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Research paper

Laboratory rats (*Rattus norvegicus*) do not use binaural phase differences to localize sound

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ABSTRACT

The ability of Norway rats to use binaural time- and intensity-difference cues to localize sound was investigated by determining their ability to localize pure tones from 500 Hz to 32 kHz. In addition, their ability to use the binaural time cues present in the envelope of a signal was determined by presenting them with a 1-kHz tone that was amplitude modulated at either 250 or 500 Hz. Although the animals were easily able to localize tones above 2 kHz, indicating that they could use the binaural intensity-difference cue, they were virtually unable to localize the lower-frequency stimuli, indicating that they could not use the binaural phase (time) cue. Although some animals showed a residual ability to localize low-frequency tones, control tests indicated that they were using the transient interaural intensity difference in the onset of a sound that exists after it reaches the near ear but before it reaches the far ear. Thus, in contrast to earlier studies, we conclude that the Norway rat is unable to use the ongoing time cues available in low-frequency tones to localize sound, raising the possibility that the rat may not use interaural time differences to localize sound.

1. Introduction

The ability of mammals to localize sound varies among species not only in acuity, but also in the use of the two binaural locus cues: the difference in the time of arrival of a sound at the two ears and the difference in the frequency-intensity spectra reaching the two ears. Although it appears that most mammals use both binaural cues, some, such as horses and cattle, use only the binaural time-difference cue, whereas others, such as house mice and big brown bats, appear to use only the binaural spectral-difference cue. A few mammals, such as some subterranean rodents, have lost the ability to localize brief sounds altogether and thus do not use either binaural cue (for a review, see Heffner and Heffner, 2003).

The ability of an animal to use the two the binaural cues can be investigated by training it to localize the source of single, brief tone pips (e.g., Masterton et al., 1975), a procedure first used with humans (Mills, 1972; Stevens and Newman, 1936). Specifically, the ability to localize pure tones too low in frequency to generate binaural intensity differences (because they bend around the head with little attenuation) indicates the ability to use the binaural phase cue, which is a binaural time cue (e.g., Zhang and Hartmann, 2006). The ability to localize pure tones too high in frequency to provide a binaural phase cue (because successive cycles arrive too quickly for the nervous system to match the arrival of the same cycle at the two ears) indicates the ability to use the intensity-difference cue, a special case of the binaural frequency-intensity spectral cue. Among species that use the binaural phase cue, the upper-frequency limit for its use spans more than three octaves, from the 500-Hz upper limit of cattle to the 6.3-kHz upper limit of the Jamaican fruit bat (Heffner and Heffner, 2003). Thus, a comparative study of the upper limit of the use of the binaural phase cue could lead to an understanding of the reasons for this variation, and perhaps of the reasons why some species forego the use of the cue altogether.

In comparing the use of the binaural locus cues by different species, we noted that there was disagreement regarding the highest frequencies at which laboratory rats can use the binaural phase cue. Specifically, Masterton and his colleagues (1975) placed the upper limit for rats between 4 and 8 kHz whereas Kelly and Kavanagh (1986) placed it between 2 and 4 kHz. Because our comparative analysis required a more precise estimate of the upper limit for binaural phase, we decided to test laboratory rats ourselves to determine which estimate was correct. What we found, however, was that we were unable to replicate either upper limit; instead, it appears that laboratory rats are unable to use the binaural phase-difference cue at all. As described in Section 4, this finding is not incompatible with the results of anatomical and physiological studies of sound localization in the rat.

Abbreviations: MSO, medial superior olive; SL, sensation level; SPL, sound pressure level.

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2. Methods

Four rats were trained to localize the source of brief pure tones at a fixed angle of 30° left and right of midline (60° total separation) using a conditioned-suppression avoidance procedure. The ability to localize pure tones below the frequency at which the phase cue becomes ambiguous indicates the use the binaural phase-difference cue whereas the ability to localize pure tones above the frequency of phase ambiguity indicates the ability to use the binaural intensity-difference cue.

2.1. Subjects

Four male hooded rats (*Rattus norvegicus*, Harlan Sprague–Dawley) were used in this study. Rats A, C, and D were 200 days old at the beginning of testing and 450 days old at the end; Rat B was 90 days old at the beginning and 200 days old at the end. They were housed in standard solid bottom cages with grid covers and pelleted corncob bedding (1/8 in. pellets, Harlan Teklad). The animals were given free access to rodent chow and their body weights were measured daily. Water was available during daily training and testing sessions. Pieces of apple were given as needed to maintain a healthy body weight.

The use of animals in this study was approved by the University of Toledo Animal Care and Use Committee.

2.2. Behavioral apparatus

Testing was conducted in a double-walled sound chamber (IAC model 1204; Industrial Acoustics Co., Bronx, NY, USA; 2.55 × 2.75 × 2.05 m), the walls and ceiling of which were lined with eggcrate foam and the floor carpeted to reduce sound reflections. The equipment used for behavioral control and stimulus generation was located outside the chamber and the rats were monitored over a closed-circuit television. The rats were tested in a cage (28 × 13 × 16 cm) constructed of half-inch (0.127 cm) wire mesh, which was mounted 98 cm above the floor on an adjustable tripod. A waterspout, consisting of 2-mm diameter brass tubing topped with a brass "lick" plate (2.5 × 1.7 cm), was mounted vertically in the front of the cage. The spout was adjusted to a level that permitted the rats to drink comfortably (4 cm above the floor of the cage). Water was delivered to the reward spout via a flexible plastic tube attached to a 60-cc syringe pump (Yale Apparatus, model YA-12, Wantagh, NY) located outside the sound chamber. The flow rate was adjusted so each animal was able to satisfy its daily water requirements in a single session of 30–45 min. A contact circuit between the waterspout and the cage floor detected when a rat made contact with the spout and activated the syringe pump. Requiring the rats to maintain contact with the spout during testing also served to keep their heads fixed within the sound field. Imbedded in the mesh wire of the floor of the cage was a thin dampened sponge that provided good electrical contact between an animal and the cage floor.

