Brown, M. C., S. G. Kujawa, and M. L. Duca. Single olivocochlear neurons in the guinea pig. I. Binaural facilitation of responses to high-level noise. J. Neurophysiol. 79: 3077–3087, 1998. Single medial olivocochlear (MOC) neurons were recorded from the cochlea of the anesthetized guinea pig. We used tones and noise presented monaurally and binaurally and measured responses for sounds up to 105 dB sound pressure level (SPL). For monaural sound, MOC neuron firing rates were usually higher for noise bursts than tone bursts, a situation not observed for afferent fibers of the auditory nerve that were sampled in the same preparations. MOC neurons also differed from afferent fibers in having less saturation of response. Some MOC neurons had responses that continued to increase even at high sound levels. Differences between MOC and afferent responses suggest that there is convergence in the pathway to olivocochlear neurons, possibly a combination of inputs that are at the characteristic frequency (CF) with others that are off the CF. Opposite-ear noise almost always facilitated the responses of MOC neurons to sounds in the main ear, the ear that best drives the unit. This binaural facilitation depends on several characteristics that pertain to the main ear: it is higher in neurons having a contralateral main ear (contra units), it is higher at main-ear sound levels that are moderate (~65 dB SPL), and it is higher in neurons with low discharge rates to main-ear stimuli. Facilitation also depends on parameters of the opposite-ear sound: facilitation increases with noise level in the opposite ear until saturating, is greater for continuous noise than noise bursts, and is usually greater for noise than for tones. Using optimal opposite-ear facilitators and high-level stimuli, the firing rates of olivocochlear neurons range up to 140 spikes/s, whereas for moderate-level monaural stimuli the rates are <80 spikes/s. At high sound levels, firing rates of olivocochlear neurons increase with CF, an increase that may compensate for the known lower effectiveness of olivocochlear synapses on outer hair cells responding to high frequencies. Overall, our results demonstrate a high MOC response for binaural noise and suggest a prominent role for the MOC system in environments containing binaural noise of high level.

INTRODUCTION

Olivocochlear (OC) neurons originate in the superior olivary complex of the brain and project to the organ of Corti in the cochlea (reviewed by Warr 1992). The OC neurons are divided into the following two groups: medial olivocochlear (MOC) neurons, which originate in the medial part of the superior olivary complex and project to outer hair cells (Fig. 1), and lateral OC neurons, which originate more laterally and project to dendrites of afferent neurons near inner hair cells. Although the functional significance of the OC systems has not been definitively established, several hypotheses for MOC function have been proposed. These are to shift the dynamic range of auditory-nerve fibers to higher sound levels, to reduce the effects of noise masking, to protect the ear from damage due to high-level sound, and to mediate selective attention (Geisler 1974a; Hernandez-Peon et al. 1956; Kawase et al. 1993; Meric and Collet 1994; Rajan 1995a; Wiederhold and Liberman 1970; Winslow and Sachs 1988; reviewed by Guinan 1996). MOC neurons respond to sound (Brown 1989; Fex 1965; Liberman and Brown 1986; Robertson and Gummer 1985) and are thus the output neurons of a sound-evoked reflex. Response characteristics of these MOC neurons are likely to give important clues to the function of the reflex.

In the present study, we recorded the responses of single MOC neurons to high-level sounds. High-level sounds were used because most of the functional hypotheses would predict an important role for MOC neurons at high levels. For instance, a role for MOC neurons in protecting the inner ear is important only for sounds that are damaging, that is, for sounds of high level. Levels for which protective effects have been shown range from 100 to 118 dB (Rajan 1995a; Rajan and Johnstone 1988; Reiter and Liberman 1995). In the present experiments, sound levels up to 105 dB SPL were used. Responses to high-level sounds have not been previously studied because of possible damage to the cochlea. In the present experiments, damage was avoided because few stimuli were presented at one time, and the stimuli were brief. We concentrated on MOC neuron responses to noise because the proposed functional hypothesis of reducing the effects of noise masking has received support from physiological and behavioral studies (Dewson 1968; Dolan and Nuttall 1988; Kawase and Liberman 1993; May and McQuone 1995; Nieder and Nieder 1970). This hypothesis would be further supported if noise was an effective stimulus for MOC neurons, yet detailed studies of MOC responses to noise have not been previously reported.

