of them point (Kadohisa and Wilson, 2006; Calu et al., 2007) toward the associative feature of the pPC in which activity can vary with the outcome associated to the odors and be the site of multisensory integration (Maier et al., 2012). The more integrative activity in the pPC may be related to the above mentioned recurrent inhibition (Luna and Morozov, 2012) but also to the different neuromodulatory and afferent/efferent connections of the pPC (Bouret and Sara, 2002; Chen et al., 2014), notably inputs coming massively from the basolateral amygdala (Sadriani and Wilson, 2015). Given these differences, it is also expected that different olfactory conditionings as well as olfactory task learning can differentially modulate the expression of beta/gamma oscillations patterns in aPC and pPC (Kay, 2014; Martin and Ravel, 2014). Further studies combining various odorant families with the acquisition of a behavioral task will be needed to determine how both factors affect the oscillatory patterns occurrence in aPC vs pPC.

Interestingly, those results confirm and deepen our understanding of the heterogeneity and characteristics of the piriform cortex in humans. Indeed, in human and following several fMRI studies (Gottfried et al., 2002, 2006; Zelano et al., 2007; Howard et al., 2009; Fournel et al., 2016), a dissociation between aPC and pPC has been proposed and it has been shown that aPC activity represents the fidelity of

information arising from the OB while the pPC is more synthetic and associative with for example the generation of predictive templates (Zelano et al., 2011).

Overall, our results confirmed the functional heterogeneity of the PC. Whereas activity in its anterior part is tightly coupled with the OB and mainly encodes odorant features, activity in its posterior part does not correlate with odorant features but is probably more involved in cognitive functions, such as memory or odor significance encoding, not involved in this experiment (Litaudon et al., 1997b; Haberly, 2001; Mouly and Gervais, 2002; Sevelinges et al., 2008; Hegoburu et al., 2009).

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References

Adrian ED (1942) Olfactory reactions in the brain of the hedgehog. *J Physiol* 100:459-473.

Beed P, Gundlfinger A, Schneiderbauer S, Song J, Böhm C, Burgalossi A, Brecht M, Vida I, Schmitz D (2013) Inhibitory gradient along the dorsoventral axis in the medial entorhinal cortex. *Neuron* 79:1197-1207.

Bouret S, Sara SJ (2002) Locus coeruleus activation modulates firing rate and temporal organization of odour-induced single-cell responses in rat piriform cortex. *Eur J Neurosci* 16:2371-2382.

Bressler SL (1984) Spatial organization of EEGs from olfactory bulb and cortex. *Electroencephalogr Clin Neurophysiol* 57:270-276.

Bressler SL, Freeman WJ (1980) Frequency analysis of olfactory system EEG in cat, rabbit, and rat. *Electroencephalogr Clin Neurophysiol* 50:19-21.

Buonviso N, Amat C, Litaudon P (2006) Respiratory modulation of olfactory neurons in the rodent brain. *Chem Senses* 31:145-154.

Buonviso N, Amat C, Litaudon P, Roux S, Royet JP, Farget V, Sicard G (2003) Rhythm sequence through the olfactory bulb layers during the time window of a respiratory cycle. *Eur J Neurosci* 17:1811-1819.

Buzsáki G, Draguhn A (2004) Neuronal oscillations in cortical networks. *Science* 304:1926-1929.

Calu DJ, Roesch MR, Stalnaker TA, Schoenbaum G (2007) Associative encoding in posterior piriform cortex during odor discrimination and reversal learning. *Cereb Cortex* 17:1342-1349.

Canier T, Amat C, Litaudon P, Garcia S, Lafaye de Micheaux P, Liqueur B, Roux S, Buonviso N (2008) Odor vapor pressure and quality modulate local field potential oscillatory patterns in the olfactory bulb of the anesthetized rat. *Eur J Neurosci* 27:1432-1440.

Canier T, David F, Litaudon P, Garcia S, Amat C, Buonviso N (2009) Respiration-gated formation of gamma and beta neural assemblies in the mammalian olfactory bulb. *Eur J Neurosci* 29:921-930.

Chabaud P, Ravel N, Wilson DA, Gervais R (1999) Functional coupling in rat central olfactory pathways: a coherence analysis. *Neurosci Lett* 276:17-20.

