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Event-related oscillations (EROs) in the parietal cortex of adult alcohol-preferring (P) and alcohol-nonpreferring (NP) rats

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Abstract

The selectively bred alcohol-preferring (P) and -nonpreferring (NP) lines were developed from Wistar rats to model high and low voluntary alcohol consumption and have been demonstrated to exhibit many of the characteristics of human alcohol dependence. Electrophysiological studies have shown P rats exhibit more electroencephalographic fast frequency activity and reduced P3 amplitude in the parietal cortex than alcohol-nonpreferring (NP) rats, findings that are more common in alcohol dependent individuals. Event-related oscillations (EROs) have been suggested to be good endophenotypes associated with ethanol dependence in clinical studies. Recently EROs have also been demonstrated to occur in rodents in response to stimuli that are similar to that used in human clinical studies. The objective of the present study was to characterize EROs in adult P and NP rats. A time-frequency representation method was used to determine delta, theta and alpha/beta ERO energy and the degree of phase variation in the parietal cortex of adult P and NP rats. The present results suggest that the decrease in P3 amplitudes previously shown in P rats were not associated with changes in ERO energy but were significantly associated with decreases in evoked delta and alpha/beta phase locking. These studies demonstrate ERO measures may also be good endophenotypes in animal models of alcoholism.

Keywords

Alcohol-preferring rats; Event-related oscillations; Ethanol; Parietal cortex; P300; Event-related potentials; Electroencephalogram

Introduction

Genetic selection studies have resulted in a number of high drinking lines of mice and rats (see Bell et al., 2006; Green and Grahame, 2008). The alcohol-preferring (P) and -nonpreferring (NP) rat lines are one of the most extensively examined animal models of alcoholism (Li et al., 1993). These rats were developed for differences in home cage ethanol consumption in order to study ethanol drinking behaviors and their consequences (Bell et al.,

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2006; Lumeng et al., 1977). Selectively bred P rats have been shown to voluntarily consume levels of 10% ethanol of >5 g/kg/day, with an ethanol preference ratio (vs. water) of greater than 2:1. The NP rats generally consume levels of 10% ethanol of <1.5 g/kg/day, with an ethanol preference ration of less than 0.2:1. These lines have been the focus of intensive study of the behavioral, neurobiological, and neurophysiological factors that contribute to ethanol consumption (for reviews, see Bell et al., 2006; Li et al., 1993; McBride and Li, 1998).

Electrophysiological differences between the rat lines have also been demonstrated (Breen and Morzorati, 1996; Ehlers et al., 1991, 1992, 1999; Morzorati et al., 1994; Robledo et al., 1993, 1994). The study of neurophysiological endophenotypes in P and NP rats with well-differentiated ethanol-related phenotypes could be an additional tool for identifying susceptibility genes for ethanol dependence. We have previously characterized the electrophysiological profile of P and NP rats and found that P rats have significantly lower amplitude of the P3 component of the event-related potential (ERP), when compared to NP rats (Ehlers et al., 1999). This finding is similar to what has been reported for human subjects at differing risk for ethanol dependence (for review, see Porjesz et al., 2005).

There is evidence to suggest that ERPs may originate from an additive, evoked activation of neural assemblies independent of ongoing EEG as well as by the phase resetting of ongoing EEG oscillations in response to sensory input (for review, see Rangaswamy and Porjesz, 2008; Sauseng et al., 2007). Considerable efforts have been made in understanding how these models may potentially explain the generation of human ERPs. For instance, it has been proposed that the P3 component arises from a series of superimposed event-related oscillations (EROs) that are induced by sensory or cognitive processes that influence the dynamics of EEG rhythms (e.g. Demiralp et al., 2001; Karakas et al., 2000; Yordanova and Kolev, 1996). EROs are estimated by performing a decomposition of the EEG signal into phase and magnitude information over a range of frequencies and then the changes in those frequencies are characterized over a millisecond time scale with respect to task events. EROs have been demonstrated to be sensitive measures of both normal and abnormal cognitive functioning in humans (see Basar et al., 1999, 2001; Gevins et al., 1998; Klimesch et al., 1997; Schurmann et al., 2001). Additionally, these oscillations have been linked to several relevant genes associated with ethanol dependence phenotypes (Begleiter and Porjesz, 2006; Edenberg et al., 2004; Jones et al., 2004).