Most previous studies of MOC neurons have used monaural sound presented either to the ipsilateral or contralateral ear. These studies indicate that MOC neurons almost always have a “main ear” that, when stimulated monaurally, causes a response. Monaural stimulation in the ear opposite the main ear usually does not evoke a response. MOC neurons can be classified on the basis of this main-ear response: ipsi units respond only to sound in the ipsilateral ear (if stimuli are kept below the acoustic cross-talk threshold), contra units respond only to sound in the contralateral ear, and
lower than the shock rates that cause optimal effects on auditory-nerve responses, although they are likely to be sufficient to protect the cochlea from overexposure (Rajan 1988; Rajan and Johnstone 1988b). A preliminary version of these results has been presented (Brown et al. 1997).

METHODS

Anesthesia and surgery

The database for this study is a total of 17 guinea pigs, ranging in weight from 256 to 730 g. Twelve guinea pigs were anesthetized with a combination of pentobarbital sodium (Nembutal; 25 mg/kg ip), fentanyl (0.2 mg/kg im), and droperidol (10 mg/kg im). Anesthetic boosters of one-third the original dose were administered every 2 h. Five other guinea pigs were anesthetized with urethan (1,500 mg/kg ip, boosters about every 8 h) plus fentanyl and droperidol as above. Of the total of 197 MOC neurons, 53 were from the 5 urethan-anesthetized preparations; this group of neurons did not obviously differ from the neurons recorded in the Nembutal-anesthetized animals except that their maximal discharge rates are somewhat lower (Brown 1989). Animals were prepared surgically for acute physiological experiments, including removal of the pinnae bilaterally and cutting the skin around the ear canals to allow coupling of the sound delivery systems to the ear canals. The bulla on the left side was exposed and opened to allow electro-physiological recordings, and the bulla on the right side was vented (driven by monaural sounds presented to the ipsilateral ear) and with a small opening. To obtain more stability of measurements, the animal was paralyzed with curare (1 mg/kg im) and ventilated with a respirator delivering room air. All surgical procedures were in accordance with the National Institutes of Health guidelines for the care and use of laboratory animals.

Acoustic stimuli

All tone and noise bursts were 50 ms in duration with rise/fall times of 2.5 ms and were presented at a rate of 10 per second. All noise was broadband and generated by a General Radio random noise generator with a 50-kHz bandwidth. Noise level is specified in overall sound pressure level (SPL, re 20 µPa); it was measured with a probe-tube microphone and a sound level meter (bandwidth 20–20,000 Hz) calibrated with a pistonphone. Calibration of the acoustic system with the probe-tube microphone in the ear canal demonstrated that the frequency response was fairly flat from 0.5 to 20 kHz (Fig. 2). Noise to the main ear always was presented

1 In our earlier studies, either-ear units were referred to as binaural units. We now introduce a new term, either-ear units, that better describes the response of these units to monaural sound, is more consistent with other classifications of neurons in the auditory CNS (Irvine 1986), and takes into account that other types of MOC units also have been determined to be binaural (Liberman 1988b).

Fig. 1. A: schematic of the medial olivocochlear (MOC) reflex pathway to one ear, showing the afferent inputs (arrows) and the origin of ipsi units (driven by monaural sounds presented to the ipsilateral ear) and contra units (driven by monaural sounds presented to the contralateral ear). Either-ear units (driven by sound in either ear, with the main ear taken as the most sensitive ear) have unknown origins and are not indicated on the figure. In addition to main-ear input (large arrows), MOC neurons receive opposite-ear facilitatory input (small arrows). MOC axons leave the brainstem in the vestibular part of the VIIIth nerve. CN, cochlear nucleus. B: schematic of MOC axons projecting from the intraganglionic spiral bundle (IGSB) to the organ of Corti to terminate on outer hair cells (OHCs). A recording electrode is shown in the IGSB, where MOC fibers spiral apically after entering at the base of the cochlea. IHC, inner hair cell.

Fig. 2. Calibration curve for the acoustic system in the external ear canal of a guinea pig. Sound pressure level was measured by a calibrated probe-tube microphone placed ~2 mm from the eardrum.
as bursts, and noise to the opposite ear was presented continuously unless otherwise noted. The interaural sound transmission ("cross-talk") in our preparation was measured and found to be \( \pm 0 \text{ dB} \) down.