Finally, a shock generator, connected between the waterspout and the cage floor, provided a mild shock. The shock was adjusted for each animal to the lowest level that produced a consistent avoidance response to a detectable signal. To provide feedback for a successful avoidance, a 25-W light bulb, placed below and in front of the cage, was turned on for the duration of the shock (0.5 s) so that turning off the light indicated that the shock was over and that the animal could return to the waterspout.

2.3. Acoustical procedures

Broadband noise bursts were used for initial training and pure tones were used for final training and testing. The sounds were presented through matched loudspeakers that were mounted at the level of the rats' ears on a perimeter bar (102-cm radius, 104-cm height).

Pure tones were generated using a signal generator (Stanford Research System model SR 770 FFT Network Analyzer) and randomly attenuated (Coulbourn S85-08 programmable attenuator) over a 3.5-dB range on each trial. The sine wave was filtered with a band-pass filter (Krohn-Hite 3550) set 1/3 octave above and below the tone's frequency. The tone was gated on (Coulbourn S84-04) using rise/fall times of 5–50 ms, depending on the particular test. Finally, the signal was amplified (Crown D-75), monitored on an oscilloscope, and then sent to one of a pair of loudspeakers. The loudspeakers used were Motorola KSN1005A piezoelectric speakers (2.8, 4, 5.5, 8, 16, and 32 kHz), 6-in. RS 2000 Infinity woofers (.500, 1, 2, 2.8, and 4 kHz) and 10-in. SM 102 Infinity woofers (1, 2 and 2.8 kHz).

Testing was performed with the loudspeakers located 60° apart (30° to the left and right of midline). The sound pressure level of the tones ranged from 15 to 50 dB above the previously published thresholds for the laboratory rat, depending on the particular test (Heffner et al., 1994; Kelly and Masterton, 1977).

In addition to pure tones, the rats were also tested on their ability to localize a 1-kHz tone sinusoidally-amplitude-modulated (100% modulation depth) at modulation rates of 250 and 500 Hz to determine if they could extract binaural time cues from the envelope of the signal.

The sound pressure level (SPL re 20 $\mu N/m^2$) of the stimulus was measured and the left and right loudspeakers were equated daily using a ¼-in. (0.64-cm) microphone (Brüel & Kjaer 4135), preamplifier (Brüel & Kjaer 2619), conditioning amplifier (Brüel & Kjaer Nexus Conditioning Amplifier 2690), and a spectrum analyzer (SR 770). Sound measurements were taken by placing the microphone at the position occupied by an animal's head when it was drinking from the waterspout and pointing the microphone directly toward a loudspeaker (0° incidence).

2.4. Behavioral procedure

The rats were initially trained to drink at a steady rate from the waterspout in the presence of broadband noise bursts (100-ms on, 400-ms off; 4 pulses per trial) presented from a loudspeaker 30° to their right ("safe trial"). They were then trained to break contact with the spout whenever noise bursts were presented from a loudspeaker located 30° to the left ("warning trial"), in order to avoid a mild electric shock. The shock (0.5 s) was delivered through the spout at the end of the warning trial. Breaking contact with the spout before the end of a warning trial indicated that the animal detected the change in locus and enabled it to avoid the shock. The shock light, which came on at the same time as the shock, provided feedback for a successful avoidance and its offset signaled that it was safe to return to the spout. After the animals learned to respond only to left sounds, the signal was reduced to a single noise burst (100-ms). Once they consistently achieved 90% or better performance with the single noise burst, the stimulus was changed to a single tone pip.

A session consisted of a series of 2-s trials that began with the onset of a stimulus. In order to slow the pace of signal presentations, each trial was followed by a 1.5-s intertrial interval. Thus, the rats received one signal every 3.5-s and had to decide whether to break contact or continue to drink. The response of an animal on each 2-s trial was defined as the duration of contact with the spout during the last 150 ms of the trial, giving the animal sufficient time to react to the signal. If the animal broke contact for more than half of this 150-ms period, an avoidance response was recorded. The response was classified as a "hit" if the signal had come from the animal's left side and as a "false alarm" if it had come from the animal's right. However, if a rat was not in contact with the spout during the 1-s preceding the trial, data from that trial were not recorded, even though the trial proceeded as usual. This eliminated trials when the rat was grooming or otherwise not engaged in the task. Trial presentation was not resumed until the animal returned to the spout.

Each trial had a 22% probability of containing a left signal. Both hit and false-alarm rates were determined for each block of trials (8–10 consecutive warning trials interspersed with 32–40 safe trials) for each frequency. The hit rate was corrected for the false-alarm rate to produce a performance measure according to the following formula: Performance = Hit Rate − (False-Alarm Rate × Hit Rate) (Heffner and Heffner, 1995). This measure varies from 0 (no hits) to 1 (100% hit rate with no false alarms). Note that this calculation proportionately reduces the hit rate by the false-alarm rate observed for each block of trials in each stimulus condition, rather than by the false-alarm rate averaged for the session as a whole. This was done because false-alarm rates vary within a session depending on the difficulty of the discrimination.

A single frequency was typically tested per session, although, if an animal was having difficulty or was unable to localize a particular frequency, either an easier frequency or the noise stimulus was presented on some trials to verify that the animal was still motivated. Each frequency was tested in two to three sessions for a minimum of 100 warning trials. An animal's performance was calculated for each trial block and the highest 50% of performance scores at each frequency was taken to reflect the best performance that the rats could sustain.