Studies have further demonstrated that delta and theta EROs are the primary contributors to the human P3 ERP component (Basar et al., 1999; Basar-Eroglu et al., 1992; Demiralp et al., 2001; Karakas et al., 2000; Schurmann et al., 2001). Reductions in P3 amplitude have been related to decreased cortical ERO energy and also to higher phase variability and weaker phase locking. For instance, it has been shown that the reduction of P3 amplitude during retrieval of a working memory task is associated with a decrease in delta ERO power and an increase in phase variability (Schack and Klimesch, 2002). In addition to their role in generating the P3 ERP component, evoked oscillations have also been shown to play a role in the generation of other ERP components, including the P1-N1 complex. There is evidence to suggest that alpha and theta evoked power and phase locking (PL) plays an important role in the generation of the P1-N1 complex (Klimesch et al., 2004). However, whether differences in ERO energy and phase variability play a role in the different neurophysiological profiles identified in animal models has been less studied

In view of the evidence from human studies of the link between alcohol dependence and ERO energy (Porjesz et al., 2005), characterizing the relationship between an ethanol preference phenotype and changes in EROs, translating this information to an animal model may provide valuable information on the mechanisms underlying these measures. The

present study extended our initial analyses of neurophysiological endophenotypes in P and NP rats to EROs generated in cortical sites in response to an auditory oddball paradigm (standard, rare and noise tones). In this study, we investigated oscillatory activity in the delta, theta, and alpha/beta frequency ranges in the parietal cortex of P and NP rats within the temporal window of the P3 ERP response. ERO and PL analyses were accomplished from the same datasets that were used to generate the ERP data reported in a previous publication (Ehlers et al., 1999). We hypothesize that differences in hippocampal P3 amplitudes previously reported in P and NP rats (Ehlers et al., 1999) are associated to differences in delta and theta ERO oscillatory activity.

Materials and methods

Animals

Twenty-five (25) rats, 14 P and 11 NP male rats, of the 42nd generation, bred at Indiana University were received at The Scripps Research Institute weighing 281–410 g. All rats had ad libitum access to food and water. A detailed description of the environmental conditions of rats can be found elsewhere (Ehlers et al., 1999). The work described herein adheres to the guidelines stipulated in the NIH *Guide for the Care and Use of Laboratory Animals* (NIH publication No. 80–23, revised 1996) and was reviewed and approved by The Scripps Research Institute's Institutional Animal Care and Use Committee.

Surgical and electrophysiological recording procedures

Surgical and electrophysiological recording procedures performed in this study were previously described (Ehlers et al., 1999). In brief, P and NP rats were deeply anesthetized with Nembutal (50 mg/kg, intraperitoneally) and surgically prepared with recording electrodes at least two weeks prior to the experimental procedures. Stainless steel single-wire electrodes were implanted into the dorsal hippocampus (AP: −3.0 mm, ML: ±3.0 mm, DV: −3.0 mm) and amygdala (AP: 1.0 mm, ML: ±5.3 mm, DV: −8.5 mm) (Pellegrino et al., 1979). A 23-gauge stainless steel guide cannula was also aimed at the lateral ventricle (AP: −1.0 mm, ML: ±1.5 mm, DV: −4.6 mm). Screw electrodes were placed in the skull overlying the frontal (AP: 3.0 mm, ML: ±3.0 mm) and parietal (AP: −3.0 mm, ML: ±4.0 mm) cortices. A midline screw "reference" electrode was placed 3 mm posterior to lambda in the skull overlying the cerebellum. Electrode connections were made to a multipin Amphenol connector and the assembly was anchored to the skull with dental acrylic and anchor screws. EEG signals were recorded with a band pass of 0.5–70 Hz with a 60-Hz notch filter in. ERP trials were digitized at a rate of 256 Hz. Potential artifacts identified by computer software were excluded only after visual analysis of raw EEG. Only neurophysiological data recorded from the parietal cortex in animals treated with saline was included in the present study. The effects of intracerebroventricular administration of neurotensin on EEG and ERP were reported in a previous publication (Ehlers et al., 1999).