**Cochlear surgery**

Most of the methods have been described in our previous study (Brown 1989). A small opening was made in the otic capsule over scala tympani of the basal turn. The bone over the spiral ganglion was pierced with a fine insect pin at a point corresponding to \( \sim 20\% \) distance from the basal end of the organ of Corti. This recording site was made on the peripheral edge of the ganglion, which is the location of the intraganglionic spiral bundle that contains MOC fibers (Fig. 1B). As a test for the effect of surgical procedures on the sensitivity of the cochlea, the compound action potential (CAP) of the auditory nerve was recorded with a silver-wire electrode placed at the round window. Stimuli to evoke the CAP were 5-ms tone pips (0.5-ms rise time, \( \cos^2 \) shaping) at 15 logarithmically spaced frequencies from 1.9 to 25.4 kHz. SPL was varied to determine the level (to within 1 dB) required to produce a CAP of 10 \( \mu \text{V} \) (amplitude of negative trough to following positive peak). Measures of the CAP before and after surgery indicated minimal alterations in CAP sensitivity (\( <5 \sim 10 \text{ dB} \)) across the frequency range tested. Animals with larger shifts were not used in this study.

**Classification of and data obtained from single neurons**

Single-fiber recordings were obtained using glass microelectrodes filled with a combination of 2 M KCl and 4% methyl blue (to visualize the electrode tip). Both MOC (afferent) and spiral ganglion (afferent) fibers were recorded from the spiral ganglion. MOC neurons were identified by their regular interspike intervals, long latency (>5 ms) responses to noise and tone bursts, and responses to contralateral sound (in some of these neurons). By intracellular labeling, such recordings have been confirmed to be from axons of MOC neurons that run in the intraganglionic spiral bundle and innervate outer hair cells in the organ of Corti (Fig. 1B) (Brown 1989; Liberman and Brown 1986; Robertson 1984). At our recording site, we sampled MOC neurons with a wide range of characteristic frequencies (CFs), from 0.59 to 24.7 kHz. This is because MOC axons are spiraling through the recording site to reach the basal, middle, and apical turns (Brown 1987b). In contrast, afferent fibers were identified by their irregular interspike intervals and their short latency responses to noise and tone bursts. We sampled afferent fibers restricted to CFs from 12 to 21 kHz because the afferent axons take a radial course from the recording site directly out to the organ of Corti (Brown 1987a). We almost certainly did not record from the axons of lateral OC neurons because these axons are very thin (\(<1 \text{ \mu m} \) diam) (Brown 1987b).

In recordings from single MOC neurons, we first classified the unit as an ipsi, contra, or either-ear unit by its response to 65 dB SPL noise bursts presented to the ipsilateral and then to the contralateral ears: ipsi units responded only when the bursts were in the ipsilateral ear, contra units when the bursts were in the contralateral ear, and either-ear units when the bursts were in either ear. The ear evoking a response was designated the main ear; in the case of either-ear units the ear evoking a response at the lowest sound level was the main ear. Of our total of 197 units, 66% were ipsi units, 27% were contra units, and 7% were either-ear units. We then obtained data in the following order: rate-level functions for monaural noise bursts in the main ear with levels spaced 10 dB apart and only 10 bursts/level (in order not to cause damage to the cochlea), rate-level functions for binaural noise (main-ear noise bursts plus simultaneous, continuous, opposite-ear noise at 85 dB SPL), tuning curves using main ear tone bursts, rate-level functions for main-ear tone bursts at the characteristic frequency (0–100 dB SPL) without and with opposite-ear noise, and spontaneous firing rate (10-s sampling period). If the unit held longer, the opposite-ear sound was varied to study its effects on facilitation. MOC noise rate-level functions usually were run from high to low level (from 105 to 15 dB SPL) to maximize the collection of data at high levels.

To compare the effect of level sweep direction on rate in three MOC units, two rate-level functions were obtained with noise bursts run from high to low levels, and two rate-level functions were obtained with bursts run from low to high levels. For sweeps in the same direction, rates were very similar: differences averaged over all levels were 3.0%. For sweeps in different directions, rates also were very similar, although there was a small, systematic difference in maximum rate: for bursts run from low to high level, there was, on average, a 4.9% lower maximum rate. This lower rate may be associated with adaptation of the response when stimulus level is varied from low to high, although the response to repeated tone bursts did not decline substantially even at the highest levels tested (e.g., Fig. 10).