2.5. Measurement of the binaural intensity difference

The interaural intensity difference available for a sound source placed 30° from the midline was measured on three rats using pure tones and 1/3-octave noise. An anesthetized animal was placed in the sound chamber and the sound was produced and measured using the same equipment and speaker placement as used in the behavioral test. The sound was turned on and the level at each ear was measured using the ¼-in. microphone placed at the base of the pinna and oriented vertically.

2.6. Measurement of the frequency of ambiguity for binaural phase

The frequency of phase ambiguity (i.e., the highest frequency at which the phase cue is available) depends on the size of an animal's head and the angle of the sound source, and can be calculated using the formula: $F = 1/[6(a/C)\sin\theta]$, where a is the radius of the head (in mm), C is the speed of sound (.3434 mm/μs), and θ is the angle (in radians) of the sound source from the animal's midline (Kuhn, 1977). Using the distance between the two ears around the head from the opening of one ear canal to the other, which was 51.5 mm, we calculated the radius of the rat's head to be 16.4 mm and the frequency of ambiguity for a sound source located 30° from midline as 6.9 kHz.

3. Results

We found that although the rats easily localized high-frequency tones, indicating that they could use the binaural intensity-difference cue, they could not localize low-frequency tones, indicating that they could not use the binaural phase cue. Because the inability to localize low-frequency tones differed from the results of the two previous studies (Masterton et al., 1975; Kelly and Kavanagh, 1986), and because the performances of some of the animals on low-frequency stimuli were ambiguous, additional testing was conducted to more fully explore this finding.

3.1. Localization of pure- and amplitude-modulated tones, 20 ms rise/fall time

The first test was of the ability to localize pure tones from 1 to 32 kHz and a 1-kHz tone amplitude modulated at 250 and 500 Hz modulation rates, using a 20-ms rise/fall time. With the exception of the 1-kHz stimuli, the tones were presented at 50 dB above the published rat thresholds (Heffner et al., 1994; Kelly and Masterton, 1977). Because rats have poor hearing below 2 kHz, the 1-kHz signals could not be presented at that level without producing overtones. Instead, the 1-kHz absolute threshold was determined for the rats used in this study and the 1-kHz stimuli were presented at 30 dB above their threshold (i.e., 30 dB sensation level or SL, 64 dB SPL). A single tone pip (20 ms rise, 80 ms ongoing, 20 ms fall) was presented on each trial from one of two speakers located 30° to the left and right of midline (60° total separation). Fig. 1 shows the best sustainable performances (the average of the top 50% of the trial blocks from three sessions) of all four animals. As can be seen, the rats were able to localize high frequencies, indicating their use of the binaural intensity-difference cue. However, they were unable to localize low frequencies and their performance declined below 4 kHz to, or near, chance levels at 1 and 2 kHz, suggesting that they could not use the binaural phase cue. The results of the amplitude modulation test were ambiguous with rats C and D performing near or at chance, respectively, whereas rats A and B performed well above chance.

The performance of the rats on the low-frequency tones suggested to us that they were unable to use the binaural phase cue but that some of them were able to score above chance on the 1-kHz pure and amplitude-modulated tones by using some other cue. One possibility was that they were actually localizing high-frequency harmonics present in the signal but too low a level to be detected by our measuring equipment. If so, that would mean they were using the binaural intensity-difference cue rather than the binaural phase-difference cue. Another possibility was that the animals were using the transient onset cue that occurs when

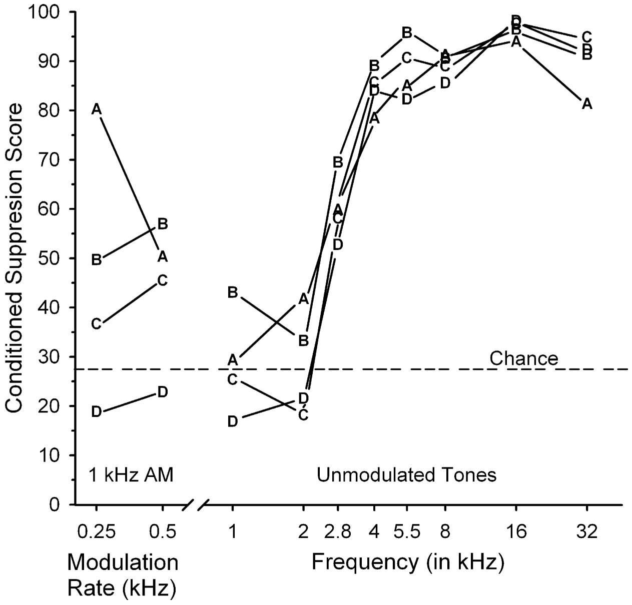

Fig. 1. Ability of four rats (A–D) to localize single 100-ms tone pips, 20-ms rise/fall time. The loudspeakers were located 30° to the left and right of midline. The 1-kHz pure tone and modulated tones were presented at 30-dB sensation level (SL), instead of 50-dB SL to avoid overtones. Note that at this angle, the binaural phase cue is theoretically available up to 6.9 kHz, although the rats do not appear to make use of it.

a signal is first turned on. This cue occurs even for low-frequency sounds that bend around the head with little or no attenuation and begins when a signal reaches the near ear and lasts until the sound has reached its full intensity at both ears; because the onset cue has been demonstrated in humans to be a short-duration intensity-difference cue (not a time-difference cue), we refer to it here as the transient binaural intensity-difference cue (Elfner and Tomsic, 1968; Perrott, 1969). Thus, the subsequent tests were conducted to determine if the animals could localize low-frequency tones when the possibility of using these alternative cues was reduced.