Chabaud P, Ravel N, Wilson DA, Mouly A-M, Vigouroux M, Farget V, Gervais R (2000) Exposure to behaviourally relevant odour reveals differential characteristics in rat central olfactory pathways as studied through oscillatory activities. *Chem Senses* 25:561-573.

Chen C-FF, Zou D-J, Altomare CG, Xu L, Greer CA, Firestein SJ (2014) Nonsensory target-dependent organization of piriform cortex. *Proc Natl Acad Sci USA* 111:16931-16936.

Cohen Y, Putrino D, Wilson DA (2015) Dynamic cortical lateralization during olfactory discrimination learning. *J Physiol* 593:1701-1714.

Courtiol E, Amat C, Thevenet M, Messaoudi B, Garcia S, Buonviso N (2011) Reshaping of bulbar odor response by nasal flow rate in the rat. *PLoS One* 6:e16445.

Datiche F, Litaudon P, Cattarelli M (1996) The intrinsic association fiber system of the rat piriform cortex: a quantitative study based on a cholera toxin B subunit (CTb) tracing in the rat. *J Comp Neurol* 376:265-277.

David FO, Hugues E, Cenier T, Fourcaud-Trocme N, Buonviso N (2009) Specific entrainment of mitral cells during gamma oscillation in the rat olfactory bulb. *PLoS Comput Biol* 5:e1000551.

Fisher NI (1993) *Statistical analysis of circular data*. Cambridge: Cambridge University Press.

Fontanini A, Bower JM (2005) Variable coupling between olfactory system activity and respiration in ketamine/xylazine anesthetized rats. *J Neurophysiol* 93:3573-3581.

Fournel A, Ferdenzi C, Sezille C, Rouby C, Bensafi M (2016) Multidimensional representation of odors in the human olfactory cortex. *Hum Brain Mapp* 37:2161-2172.

Franks KM, Russo MJ, Sosulski DL, Mulligan AA, Siegelbaum SA, Axel R (2011) Recurrent circuitry dynamically shapes the activation of piriform cortex. *Neuron* 72:49-56.

Freeman WJ (1959) Distribution in time and space of prepyriform electrical activity. *J Neurophysiol* 22:644-665.

Freeman WJ (1960) Correlation of electrical activity of prepyriform cortex and behavior in cat. *J Neurophysiol* 23:111-131.

Gire DH, Whitesell JD, Doucette W, Restrepo D (2013) Information for decision-making and stimulus identification is multiplexed in sensory cortex. *Nat Neurosci* 16:991-993.

Gottfried JA, Deichmann R, Winston JS, Dolan RJ (2002) Functional heterogeneity in human olfactory cortex: an event-related functional magnetic resonance imaging study. *J Neurosci* 22:10819-10828.

Gottfried JA, Winston JS, Dolan RJ (2006) Dissociable codes of odor quality and odorant structure in human piriform cortex. *Neuron* 49:467-479.

Gschwend O, Beroud J, Carleton A (2012) Encoding odorant identity by spiking packets of rate-invariant neurons in awake mice. *PLoS One* 7:e30155.

Haberly LB (1973) Summed potentials evoked in opossum prepyriform cortex. *J Neurophysiol* 36:775-788.

Haberly LB (2001) Parallel-distributed processing in olfactory cortex: new insights from morphological and physiological analysis of neuronal circuitry. *Chem Senses* 26:551-576.

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.

Hagiwara A, Pal SK, Sato TF, Wienisch M, Murthy VN (2012) Optophysiological analysis of associational circuits in the olfactory cortex. *Front Neural Circuits* 6:18.

Hegoburu C, Sevelinges Y, Thévenet M, Gervais R, Parrot S, Mouly A-M (2009) Differential dynamics of amino acid release in the amygdala and olfactory cortex during odor fear acquisition as revealed with simultaneous high temporal resolution microdialysis. *Learn Mem* 16:687-697.

Hermer-Vazquez R, Hermer-Vazquez L, Srinivasan S, Chapin JK (2007) Beta- and gamma-frequency coupling between olfactory and motor brain regions prior to skilled, olfactory-driven reaching. *Exp Brain Res* 180:217-235.