From afferent fibers, we recorded tuning curves, spontaneous rates, and rate-level functions for tone bursts at the characteristic frequency and for noise bursts. Firing rates are specified as total rate without subtraction of any spontaneous rate. For afferents, level functions were obtained with bursts run from low to high levels. For afferent level functions, rate was measured in the window of time that contained the 50-ms–duration tone burst, and the rate during the 50-ms silent interval was ignored. For MOC neurons, which have significantly greater latencies and latencies that greatly depend on sound level, rate for level functions was measured using an algorithm that determined the 50-ms window that contained the maximal firing (Liberman 1988b). For MOC tuning
curves, the 50-ms ‘‘on’’ window was arbitrarily set to begin 10 ms after the beginning of the tone burst.

RESULTS

Responses to monaural noise and tones

Rate versus level functions in response to monaural sound (Fig. 3) illustrate several differences between MOC neurons and afferent fibers. The first difference was the rate of response to noise bursts versus tone bursts. For MOC neurons, there was often a higher rate to noise bursts than to tone bursts at high sound levels (Fig. 3A). For afferent fibers, response rates to noise bursts and tone bursts were usually similar at high stimulus levels (Figs. 3B and 4B). In the 33 MOC neurons tested with both noise and tone bursts, maximum rates over the range of sound levels tested were in many units greater for noise bursts than for tone bursts (Fig. 4A). This tendency was more common in high-CF neurons than in low-CF neurons (Fig. 4C).

A second important difference between MOC and afferent responses was in the shape of the rate-level functions. Our data include responses to noise bursts from 65 MOC neurons and 18 afferent fibers and responses to tone bursts from 65 MOC neurons and 56 afferent fibers. MOC level functions often had large dynamic ranges, and in some units, rates increased even at the highest levels that were tested (Fig. 3A). Level functions from afferent fibers, however, had smaller dynamic ranges and often completely saturated at high levels (Fig. 3B), as has been demonstrated previously (Sachs and Abbas 1974). Our metric to quantify differences in saturation was to fit lines to the low-level portions of the functions and extrapolate the lines to high levels (Figs. 3A and 5A, inset). The difference between the extrapolated and observed firing rates was normalized by dividing by the extrapolated rate and is plotted against sound level in Fig. 5A. This normalized metric is zero for a straight line but is higher for saturated functions. The averaged normalized differences increased with sound level (Fig. 5A) because many of the functions saturate. The normalized differences of MOC neurons are smaller than those of afferent fibers because MOC functions generally show less saturation. Analysis of variance procedures (two-way ANOVA tests) were performed to test the effects of level and unit type (MOC vs. afferent) on these normalized differences. Where we have the most data (15 MOC and 25 afferent units over levels 30–80 dB above threshold), differences for MOC units were significantly smaller ($P = 0.003$) than those for afferent units. Afferents of low- and medium-spontaneous rate are known to have less saturated tone level functions than other afferents (Sachs and Abbas 1974); those within our sample ($n = 11$ units) did in fact have smaller normalized differences than units with high spontaneous rate ($n = 17$ units). However, MOC neurons had normalized differences that were even smaller than those of low- and medium-spontaneous rate afferents. Noise level functions from MOC neurons tend to have smaller normalized differences than tone functions from MOC neurons, but ANOVA tests did not reveal significant differences. For MOC level functions, there was a weak trend for neurons of low CF to have the largest normalized differences and the most saturated level functions. This trend can be observed in Fig. 5, B and C, where data are plotted for 60 dB above threshold; similar plots were obtained at other levels although there are fewer data points at the higher levels. Overall, these data demonstrate that maximal rates from MOC neurons will be elicited by high-level noise bursts because their rate-level functions show the least tendency to saturate.