3.2. Localization of pure tones at 15 dB SL

As previously noted, the ability of some of the animals to localize the 1-kHz tones in the preceding test may have been due to either the presence of high-frequency harmonics that would permit the use of the binaural intensity-difference cue or the transient binaural intensity-difference cue. Because high-frequency harmonics occur when a loudspeaker is overdriven, they can be eliminated by reducing the amplitude of the tones to below the level that produces distortion. Amplitude also plays a role in the transient binaural intensity difference as the magnitude of this cue depends in part on how fast the amplitude is increasing (the number of decibels it is increasing per millisecond, which will be greater for higher amplitudes at a given rise/decay rate). For example, a sound that is increasing by 10 dB/ms will generate a larger transient intensity difference than one that is increasing by 1 dB/ms. (Indeed, as noted by Heil and Irvine, 1997, the latency of the auditory nerve varies as a function of the maximum acceleration of peak pressure.) Thus, reducing the amplitude of the sound, while holding the rise time constant, would reduce the magnitude of the transient intensity difference.

To reduce the possibility of the rats using these cues, we determined their ability to localize .5, 1, and 4 kHz at 15 dB SL, rather than the 30–50 dB SL used in the previous test (60° separation, 20-ms rise/fall, 120-ms total duration). The 500-Hz tone was included because it could be generated at a level of 15 dB SL—69 dB SPL—without the overtones that were detectable at higher amplitudes. Fig. 2 illustrates each animal's best performances (the average of the top 50% of the trial blocks from three sessions). As can be seen, although reducing the intensity of the tones to 15 dB SL had little effect on their ability to localize the 4-kHz tone (cf. Figs. 1 and 2), none of the rats were able to localize the 1-kHz tone. In addition, the animals could not localize the 500-Hz tone, indicating that they could not use the binaural phase cue at this frequency either. These results support the interpretation that rats can use the binaural intensity-difference cue but not the binaural phase-difference cue. That none of the rats could now localize the 1-kHz stimuli above chance was most likely due to the reduction of the transient intensity-difference cue, as the next two tests demonstrate.

3.3. Localization of pure- and amplitude-modulated tones, 5 and 50 ms rise/fall times

Another way to change the size of the transient binaural intensity difference is to change the duration of the rise time. A signal that is turned on quickly will reach a higher intensity at the near ear before reaching the far ear than will a sound that is turned on more slowly (Elfner and Tomsic, 1968; Perrott, 1969—these authors also note that the effect of rise time on the difference in the arrival time at the two ears is the opposite, such that turning a signal on quickly reduces the arrival time difference). To demonstrate the effect of rise time, the rats were compared on their ability to localize pure- and amplitude-modulated tones using 5 and 50-ms rise/fall times (total durations were 105 and 150 ms, respectively). For this test, all tones were presented at 30 dB SL and trial blocks of 8–10 warning trials were alternated between the two rise/fall times. Fig. 3 illustrates the effect of rise time on the ability of the rats to localize the tones. The best performance (the average of the top 50% of the trial blocks for two sessions) for each animal showed that the different rise times had no effect on performance at frequencies above 1 kHz. On the other hand, rise time had a definite effect on performance for the 1 kHz tone and amplitude-modulated tones; whereas all of the rats were able to localize at least some of the 1-kHz stimuli above chance when a 5-ms rise/fall time was used, none could do so when a 50 ms rise/fall was used. Because lengthening the rise time reduces the transient binaural intensity (but increases the arrival time difference), this result supports the idea that the rats were using the transient binaural intensity-difference cue to localize the 1-kHz tone.

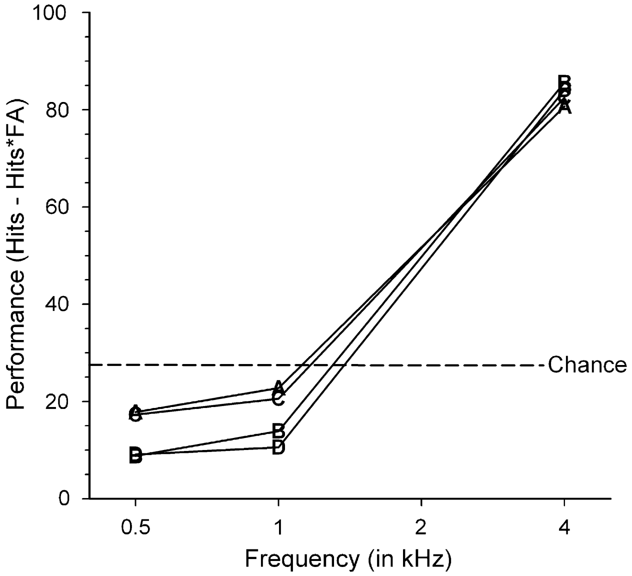

Fig. 2. Ability of the four rats to localize .500, 1, and 4 kHz at 15 dB SL, 60° separation. The stimulus was a single 100-ms tone pip, 20 ms rise/fall. The rats were able to localize the 4-kHz tone, indicating that they could use the interaural intensity difference available at that frequency, but were unable to localize 0.5 and 1 kHz, frequencies at which the interaural intensity differences were presumably too small to be useable.

3.4. Localization of 1 kHz with and without the ongoing portion of the signal

If the rats were using the transient interaural intensity difference to localize the 1-kHz stimuli, then they should still be able to localize the tones if the ongoing portion were removed. At this low frequency, once the signal reached full amplitude at both ears, the binaural intensity difference would be too small to indicate location; thus, removing the ongoing portion of the signal could make the signal easier to localize even though the total duration of the signal would be reduced.