General procedures

Electrophysiological recordings were collected as previously described (Ehlers et al., 1999). In brief, a three-tone auditory 'oddball' paradigm originally developed to directly model studies employed in humans was used (Ehlers and Chaplin, 1992; Ehlers et al., 1991, 1994). The auditory ERP session consisted of 312 individual tone presentations. Three tone types were presented: standard tones (1000 Hz square wave, 70 dB, 84% probability), rare tones (2000 Hz square wave, 85 dB, 10% probability), and noise tones (white noise, 100 dB, 6% probability). Individual trials were 1000 ms in duration (100 ms pre-stimulus + 900 ms post-stimulus) and were separated by variable intervals ranging from 500 to 1000 ms. Rare tones were interspersed with standards such that no two rare tones occurred successively. The

noise tone occurred every 16th trial. Further details about the auditory ERP sessions were described previously (Ehlers et al., 1999).

ERO and PLI analyses

ERO and phase-locking index (PLI) analyses were accomplished from the same datasets that were used to generate the cortical ERP data reported in a previous publication (Ehlers et al., 1999). Data from each trial generated by the stimuli were processed by a time-frequency analysis algorithm, which utilizes the S-transform (Stockwell et al., 1996), a generalization of the Gabor transform (Gabor, 1946), defined as:

$$S\left[jT, \frac{n}{NT}\right] = \sum_{m=0}^{N-1} H\left[\frac{m+n}{NT}\right] e^{\frac{-2\pi^2 m^2}{n^2}} e^{\frac{i2\pi mj}{N}} \qquad n \neq 0$$

The equation for calculation of the *S*-transform of discrete time series $h(kT)$ at time jT and frequency n/NT is where T is the sample period of the discrete time series, j is the sample index, N is the number of samples in the time series, n is the frequency index, and $H[\ ]$ is the Fourier spectrum of the discrete time series. The computer code used is based closely on a C language S-transform subroutine available from the NIMH MEG Core Facility web site (http://kurage.nimh.nih.gov/meglab/). The defining equation of the S-transform is a convolution integral in continuous time. The method used is equivalent to the finite discrete time version of this, but for computational efficiency, multiplications in frequency domain are used rather than convolution in time domain. The inputs to the S-transform are real, but the outputs are complex. We use the magnitudes squared of the time-frequency output values, discarding the corresponding phase angles.

The PLI was calculated to measure phase variability in relation to stimulus onset, as previously described (Schack and Klimesch, 2002). The PLI, which ranges between zero and one. An increased PLI indicates less phase variability and stronger phase locking to the onset, whereas a reduced PLI indicates higher phase variability and weaker phase locking (Schack and Klimesch, 2002).

To reduce consequences of resulting discontinuities, we use a cosine window over the initial and final 100 msec of the input time series of each trial. The output of the transform for each stimuli and electrode site was calculated by averaging the individual trials containing the time-frequency energy distributions. To quantify S transform magnitudes, a region of interest (ROI) was identified by specifying the band of frequencies and the time interval contained in the rectangular ROI and the energy in that region was estimated. PLI was estimated at the peak amplitude within the ROI. These analyses are similar to what has been previously described (Jones et al., 2004; Schack and Klimesch, 2002). Baseline corrected post-stimulus activity (900 ms) was calculated by subtracting averaged pre-stimulus ERO energy values (100 ms) from the post-stimulus ROI values, as previously described (Padmanabhapillai et al., 2006). Normalized pre-stimulus ERO energy values for each ROI was determined by calculating a normalized baseline, defined as: $V_1 - (H_b \times A_1)$, where V_1 is the volume energy of ROI_1, H_b is the average height of the baseline for ROI_1, and A_1 is area of ROI_1. The area of ROI_1 (A_1) is calculated as the frequency range of ROI_1 × the total duration of ROI_1. H_b is defined as: $V_b \div A_b$, where V_b is the volume of the baseline for ROI_1, and A_b is the area of the baseline for ROI_1. The ROI frequencies were: delta (1–4 Hz), theta (4–8 Hz), alpha/beta (8–32 Hz). The ROI time intervals correspond to the P3 component (250–325 ms) and are consistent with our previous ERP studies (Ehlers et al., 1999).