![Fig. 4. Maximum firing rates for noise and tone bursts tested in the same units. Firing rates for 33 MOC neurons (A), and 15 afferent fibers (B). For MOC neurons, sound was presented to the main ear, the ear that evoked a response at the lowest sound level. For afferent fibers, sound was presented to the ipsilateral ear. Tone bursts were presented at the CF. C: for MOC neurons, ratio of maximum rate to noise to maximum rate to tones plotted as a function of CF.](http://jn.physiology.org/DownloadedFrom/10.220.33.2/1192-2016-neuropys/538-7/9k29$$ju17.jpg)
Responses to binaural noise: dependence of facilitation on unit class and main-ear sound level

MOC responses to main-ear stimuli are increased, or facilitated, by sound presented to the opposite ear. For instance, opposite-ear noise facilitates the response of the neuron illustrated in Fig. 6A for most noise levels of the main ear. In this particular neuron, the rate-level function for the main ear alone shows saturation, but opposite-ear noise facilitates the response even at levels above saturation. This finding rules out the possibility that the binaural facilitation is generated by acoustic cross-talk. Facilitation of responses to main-ear tone bursts also was observed (data not shown).

Facilitation first was studied by fixing the level of the opposite-ear noise at 85 dB SPL and varying the main-ear stimulus level. We quantify facilitation as the difference in rate between the binaural and monaural response (Fig. 6A, vertical arrows). On average, facilitation is somewhat greater for contra units than for ipsi units (Fig. 6B). These units did not differ in other ways; for instance, thresholds and firing rates to monaural stimuli were very similar. Facilitation also varies with the noise level in the main ear: it is maximal at midlevels and less at low and high levels (Fig. 6B). Facilitation tends to be greatest in neurons that respond with the lowest rates to monaural sound.

Although most of our experiments used Nembutal-anesthetized preparations, we also tested whether there was facilitation in urethan-anesthetized preparations. There was little difference in facilitation for the two anesthetics. When the data from Fig. 6B were plotted separately for the Nembutal-anesthetized animals (48 ipsi and 27 contra units) and the urethan-anesthetized animals (12 ipsi and 4 contra units), the patterns were similar. Also, the finding that the monaural noise response is greater than the monaural tone response (Fig. 4A) holds for units from each anesthetic. Consistent with our earlier report, however, maximal discharge rates of units from urethan-anesthetized animals are somewhat lower than units from Nembutal-anesthetized animals (Brown 1989).

Dependence of facilitation on opposite-ear sound level and stimulus type

In the experiments described so far, the opposite-ear noise was fixed at 85 dB SPL. When the level of the opposite-ear noise was changed, average facilitation was observed to be very small for opposite-ear levels of 25 dB, to rise until ~65 dB, and to saturate between 65 and 85 dB SPL (Fig. 8A).
low-CF neurons, but not mid- or high-CF neurons, to be facilitated a small amount by opposite-ear tone bursts.

Time course of facilitation

By counting the number of spikes in response to individual bursts presented to the main ear, we determined that facilitation takes place within 50 ms of the onset of the facilitator. For instance, when the main ear is stimulated alone, the neuron shown in Fig. 10 fires two spikes for each of the bursts (●). There is no adaptation of the response to consecutive noise bursts. When opposite-ear noise is added starting at the same time as the first main-ear burst (Fig. 10, inset), the neuron fires three spikes for each burst (Fig. 10, ○). This facilitation of the rate is seen during the first noise burst (within 50 ms) and remains constant for ≥10 bursts (lasting a total of 1 s), demonstrating that there is little adaptation of the facilitated response. Similar results were obtained in 28 other neurons.

Dependence of rate and facilitation on CF

Although there is considerable variation from unit to unit, saturation of facilitation was evident in functions from individual neurons as well as in the average curve (Fig. 8A). In contrast, saturation is not seen in the average firing rates of MOC neurons in response to noise in the main ear (Fig. 8B). This behavior results from the wide dynamic range of individual rate-level functions of MOC neurons and from the fact that high-threshold neurons begin to respond as some low-threshold neurons begin to saturate.