The effect of removing the ongoing portion of a 1-kHz pure tone was determined by testing the animals using a 40 ms duration tone pip (20 ms rise/fall, 30 dB SL, 60° separation). The results were then compared with the animals' performances for localizing the 120 ms duration tone used in the first test (Fig. 1). The results, shown in Fig. 4, indicate that removing the ongoing portion of the 1-kHz signal had either little effect on performance (rat B) or else noticeably improved performance (rats A, C, and D). We interpret these results as indicating that rats are unable to use the bin-

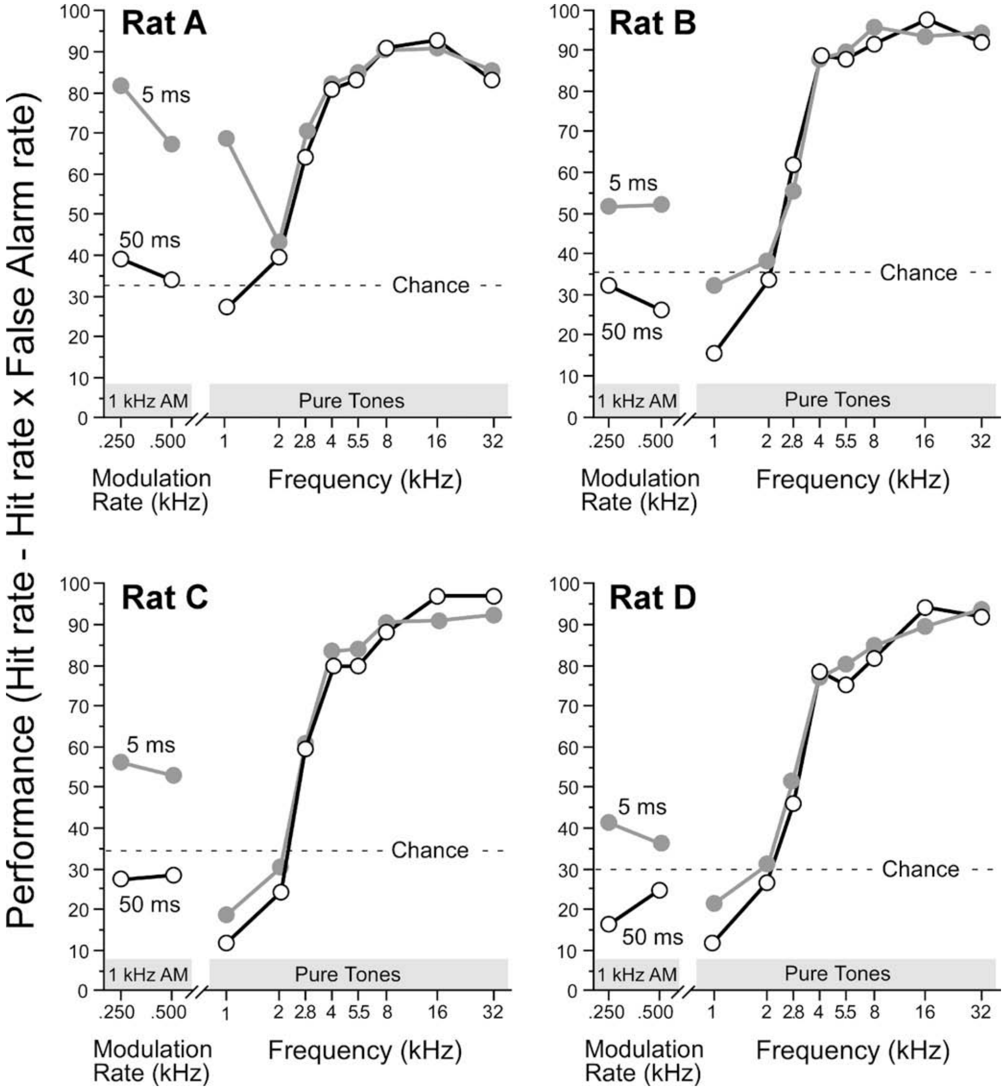

Fig. 3. Comparison of the ability of the rats to localize pure- and amplitude-modulated tones presented with a 5 or 50 ms rise/fall. All tones were presented 30 dB SL at a separation of 60°. The inability of the rats to localize the 1-kHz tones when a 50-ms rise-fall time was used is attributed to the reduced availability of the transient interaural intensity difference that occurs during signal onset.

aural phase cue, but can localize low frequency pure tones, albeit poorly, if the onset is sufficiently rapid to provide a transient binaural intensity cue.

3.5. Measurement of the binaural intensity difference

To further explore the possibility that laboratory rats use only the binaural intensity-difference cue, we measured the binaural intensity difference at the ears of three rats for tones and noise (Fig. 5) for a sound source located 30° from midline. Although measuring the intensity of a sound at the base of the pinna may be an imperfect measure of the intensity reaching the eardrum, it does give some indication of the relative attenuation of the head and pinnae for different frequencies. Comparing these measurements with the behavioral performances shown in Figs. 1 and 3 indicate the following points: first, the best localization performance occurs at 16 kHz, which is also the frequency at which the largest measured interaural intensity difference. Second, localization performance remains relatively good down to 4 kHz, at which the average measured interaural intensity difference is about 3 dB, indicating that an interaural intensity difference of 3 dB or greater is sufficient to support good performance. Third, when the measured interaural difference falls below 3 dB, localization performance declines noticeably, falling to chance at and below 2 kHz at which frequencies the interaural intensity difference is either too small or too unreliable to provide a cue for sound localization. Thus, the ability of rats to localize pure tones, when onset cues are minimized, follows the availability of binaural intensity differences.