Howard JD, Plailly J, Grueschow M, Haynes J-D, Gottfried JA (2009) Odor quality coding and categorization in human posterior piriform cortex. *Nat Neurosci* 12:932-938.

Kadohisa M, Wilson DA (2006) Separate encoding of identity and similarity of complex familiar odors in piriform cortex. *Proc Natl Acad Sci USA* 103:15206-15211.

Kashiwadani H, Sasaki YF, Uchida N, Mori K (1999) Synchronized oscillatory discharges of mitral/tufted cells with different molecular ranges in the rabbit olfactory bulb. *J Neurophysiol* 82:1786-1792.

Kay LM (2014) Circuit oscillations in odor perception and memory. *Prog Brain Res* 208:223-251.

Kay LM, Beshel J, Brea J, Martin C, Rojas-Líbano D, Kopell N (2009) Olfactory oscillations: the what, how and what for. *Trends Neurosci* 32:207-214.

Kay ML, Freeman WJ (1998) Bidirectional processing in the olfactory-limbic axis during olfactory behaviour. *Behav Neurosci* 112:541-553.

Kronland-Martinet R, Morlet J, Grossmann A (1987) Analysis of sound patterns through wavelet transforms. *Int J Patt Recogn Art Intell* 1:273-302.

Lagier S, Carleton A, Lledo P-M (2004) Interplay between local GABAergic interneurons and relay neurons generates γ oscillations in the rat olfactory bulb. *J Neurosci* 24:4382-4392.

Large AM, Vogler NW, Canto-Bustos M, Friason FK, Schick P, Oswald A-MM (2018) Differential inhibition of pyramidal cells and inhibitory interneurons along the rostrocaudal axis of anterior piriform cortex. *Proc Natl Acad Sci USA* 115:E8067-E8076.

Litaudon P, Amat C, Bertrand B, Vigouroux M, Buonviso N (2003) Piriform cortex functional heterogeneity revealed by cellular responses to odours. *Eur J Neurosci* 17:2457-2461.

Litaudon P, Bouillot C, Zimmer L, Costes N, Ravel N (2017) Activity in the rat olfactory cortex is correlated with behavioral response to odor: a microPET study. *Brain Struct Funct* 222:577-586.

Litaudon P, Cattarelli M (1995) Piriform cortex late activity revealed functional spatial heterogeneity. *NeuroReport* 6:1377-1380.

Litaudon P, Cattarelli M (1996) Olfactory bulb repetitive stimulations reveal non-homogeneous distribution of the inhibitory processes in the rat piriform cortex. *Eur J Neurosci* 8:21-29.

Litaudon P, Datiche F, Cattarelli M (1997a) Optical recording of the rat piriform cortex activity. *Prog Neurobiol* 52:485-510.

Litaudon P, Garcia S, Buonviso N (2008) Strong coupling between pyramidal cell activity and network oscillations in the olfactory cortex. *Neuroscience* 156:781-787.

Litaudon P, Mouly A-M, Sullivan R, Gervais R, Cattarelli M (1997b) Learning-induced changes in rat piriform cortex mapped using multisite recording with voltage-sensitive dye. *Eur J Neurosci* 8:1593-1602.

Löscher W, Lehmann H, Ebert U (1998) Differences in the distribution of GABA- and GAD-immunoreactive neurons in the anterior and posterior piriform cortex of rats. *Brain Res* 800:21-31.

Lowry CA, Kay LM (2007) Chemical factors determine olfactory system beta oscillations in waking rats. *J Neurophysiol* 98:394-404.

Luna VM, Morozov A (2012) Input-specific excitation of olfactory cortex microcircuits. *Front Neural Circuits* 6:69.

Luna VM, Pettit DL (2010) Asymmetric rostro-caudal inhibition in the primary olfactory cortex. *Nat Neurosci* 13:533-535.

Luna VM, Schoppa NE (2008) GABAergic circuits control input-spike coupling in the piriform cortex. *J Neurosci* 28:8851-8859.

Maier JX, Wachowiak M, Katz DB (2012) Chemosensory convergence on primary olfactory cortex. *J Neurosci* 32:17037-17047.

Mardia KV (1972) *Statistics of directional data*. London: Academic Press.