Statistical Analysis

Statistical analyses were performed by using SPSS for the Macintosh (SPSS, Inc., Chicago, IL). Values are mean ± standard error of the mean (SEM). Data analyses were performed on parietal ERO energy and PLI for the ROIs in response to standard, rare and noise tones. Group (P vs. NP) was assessed as a between subject variable. Tone (standard, rare and noise) was assessed as within subject repeated measures. For all repeated measures analyses, Greenhouse-Geisser corrected *P*-values were reported to account for violations of sphericity. Post hoc analysis of two-way repeated measures ANOVA (Tone) utilized pairwise comparisons. One-way ANOVA was used to assess strain differences. For these analyses, *P*-value was set at $P < 0.05$ to determine the levels of statistical significance.

Results

ERO mean energy and phase locking in P and NP rats

Effect of tone type on ERO energy and PLI—Two-way repeated measures ANOVA with ERO energy as dependent variable revealed a significant main effect of Tone in the theta and alpha/beta frequency bands in the parietal cortex (Table 1). Post hoc pairwise comparisons showed lower ERO energy in the parietal theta and alpha/beta bands occurred in response to rare and noise tones, compared to standard tones (Table 1).

Two-way repeated measures ANOVA with PLI as dependent variable revealed a significant main effect of Tone in the delta, theta and alpha/beta frequency bands in the parietal cortices, when collapsing across P and NP groups (Table 2). Post hoc pairwise comparisons showed lower PLI in response to standard tones (vs. rare and noise tones) in the parietal delta and theta bands. Lower PLI in response to rare tones (vs. noise tones) was also found in the parietal alpha/beta band (Table 2).

ERO differences between P and NP rats: Baseline activity—Baseline ERO energy in the parietal delta band was not different between P and NP rats (Data not shown). Baseline ERO energy in the parietal theta band was lower in NP than in P rats in response to standard tones [P rats: 337.1 ± 48.2 vs. NP rats: 188.5 ± 32.7; $F(1,20)=4.9$, $P<0.05$]. Lower baseline ERO energy in the parietal alpha/beta band was also observed in NP rats in response to standard [P rats: 880.1 ± 62.4 vs. NP rats: 516.3 ± 42.2; $F(1,20)=17.6$, $P<0.001$], rare [P rats: 1095.0 ± 97.8 vs. NP rats: 625.2 ± 51.8; $F(1,20)=12.6$, $P<0.005$] and noise [P rats: 1209.1 ± 87.7 vs. NP rats: 715.4 ± 94.8; $F(1,20)=13.5$, $P<0.005$] tones.

ERO differences between P and NP rats: ERO energy and PLI in the 250–325 ms window

ERO Energy: ERO energy in the parietal delta band was not different between NP than in P rats (Table 3). ERO energy in the parietal theta and alpha/beta bands was lower in NP than in P rats in response to standard tones (Table 3).

PLI: PLI in the parietal delta and alpha/beta bands was lower in P than in NP rats in response to noise tones (Table 4). PLI in the parietal theta band was not different between NP and P rats in response to standard, rare and noise tones (Table 4). Figure 1A–B illustrates grand-averaged PLI time-frequency representations of the noise tones for the delta (*a*, *c*), theta (*b*) and alpha/beta (*d*) frequency bands.

Discussion

Brain oscillations have been proposed to represent neurophysiological correlates of human information processing and cognitive function (Basar et al., 1999, Karakas et al., 2000).

They have also been considered endophenotypes for complex genetic disorders, including drug addiction and psychiatric disorders (for reviews, see Begleiter and Porjesz, 2006; Porjesz et al., 2005). There is evidence to suggest that individuals with a positive family history of alcoholism have decreased P3 amplitude prior to significant ethanol drinking (Bauer et al., 1994; Begleiter et al., 1984; Pfefferbaum et al., 1991). Findings from the Collaborative Study on the Genetics of Alcoholism (COGA) have achieved significant progress identifying EROs associated with the human P3 component and several genes potentially involved in their regulation (for reviews, see Begleiter and Porjesz, 2006; Porjesz et al., 2005; Rangaswamy and Porjesz, 2008). Those studies have shown that ethanol dependent individuals manifest significantly less evoked delta and theta ERO power than age-matched controls (Jones et al., 2006a). Rangaswamy et al. (2007) have shown that adolescent offspring of ethanol dependent individuals have reduced delta and theta ERO power. These results suggest that a decrease in delta and theta EROs may antecede the development of ethanol dependence. Evidence from the COGA project has also shown a significant linkage and association between parietal delta ERO power and the cholinergic muscarinic receptor gene (*CHRM2*) on chromosome 7 (Jones et al., 2004, 2006b). These findings have provided a better understanding of the neurophysiological mechanisms and genes contributing to the human P3 component (for reviews, see Begleiter and Porjesz, 2006; Porjesz et al., 2005; Rangaswamy and Porjesz, 2008).