Thus far we have described facilitation resulting from a continuous opposite-ear noise. When the opposite-ear stimulus was changed to noise bursts, there was usually little facilitation (Fig. 9A). In a few units, noise bursts actually inhibited the monaural response (negative values of facilitation on Fig. 9A). We also compared the facilitation produced by continuous noise to that produced by continuous tones at the neuron’s CF (Fig. 9B). In some neurons, tones could facilitate the response as well as noise, but in most neurons, there was less facilitation. In one neuron, continuous opposite-ear tones were inhibitory. There was a tendency for low-CF neurons to be more effectively facilitated by tones than high-CF neurons (data not shown), as reported previously (Liberman 1988b). We have little new data on facilitation by tone bursts. However, a review of the data from our previous study (Brown 1989) also indicates a tendency for
RESPONSES OF OLIVOCOCHLEAR NEURONS TO BINAURAL NOISE

FIG. 9. Plots of facilitation for continuous noise versus facilitation for noise bursts (A) or continuous tones (B). A: scatter plot for 12 neurons tested both with opposite-ear continuous noise and noise bursts at 85 dB SPL (main-ear stimulus was CF tone bursts at 60 dB SPL). B: scatter plot for 13 neurons tested both with opposite-ear continuous noise at 85 dB SPL and continuous CF tones at 80 dB SPL (main-ear stimulus was CF tone bursts at 60 dB SPL).

A: scatter plot for 12 neurons tested both with opposite-ear continuous noise and noise bursts at 85 dB SPL (main-ear stimulus was CF tone bursts at 60 dB SPL). B: scatter plot for 13 neurons tested both with opposite-ear continuous noise at 85 dB SPL and continuous CF tones at 80 dB SPL (main-ear stimulus was CF tone bursts at 60 dB SPL).

Variously for the highest level tested, 105 dB SPL (Fig. 11D). This CF dependence is also not well fit by a straight line. Facilitation, the difference between the firing rates for the binaural and monaural stimulus, is fairly constant across CF (Fig. 11, E and F) but increases slightly for CFs &lt; 3 kHz (Fig. 11E); however, this effect was not statistically significant as shown by a t-test of the difference in facilitation at 65 dB for units with CFs &lt; 3 kHz (n = 12) versus units with higher CFs (n = 60). The firing rates for the highest-level binaural noise (Fig. 11D) are maximal firing rates for MOC neurons under our testing conditions. This is because the main-ear stimulus is the highest level tested and because the opposite-ear facilitator is the most effective facilitator that was tested. On average, the firing rates are ~60 spikes/s at low CFs and 110 spikes/s at high CFs, and extend to almost 140 spikes/s for some neurons of high CF.

DISCUSSION

This study demonstrates a number of new findings about guinea-pig MOC neurons: 1) responses are often higher to noise bursts than to tone bursts; 2) response facilitation by opposite-ear noise depends on main-ear level and whether

High rates to monaural and binaural noise

Our studies indicate that noise is a particularly effective main-ear stimulus, as well as an effective binaural facilitator for the responses of MOC neurons. Functionally, higher MOC responses should translate into higher feedback effects on the periphery. Indeed, it has been shown that OC effects on auditory-nerve response can be greater when elicited by noise than when elicited by tones (Liberman 1989; Warren and Liberman 1989) and contralateral noise has become a standard activator for OC effects (Giraud et al. 1995; Kawase et al. 1993; Kujawa et al. 1993, 1994; Puel and Rebillard 1990; Williams et al. 1994). In accord with present results demonstrating that binaural facilitation is greatest for noise, binaural stimuli were shown to have the largest OC-mediated effects on peripheral phenomena such as cochlear otoacoustic emissions and protection from acute overstimulation (Berlin et al. 1995; Cody and Johnstone 1982; Liberman et al. 1996; Rajan 1995b). Finally, the MOC neuron’s high response to noise is consistent with an MOC role in reducing the masking effects of noise (Dolan and Nuttall 1988; Kawase and Liberman 1993; Nieder and Nieder 1970), resulting in improved behavioral performance (Dewson 1968; May and McQuone 1995). Our study indicates that responses to noise in some MOC neurons increase even at the highest levels tested (105 dB SPL). However, the MOC role in reducing the effects of noise is likely to be greatest for noise of moderate levels, because it is at these levels where MOC action can reduce the response to noise in auditory-nerve fibers and therefore reduce adaptation (Kawase et al. 1993).