4. Discussion

The original purpose of this study was to determine the highest frequency at which rats could use the binaural phase cue to localize sound. Instead, the results of our tests indicated that the rats could not localize low-frequency tones and therefore were incapable of using phase cues to localize sound. Although there was some residual ability to localize 1-kHz tones (Figs. 1 and 3), control tests indicated that this was due to the transient interaural intensity difference that exists between the time that a sound reaches the near ear until it reaches the far ear. Specifically, reducing the transient interaural intensity difference by either lowering the amplitude

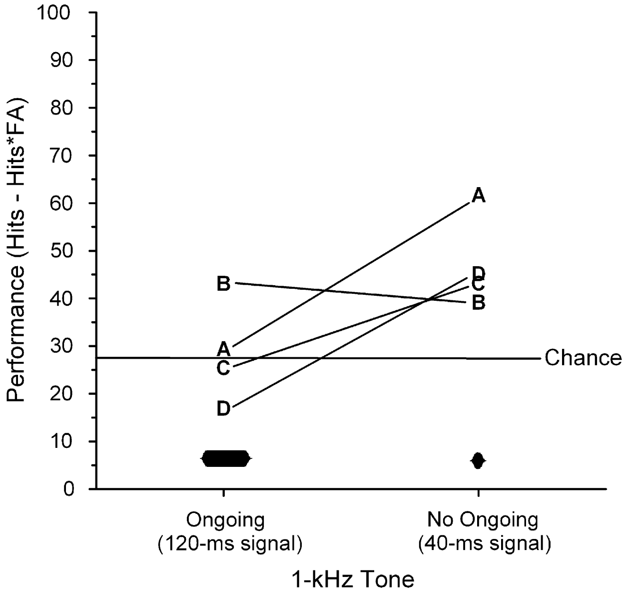

Fig. 4. Tone localization performance of four rats localizing a 1-kHz pure tone at ±30° around midline. Both signals had rise/fall times of 20 ms, but the ongoing signal included 80-ms at full intensity (30 dB above detection threshold). The performance scores for the ongoing signal are those from the initial test. Note that the "No-Ongoing" signal, despite being much briefer, was easier for three of the rats to localize. These results are consistent with the hypothesis that rats localize low-frequency tones using the transient interaural intensity-difference cue.

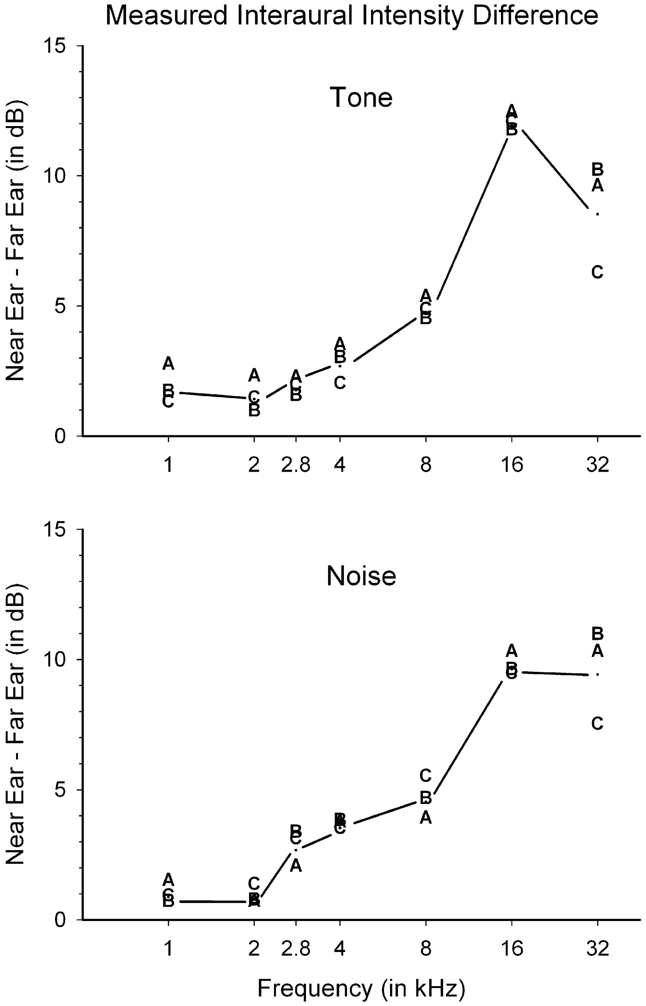

Fig. 5. Interaural intensity difference for pure tones (top) and 1/3-octave noise bands (bottom) for a sound source located 30° from midline. Measurements were conducted on three rats, labeled A, B, and C.

of the stimuli or increasing the rise/fall time completely abolished the rats' ability to localize the 1-kHz tones (Figs. 2 and 3); in addition, the finding that removing the ongoing portion of a 1-kHz tone either had no effect on or else improved performance further indicated that the rats were localizing the transient portion of the signal (Fig. 4). Finally, measurements of the intensity of sounds at the two ears indicated that the ability of the rats to localize high-frequency tones, and the subsequent decline in performance at lower frequencies, could be explained by the magnitude of the interaural intensity differences (Fig. 5). To be sure, we cannot rule out the possibility that rats use binaural time cues for localizing high frequencies. However, we can think of no reason why rats would retain the ability to use binaural time differences to localize high frequencies for which binaural intensity differences are readily available and relinquish the time cue at low frequencies for which no other localization cue is available. Moreover, a re-examination of the behavioral and physiological literature shows that the evidence supporting the use of binaural time differences by rats is not as convincing as we once believed (see the following sections).

Before proceeding, it is worth noting the evidence for why the transient onset cue is properly viewed as an intensity-difference cue rather than a time-difference cue. In investigating the role of onset in sound localization, Lloyd Elfner and his colleagues pointed out that changing the rise time of a signal has opposite effects on the size of the arrival time difference and the size of the transient interaural intensity difference (Elfner and Tomsic, 1968; Perrott, 1969). Specifically, increasing the rise time of a signal (i.e., turning it on more slowly) increases the difference in the arrival time of a sound at the two ears, but decreases the transient interaural intensity difference. The question of whether the auditory system analyzes the onset cue in terms of time or intensity, then, can be addressed by determining the effect of rise time on sound localization ability. What Elfner and his colleagues found was that *increasing* the rise time of a signal *decreased* the ability of subjects to use to the onset cue to either localize or lateralize sound, leading them to conclude that, in humans, signal onset is best viewed as a short-duration binaural intensity-difference cue (Elfner and Tomsic, 1968; Perrott, 1969). As with humans, we found that increasing the rise time of low-frequency tones decreased the ability of rats to localize the tones (Fig. 2), indicating that rats also analyze the onset cue as a transient binaural intensity difference. In short, although one may present an animal with an interaural time difference, the animal's auditory system may process the transient portions of the signal as an intensity difference.