In contrast to the considerable progress understanding the relationship between human brain oscillations and an increased risk for ethanol dependence, brain oscillations have not been well characterized in animal models of high ethanol preference. The present study is part of our ongoing investigation characterizing cortical oscillatory activity in rodent models of high and low ethanol preference (see Criado and Ehlers, 2009; Ehlers and Criado 2009). Results from our earlier studies suggested that P rats have significantly lower P3 amplitudes than NP rats (Ehlers et al., 1999). The P3 component in rats is a broad positive going potential that peaks between 250 and 400 ms (e.g., Ehlers et al., 1994; Shinba, 1997). The present findings show that the decrease in parietal P3 amplitudes found in P rats in response to noise tones (Ehlers et al., 1999) is related to decreases in evoked delta and alpha/beta phase locking. Our findings also showed that ERO energy in the parietal theta and alpha/beta bands was lower in NP than in P rats. However, these differences were only observed in response to the standard tones, whereas reductions in P3 amplitudes in P rats were found in response to the noise tones. The results suggesting that baseline ERO energy in the parietal alpha/beta bands was higher in P than in NP rats are consistent with our previous studies characterizing EEG power in P and NP rats (Ehlers et al., 1999). These differences in baseline ERO energy in the alpha/beta bands were observed in response to standard, rare and noise tones and are likely independent to the reductions in P3 amplitude in P rats in response to noise tones (Ehlers et al., 1999).

Consistent with the present results, we recently showed that reductions in evoked delta phase locking in the parietal cortex are related to the decrease in P3 amplitudes in high ethanol preference C57BL/6 (B6) mice, compared to low ethanol preference DBA/2J (D2) mice (Criado and Ehlers, 2009). This previous study also demonstrated that reductions in evoked delta ERO energy and theta phase locking in the parietal cortex are associated with a decrease in P3 amplitudes in B6 mice (Criado and Ehlers, 2009). In contrast, the present study found that differences in ERO energy between P and NP rats do not play an important role in the decrease in P3 amplitudes found in P rats. These findings indicate that reduced P3 amplitudes in rat models of high ethanol preference may have different neurophysiological profiles than humans. These data also suggest different neurophysiological mechanisms associated with a reduction of P3 amplitudes in rat and mouse models of high ethanol preference (Ehlers et al., 1999; Ehlers and Somes, 2002; Slawecki et al., 2003).

Like most ERP studies using rodents as subjects a “passive” auditory oddball paradigm has been used to generate ERPs in rats. The advantages of a passive paradigm are that it can be administered to human and other animal subjects without extensive prior training, and it does not require the subject to respond to the stimuli. While ERPs have been successfully recorded in a number of animal species the use of ERO technology to study brain function in animal models has been less applied. The present studies extend and confirm our previous findings demonstrating that EROs can be recorded in rodents (Ehlers and Criado, 2009; Criado and Ehlers, 2009). Collapsing across lines, our findings showed that parietal theta and alpha/beta ERO energy was significantly reduced in response to the rare and noise tones, compared to the standard tones. Results from the present study also found that PLI in the parietal delta and theta bands was significantly increased in response to rare and noise tones, compared to the standard tones. These findings suggest that presentation of the standard tone produces an evoked response characterized by higher theta and alpha/beta ERO energy, but also shows an increase in delta and theta phase variability, compared to the noise and rare tones. The relationship between brain oscillations and P3 amplitudes has not been well characterized in animal models of high and low ethanol preference. Future studies are needed in these models to determine the relationship between their genetic and phenotypic profile with the expression of their different neurophysiological endophenotypes associated with reduced P3 amplitudes.