Martin C, Gervais R, Hugues E, Messaoudi B, Ravel N (2004) Learning modulation of odor-induced oscillatory responses in the rat olfactory bulb: a correlate of odor recognition? *J Neurosci* 24:389-397.

Martin C, Gervais R, Messaoudi B, Ravel N (2006) Learning-induced oscillatory activities correlated to odour recognition: a network activity. *Eur J Neurosci* 23:1801-1810.

Martin C, Ravel N (2014) Beta and gamma oscillatory activities associated with olfactory memory tasks: different rhythms for different functional networks? *Front Behav Neurosci* 8:218.

Mori K, Manabe H, Narikiyo K, Onisawa N (2013) Olfactory consciousness and gamma oscillation couplings across the olfactory bulb, olfactory cortex, and orbitofrontal cortex. *Front Psychol* 4:743.

Mouly A-M, Fort A, Ben-Boutayab N, Gervais R (2001) Olfactory learning induces differential long-lasting changes in rat central olfactory pathways. *Neuroscience* 102:11-21.

Mouly AM, Gervais R (2002) Polysynaptic potentiation at different levels of rat olfactory pathways following learning. *Learn Mem* 9:66-75.

Nagayama S, Enerva A, Fletcher ML, Masurkar AV, Igarashi KM, Mori K, Chen WR (2010) Differential axonal projection of mitral and tufted cells in the mouse main olfactory system. *Front Neural Circuits* 4:120.

Neville KR, Haberly LB (2003) Beta and gamma oscillations in the olfactory system of the urethane-anesthetized rat. *J Neurophysiol* 90:3921-3930.

Perez-Orive J, Mazor O, Turner GC, Cassenaer S, Wilson RI, Laurent G (2002) Oscillations and sparsening of odor representations in the mushroom body. *Science* 297:359-365.

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

Poo C, Isaacson JS (2011) A major role for intracortical circuits in the strength and tuning of odor-evoked excitation in olfactory cortex. *Neuron* 72:41-48.

Roesch MR, Stalnaker TA, Schoenbaum G (2007) Associative encoding in anterior piriform cortex versus orbitofrontal cortex during odor discrimination and reversal learning. *Cereb Cortex* 17:643-652.

Roux SG, Cenier T, Garcia S, Litaudon P, Buonviso N (2007) A wavelet-based method for local phase extraction from a multi-frequency oscillatory signal. *J Neurosci Meth* 160:135-143.

Roux SG, Garcia S, Bertrand B, Cenier T, Vigouroux M, Buonviso N, Litaudon P (2006) Respiratory cycle as time basis: an improved method for averaging olfactory neural events. *J Neurosci Meth* 152:173-178.

Sadrian B, Wilson DA (2015) Optogenetic Stimulation of Lateral Amygdala Input to Posterior Piriform Cortex Modulates Single-Unit and Ensemble Odor Processing. *Front Neural Circuits* 9:81.

Schoenbaum G, Eichenbaum H (1995) Information coding in the rodent prefrontal cortex.1. Single-neuron activity in orbitofrontal cortex compared with that in pyriform cortex. *J Neurophysiol* 74:733-750.

Schwob JE, Price JL (1978) The cortical projections of the olfactory bulb: development in fetal and neonatal rats with additional observations in the adult. *Brain Res* 151:369-374.

Sevelinges Y, Gervais R, Messaoudi B, Granjon L, Mouly A-M (2004) Olfactory fear conditioning induces field potential potentiation in rat olfactory cortex and amygdala. *Learn Mem* 11:761-769.

Sevelinges Y, Sullivan RM, Messaoudi B, Mouly A-M (2008) Neonatal odor-shock conditioning alters the neural network involved in odor fear learning at adulthood. *Learn Mem* 15:649-656.

Srinivasan S, Stevens CF (2018) The distributed circuit within the piriform cortex makes odor discrimination robust. *J Comp Neurol* 526:2725-2743.

Stopfer M, Bhagavan S, Smith BH, Laurent G (1997) Impaired odour discrimination on desynchronization of odour-encoding neural assemblies. *Nature* 390:70-74.