4.1. Comparison with previous behavioral studies

The first tone localization test with laboratory rats was conducted by Masterton and his colleagues in 1975. Using a two-choice procedure in which the animals licked a center water spout to turn on a brief sound (40 dB SL, 40-ms rise/fall, 140 ms total duration) and then walked to the source of the sound (one of two loudspeakers located ±30° around midline), they found that the two rats they tested could localize both low and high frequencies, but not 8 kHz (Fig. 6). Although we cannot explain the inability of their rats to localize 8 kHz, their ability to localize low frequencies is most likely due to the presence of overtones in their signals. This is because at 40 dB above threshold, the sound pressure level of the 1 kHz tone would have been 66 dB, the 500 Hz tone 94 dB, and the 250 Hz tone over 100 dB (Kelly and Masterton, 1977). These levels may well have produced overtones in the 1-kHz tone and would certainly have done so at 500 and 250 Hz.

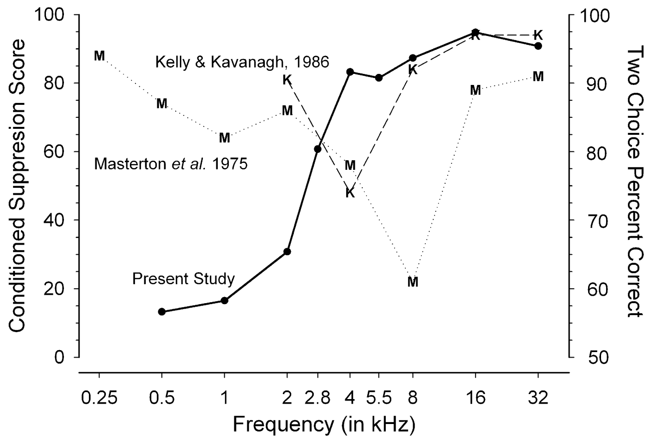

Fig. 6. Comparison of three tone localization studies of rats. The present results are the scores for the 50-ms rise/fall stimuli from Fig. 3 and the 500-Hz results from Fig. 2. Both Kelly and Kavanagh (1986) (K) and Masterton et al. (1975) (M) used a two-choice procedure in which the animals went to the source of the sound. The loudspeakers in all three studies were placed at ±30°. The left vertical axis is scaled for the Present Study, which used conditioned suppression, and the right vertical axis is scaled for the other two studies, which used the two-choice procedure.

Thus, the good low-frequency performance of the rats in their study was likely due to overtones that made it possible for them to use the binaural intensity-difference cue to localize.

A later study conducted by Kelly and Kavanagh (1986), used the same two-choice procedure and the same angle of separation and sound level; however, they used a shorter rise/fall time (20 ms) and shorter total duration (65 ms). The average score for their two normal animals is shown in Fig. 6 (they also tested five rats with cortical ablations with similar results). Unlike Masterton and his colleagues, Kelly and Kavanagh found that the rats could easily localize 8 kHz, but had difficulty with 4 kHz, although their performances remained above chance. In comparison to the present study, Kelly and Kavanagh's rats performed well at 2 kHz whereas our animals performed at or near chance. Kelly and Kavanagh checked their sounds with a spectrum analyzer so the presence of overtones in their signal is unlikely. Thus, the only explanation we can offer is that their animals may have been better able to use the transient interaural intensity difference due to the shorter signal duration and rise/fall time.

One issue is whether our failure to replicate either of the previous two studies is due to our using a different behavioral procedure: conditioned suppression as opposed to a two-choice procedure. This appears unlikely for two reasons. First, previous studies have indicated that the two procedures give the similar results on sound localization tests (e.g., Heffner and Heffner, 1988). Second, as can be seen in Fig. 6, rats were able to perform well on some frequencies with both procedures, indicating that they had no difficulty with the requirements of either task. Thus, the difference between the studies is in the frequencies that the animals were able to localize, not in their asymptotic performances.

Finally, rats have been tested on their ability to perceive the locus of clicks presented from two loudspeakers separated by 180° in which the click from one speaker preceded the other by a small time difference (Kelly, 1974); in humans, such a stimulus is usually perceived as a single click coming from the location of the speaker emitting the leading click and that percept is referred to as the "precedence effect" (Wallach et al., 1949). The results of this study showed that, like humans, rats appeared to perceive the paired clicks as coming from the leading speaker. Moreover, they were able to discriminate left-leading from right-leading click pairs for time differences as small as 62 μs. However, before concluding that these results indicate that rats use binaural time differences, it should be noted that the precedence effect can be viewed as an interaural intensity difference (Elfner and Tomsic, 1968). Indeed, this view is supported by the observation that, like the transient onset cue, the precedence effect works best for signals with fast onsets, such as clicks and does not work for sounds that are turned on gradually (Wallach et al., 1949). Thus, the results of the precedence test do not provide unequivocal support for the idea that rats use binaural time cues for sound localization.