The phase-locking index, or PLI, reflects the degree of phase variation over trials and may have a significant effect on the amplitudes and latencies of ERP components (Gruber et al., 2005; Sauseng et al., 2007; Schack and Klimesch, 2002). PLI is similar to other measures of phase variation including ‘inter-trial coherence’ (Makeig et al., 2002), ‘phase-locking factor’ (Tallon-Baudry et al., 1996), and ‘phase-locking value’ (Rodriguez et al., 1999). Findings from the present study suggest that the decrease in P3 amplitudes in P rats is associated with a decrease in delta and alpha/beta band PLI. The mechanisms mediating the lower evoked delta and alpha/beta phase locking in adult P rats and their potential role increasing the risk for ethanol dependence are not clearly understood. Studies in humans have demonstrated that delta and theta EROs are the primary contributors to the human P3 ERP component (Basar et al., 1999; Basar-Eroglu et al., 1992; Demiralp et al., 2001; Karakas et al., 2000; Schurmann et al., 2001; Stampfer and Basar, 1985; Yordanova and Kolev, 1996). However, the primary contributors to the P3 ERP component in P and NP rats have not been determined. Further research needs to be done to understand the relationship between PLI, ERO energy and ERP amplitude.

Studies have demonstrated that, relative to NP rats, the P rat exhibit several phenotypes associated with alcohol abuse and alcoholism and meets the criteria of a valid animal model to assess alcohol-preference and excessive drinking (for review, see McBride et al., 2005; Bell et al., 2006). Consistent with studies in human subjects at risk for ethanol dependence (for review see Porjesz et al., 2005), our previous study showed that P rats have significantly lower P3 amplitude, when compared to NP rats (Ehlers et al., 1999). However, the relationship between an ethanol preference phenotype and changes in EROs are not well understood in genetic mouse models of high and low alcohol preference. There is evidence to suggest that multiple neurotransmitter systems contribute to differences in ethanol preference between P and NP rats (for review, see McBride et al., 2005; Bell et al., 2006). For instance, early-onset of ethanol drinking in P rats has been associated with higher density of cortical and hippocampal seronin-1A (5-HT1A) receptors and lower density in the expression of dopamine (DA) D2 receptors in the ventral tegmental area (VTA) (for review, see McBride et al., 2005). Previous studies in our laboratory in P and NP rats have also shown that differences in glutamate and GABA function may play an important role in their ethanol preference. We found that the acute effects of MK-801, an NMDA receptor antagonist, and diazepam, a GABA/benzodiazepine receptor agonist, on cortical and

hippocampal EEG are significantly attenuated in P rats, in comparison to NP rats (Robledo et al., 1994). Whether deficits in these neurotransmitter systems play a role in the attenuation in evoked delta and alpha/beta phase locking in P rats remains unclear. While findings from the present studies contribute to our understanding of the neurophysiological mechanisms regulating the reduction in P3 amplitudes in P rats, further studies are needed to determine the relationship between the expression of these neurophysiological endophenotypes and the genetic profile of the P and NP rats. Understanding the relationship between evoked oscillatory activity, phase resetting and ERP responses in P and NP rats may provide insight into the brain processes underlying susceptibility to alcohol dependence.

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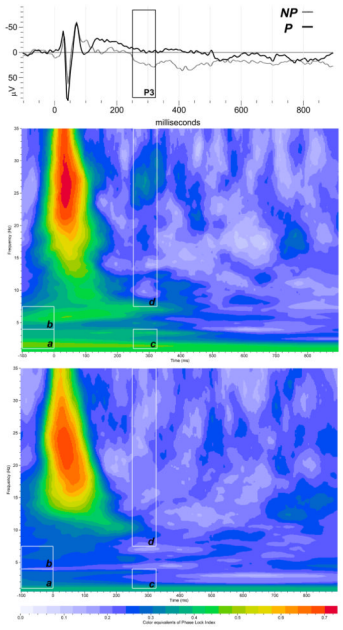

Figure 1.