Suzuki N, Bekkers JM (2010) Distinctive classes of GABAergic interneurons provide layer-specific phasic inhibition in the anterior piriform cortex. *Cereb Cortex* 20:2971-2984.

Zelano C, Mohanty A, Gottfried JA (2011) Olfactory predictive codes and stimulus templates in piriform cortex. *Neuron* 72:178-187.

Zelano C, Montag J, Johnson B, Khan R, Sobel N (2007) Dissociated representations of irritation and valence in human primary olfactory cortex. *J Neurophysiol* 97:1969-1976.

Zibrowski EM, Vanderwolf CH (1997) Oscillatory fast wave activity in the rat pyriform cortex: relations to olfaction and behaviour. *Brain Res* 766:39-49.

Zinyuk LE, Datiche F, Cattarelli M (2001) Cell activity in the anterior piriform cortex during an olfactory learning in the rat. *Behav Brain Res* 124:29-32.

Table 1. Panel of odors used in this study

Carbon chain length	Odorant	Symbol	VP (Pa)
Alcohol			
5	Pentanol	A05	293
6	Hexanol	A06	124
7	Heptanol	A07	29
10	Decanol	A10	1
Ester			
5	Ethyl-valerate	E05	639
6	Ethyl-hexanoate	E06	240
7	Ethyl-heptanoate	E07	91
10	Ethyl-decanoate	E10	6
Ketone			
7	2-heptanone	K07	514
Aldehyde			
7	Heptanal	D07	469

Table 2: Comparison of oscillatory episodes features between PC areas

Oscillation feature	Anova with PC area as the main factor
Gamma band	
Frequency	NS ($F_{1,80}=0.48$)
Duration	NS ($F_{1,80}=2.09$)
Amplitude	$p<0.005$ (Ant>Post) ($F_{1,80}=10.94$)
Respiratory phase	$p<10^{-3}$ (earlier in aPC)- Watson F-test
Beta band	
Frequency	NS ($F_{1,159}=0.35$)
Duration	NS ($F_{1,159}=0.69$)
Amplitude	NS ($F_{1,159}=2.53$)
Respiratory phase	NS- Watson F-test

Oscillation features (frequency, duration, amplitude) were statistically compared using Anova and respiratory phase was compared using Watson F-test