4.2. Physiological responses to interaural differences in rats

Because early behavioral tests concluded that rats use the interaural time-difference cue (Masterton et al., 1975; Kelly and Kavanagh, 1986), several physiological studies have focused on the auditory structures in the rat that might underlie binaural temporal processing. These studies have found neurons from the medial superior olive (MSO) to auditory cortex that respond differentially as a function of interaural time delays (e.g., Inbody and Feng, 1981; Kelly and Kidd, 2000; Kelly and Phillips, 1991; Kidd and Kelly, 1996; Paolini et al., 2001). However, as noted by Kelly and Phillips (1991), there is a mismatch between the range of binaural time differences experienced by the rat and the time differences to which the neurons respond. Norway rats have maximum interaural delays of about 130–160 μs (Koka et al., 2008), yet the time differences used in physiological experiments include values well outside this biologically relevant range. If only the range naturally available for sound localization is considered, only a 30% change in firing rat, on average, can be elicited (Kelly and Phillips, 1991). Not only are the thresholds of these neurons too large to account for the rat's sound localization threshold of 12° (Heffner and Heffner, 2003; Kavanagh and Kelly, 1986), but the neurons respond to time differences well beyond the range of the binaural locus cues generated by the rat's head. Moreover, although it is the time difference between the sounds reaching the two ears that is being manipulated in these studies, it is possible that the neurons are responding to the transient interaural intensity difference (the onset cue) that necessarily accompanies the stimulus. Thus, the response of the rats' neurons to interaural time differences does not provide convincing evidence that they use binaural time cues for sound localization.

There are several possible explanations of the response of neurons to large interaural time differences that that lie outside the natural physiological range. For example, the change in firing rate of central auditory neurons as a function of long interaural delays may be involved in echo suppression. Alternatively, the possibility that such neural responses are epiphenomenal has been argued (Grothe and Neuweiler, 2000). In either case our finding that rats are unable to use the binaural phase-difference cue are consistent with physiological studies suggesting that rats may not be capable of resolving the small interaural time differences needed for localizing sounds. By clarifying this behavioral function of the system, it may now be easier to interpret the neurophysiological results and to begin to better understand species differences among mammals, particularly those that do and those that do not hear low frequencies (Heffner et al., 2001).

Recently, others have begun to question the rat's ability to use interaural time differences on the basis of anatomical and physiological evidence. Kapfer and colleagues (2002) pointed out that rats (as well as some other species that do not hear low frequencies) have MSO's that do not show the highly ordered cell arrangements and dendritic orientations found in rodents (and other mammals) that hear low frequencies and use interaural time differences for localization. Furthermore, the distribution of inhibitory input to MSO cells, important for the precise timing needed for sound localization, is not restricted to cell bodies as it is in species known to use time cues (see discussion by Grothe, 2003). Thus it seems that rats may not have the highly accurate timing of input to the medial superior olive that seems crucial for shaping the interaural time delay functions in the MSO so apparent in species known to use time cues (Grothe, 2003).

4.3. Implications for the role of auditory cortex in sound localization

For a number of years, we have tried to understand why auditory cortex lesions cause a profound sound-localization deficit in some mammals, but not in others. Specifically, it is well established that bilateral auditory cortex lesions abolish the ability to localize sound in cats, dogs, ferrets, macaques, and squirrel monkeys (opossums, hedgehogs, and bushbabies have also been studied, but the results are inconclusive; for a review, see Heffner and Heffner, 1990). However, auditory cortex lesions have little or no effect on sound localization in either the laboratory rat or the wild wood rat (Heffner, 1981; Kelly, 1980; Kelly and Kavanagh, 1986). One possibility is that the role of auditory cortex varies with phylogeny, with carnivores and primates requiring auditory cortex for sound localization, but not rodents. Another possibility, suggested by Kelly and Kavanagh (1986), is that the species difference in the effect of cortical lesions depends on whether or not an animal can localize sound within a hemifield. Unlike primates and carnivores, rats have great difficulty localizing brief sounds within a hemifield. Because one of the main effects of auditory cortex lesions in primates and carnivores is to abolish their ability to localize sound within a hemifield, the negligible effect of cortical lesions in rats may be because they don't possess the ability to localize sound within a hemifield in the first place. As compelling as this explanation appears, it is currently confounded with another species difference in the effect of auditory cortex lesions: in macaques and ferrets, but not in rats, auditory cortex lesions abolish the perception of locus such that the animals have to relearn to associate sounds coming from the left or right with the response of going to the left or right (Heffner and Heffner, 1990; Kavanagh and Kelly, 1987; Kelly, 1980). With the discovery that laboratory rats perhaps do not use binaural time cues, we now have another possible explanation of the species difference in the effect of cortical lesions on the perception of locus.

In 1964, Bruce Masterton placed headphones on cats and tested their ability to perceive the locus of monaural and binaural clicks before and after bilateral ablation of auditory cortex (Masterton and Diamond, 1964). He found that, unlike normal animals, the operated animals did not generalize from a monaural click in the left or right ear to binaural clicks in which the left or right ear received the leading sound. This result suggested that a binaural time difference no longer gave the perception of location in space. In contrast, the operated animals had little or no difficulty discriminating binaural clicks that differed in intensity, suggesting that they retained the ability to use the binaural intensity-difference cue. Thus, in cats, auditory cortex has a greater involvement in the binaural time cue than it does in the binaural intensity cue.

In light of the present results, we now suggest that auditory cortex lesions may have their greatest effect on sound localization in animals that use the binaural time cue. Of those animals in which auditory cortex lesions affect sound localization, cats, macaques, and squirrel monkeys are known to use binaural time cues (Masterton and Diamond, 1964; Heffner and Masterton, 1978; Heffner and Heffner, unpublished; Houben and Gourevitch, 1979). Although ferrets have not been specifically tested, there is reason to believe that they use binaural time cues. This is because they have good low-frequency hearing, which is associated with the use binaural time cues (Heffner et al., 2001; Kelly et al., 1986), and their close relative, the least weasel, does use binaural time cues (Heffner and Heffner, 1987). Of the two species in which auditory cortex lesions do not significantly affect sound localization, the laboratory rat does not to use binaural time cues, at least at low frequencies, and the poor low-frequency hearing of the wood rat makes it a candidate for a similar inability (Heffner et al., 2001, 2010). Thus, it may be that damage to auditory cortex affects sound localization by disrupting the binaural time cue and that the binaural intensity cue, which must be integrated with the time cue, is not sufficient to preserve sound localization.

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