Time-frequency responses of evoked delta (*a*, *c*), theta (*b*) and alpha/beta (*d*) band PLI distribution to noise stimuli in P (A) and NP (B) rats in the parietal cortex. Time-frequency ROI windows used were −100 to 0 ms (baseline) and 250–325 ms (white squares). The inset shows representative ERP grand averages from NP (black line) and P (gray line) groups from the parietal cortex in response to the noise tones.

Table 1

Tone main effects of event-related oscillations (ERO) energy in P and NP rats in the parietal cortex

	Standard Tone	Rare Tone	Noise Tone	Tone Effects
Delta Band	61.3 ± 8.7	49.2 ± 12.4	48.7 ± 14.8	$F(1.4,27.2)=1.0$, $P>0.05$
Theta Band	161.8 ± 16.1*	96.9 ± 20.2	40.9 ± 30.3	$F(1.8,33.9)=11.5$, $P<0.001$
Alpha/Beta Band	513.8 ± 31.6*	335.5 ± 49.6	266.3 ± 48.4	$F(1.9,36.9)=14.4$, $P<0.001$

Represent statistically significant difference;

*standard vs. rare and noise tones

Table 2

Tone main effects of phase-locking index (PLI) in P and NP rats in the parietal cortex

	Standard Tone	Rare Tone	Noise Tone	Tone Effects
Delta Band	0.135 ± 0.013*	0.399 ± 0.033	0.514 ± 0.026	$F(1.6,30.4)=56.9$, $P<0.001$
Theta Band	0.134 ± 0.010*	0.368 ± 0.028	0.459 ± 0.033	$F(1.8,33.5)=47.7$, $P<0.001$
Alpha/Beta Band	0.128 ± 0.004*	0.381 ± 0.016**	0.487 ± 0.019	$F(1.9,36.3)=202.0$, $P<0.001$

Represent statistically significant difference,

* standard vs. rare and noise tones;

** rare vs. noise tones.

Table 3

ERO energy in P and NP rats during the time interval corresponding to the P3 component (250–325 ms) in the parietal cortex.

	Standard Tone	Rare Tone	Noise Tone
Delta Band	$F(1,20)=2.4$, NS	$F(1,20)=1.3$, NS	$F(1,20)=0.4$, NS
P	71.8 ± 11.2	63.2 ± 16.7	58.5 ± 21.3
NP	50.7 ± 12.9	35.2 ± 16.1	38.9 ± 14.4
Theta Band	$F(1,20)=4.6$, $P<0.05$	$F(1,20)=0.1$, NS	$F(1,20)=0.3$, NS
P	196.4 ± 22.8	102.6 ± 30.4	58.5 ± 45.2
NP	127.2 ± 17.1	91.2 ± 13.2	23.2 ± 21.6
Alpha/Beta Band	$F(1,20)=9.2$, $P<0.01$	$F(1,20)=0.2$, NS	$F(1,20)=2.5$, NS
P	609.6 ± 45.0	355.7 ± 73.5	343.3 ± 68.8
NP	418.0 ± 32.3	315.2 ± 38.5	189.3 ± 50.9

Table 4

PLI in P and NP rats during the time interval corresponding to the P3 component (250–325 ms) in the parietal cortex.

	Standard Tone	Rare Tone	Noise Tone
Delta Band	$F(1,20)=1.8$, NS	$F(1,20)=0.1$, NS	$F(1,20)=5.1$, $P<0.05$
P	0.152 ± 0.019	0.392 ± 0.041	0.455 ± 0.027
NP	0.117 ± 0.010	0.406 ± 0.050	0.572 ± 0.049
Theta Band	$F(1,20)=0.3$, NS	$F(1,20)=0.2$, NS	$F(1,20)=3.8$, NS
P	0.139 ± 0.015	0.380 ± 0.037	0.396 ± 0.036
NP	0.128 ± 0.012	0.355 ± 0.035	0.522 ± 0.060
Alpha/Beta Band	$F(1,20)=1.0$, NS	$F(1,20)=0.3$, NS	$F(1,20)=4.4$, $P=0.05$
P	0.125 ± 0.004	0.373 ± 0.019	0.448 ± 0.020
NP	0.132 ± 0.008	0.389 ± 0.024	0.526 ± 0.034

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