Figure 5

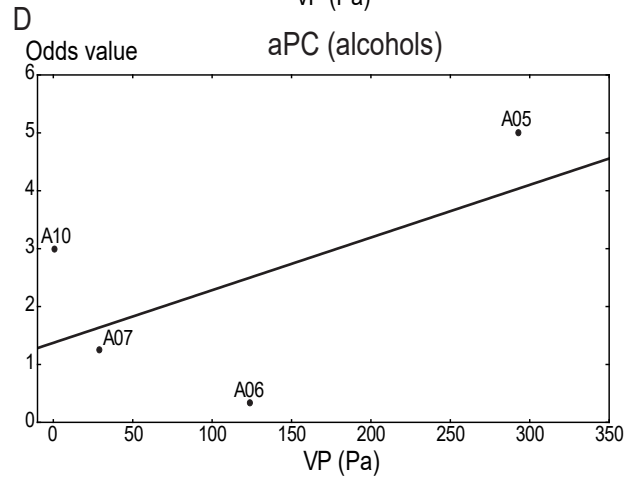
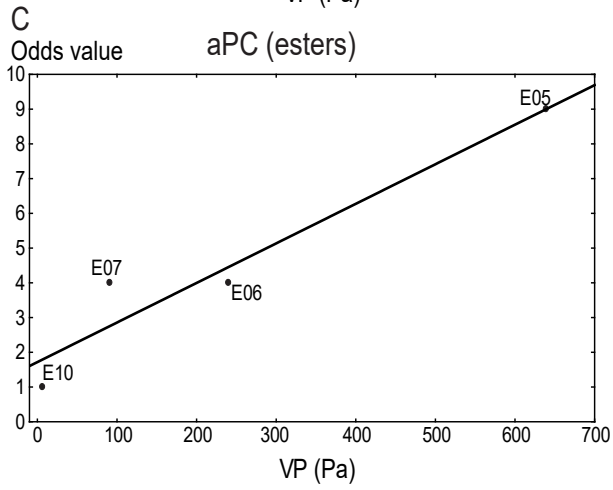
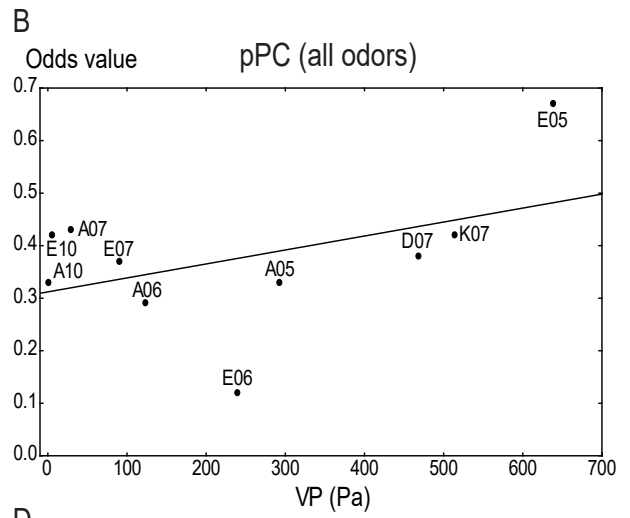
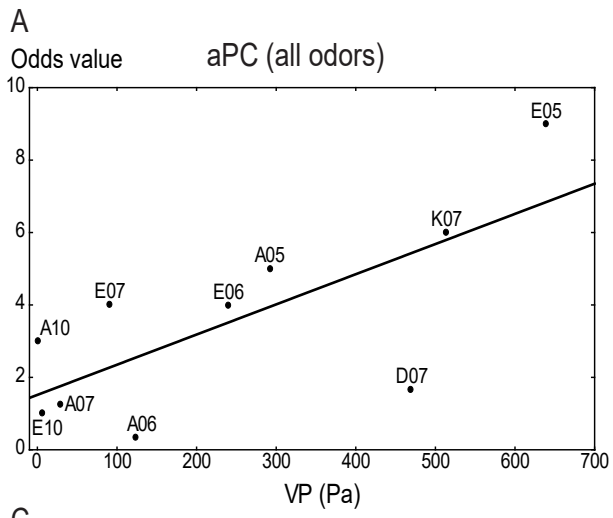
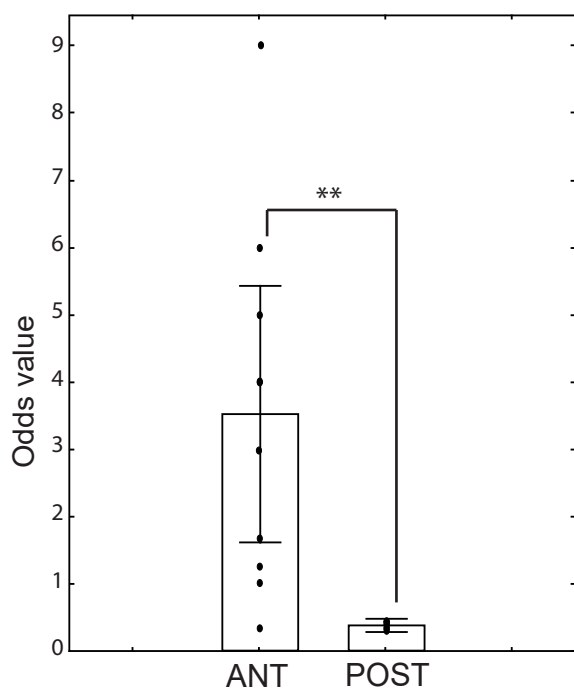


Figure 4



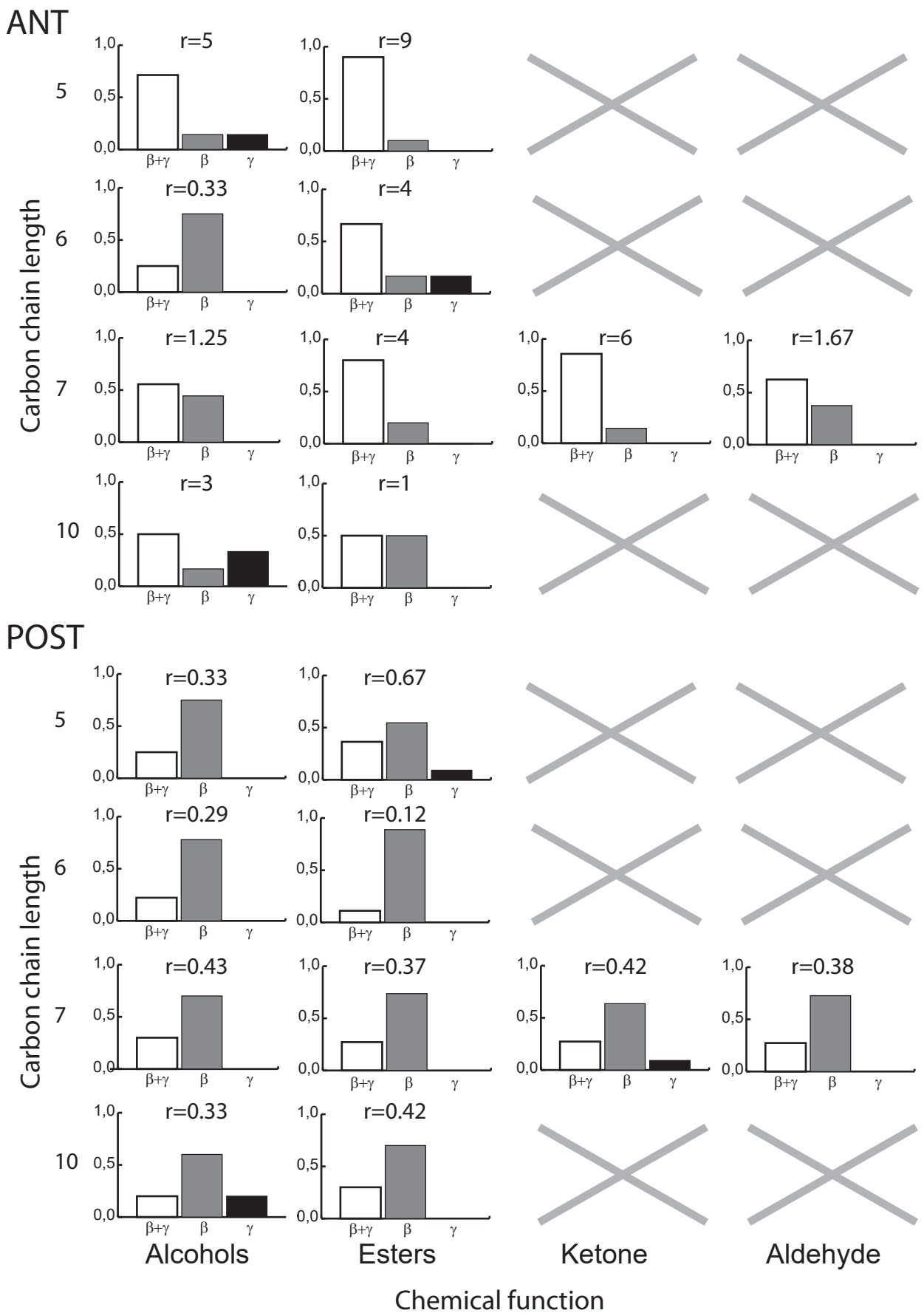


Figure 3

Figure 2

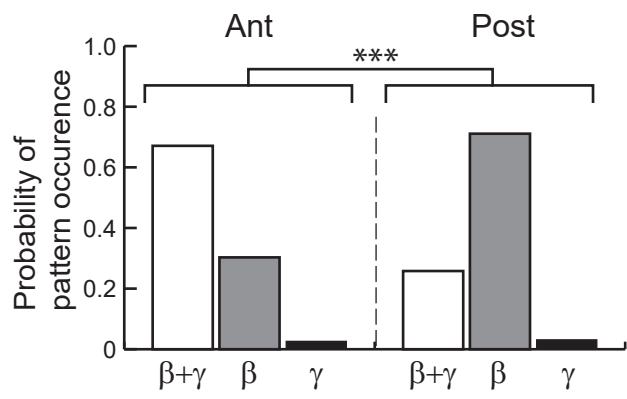


Figure 1