Response differences between MOC neurons and afferent
fibers indicate that fundamental changes occur in the reflex pathway between afferent fibers and MOC neurons. For auditory-nerve fibers, rates to noise can be much lower than rates to tones, especially for a narrowband of noise centered on either side of the tuning curve (Ruggero 1973; Schalk and Sachs 1980). This noise contains energy within the twotone suppression areas that reduces the response to energy within the excitatory response area. In our study, afferent rates to noise were not reduced compared with tones, presumably because the broadband noise did not have significant energy in suppression areas (our sound system rolls off above 20 kHz and thus our high-CF afferents would receive little suppression above CF). Our MOC units, however, had distinctly higher rates to noise, especially for high-CF neurons. How does the MOC reflex generate higher rates to noise than to tones? Possibly, MOC neurons receive convergent input from on-CF and weaker off-CF sources. This hypothesis explains higher firing rates to noise because of an activation of all inputs by the noise and because the twotone suppression area of one input would be cancelled by rates to tones, especially for a narrowband of noise centered on either side of the tuning curve (Ruggero 1973; Schalk and Sachs 1980). This noise contains energy within the twotone suppression areas that reduces the response to energy within the excitatory response area. In our study, afferent rates to noise were not reduced compared with tones, presumably because the broadband noise did not have significant energy in suppression areas (our sound system rolls off above 20 kHz and thus our high-CF afferents would receive little suppression above CF). Our MOC units, however, had distinctly higher rates to noise, especially for high-CF neurons. How does the MOC reflex generate higher rates to noise than to tones? Possibly, MOC neurons receive convergent input from on-CF and weaker off-CF sources. This hypothesis explains higher firing rates to noise because of an activation of all inputs by the noise and because the twotone suppression area of one input would be cancelled by rates to tones, especially for a narrowband of noise centered on either side of the tuning curve (Ruggero 1973; Schalk and Sachs 1980). This noise contains energy within the twotone suppression areas that reduces the response to energy within the excitatory response area. In our study, afferent rates to noise were not reduced compared with tones, presumably because the broadband noise did not have significant energy in suppression areas (our sound system rolls off above 20 kHz and thus our high-CF afferents would receive little suppression above CF). Our MOC units, however, had distinctly higher rates to noise, especially for high-CF neurons. How does the MOC reflex generate higher rates to noise than to tones? Possibly, MOC neurons receive convergent input from on-CF and weaker off-CF sources. This hypothesis explains higher firing rates to noise because of an activation of all inputs by the noise and because the twotone suppression area of one input would be cancelled by rates to tones, especially for a narrowband of noise centered on either side of the tuning curve (Ruggero 1973; Schalk and Sachs 1980).
off-CF inputs would contribute at higher sound levels. Less saturation also could result, however, if predominant input is from low spontaneous-rate afferents (Liberman 1988a) that have less saturation of their level functions than other classes. The interneurons of the MOC reflex pathway are unknown but likely include neurons in the posteroventral division of the cochlear nucleus (Thompson and Thompson 1991). Within this pathway, convergence of on-CF and off-CF inputs might occur at one of several sites: from a variety of auditory-nerve fibers to a single cochlear-nucleus neuron [as is characteristic of cochlear-nucleus Onset units (Rhode and Smith 1986; Winter and Palmer 1995)], or from a variety of reflex interneurons onto MOC somata.

Mechanisms of facilitation by opposite-ear stimuli

Present results suggest that a single neuron’s facilitation by opposite-ear sound differs from its response to main-ear sound (Fig. 8). Facilitation increases with the level of the opposite-ear noise until it saturates; this is true for average data as well as individual neuron data (Fig. 8A). By contrast, the level dependence of firing rates for main-ear input shows almost no saturation in average data (Fig. 8B) and ranges in individual neurons from almost no saturation (Fig. 3A) to large saturation (Fig. 6A). Another difference between facilitation and main-ear response is the small amount of facilitation observed for opposite-ear noise bursts (Fig. 9A) as compared with the large firing observed for main-ear noise bursts. An hypothesis that could explain these differences is that there are two separate pathways in the MOC reflex, one that produces the main-ear response and another that produces the opposite-ear facilitation. Only one pathway, through the posteroventral division of the cochlear nucleus, has been identified (Thompson and Thompson 1991); whether this pathway serves the main ear or opposite ear has not been determined.

Facilitation also depends on the level of the main-ear stimulus (Fig. 6B); it is maximal at middle levels of the main-ear stimulus for an opposite-ear noise of 85 dB SPL. We have defined facilitation as an increase in spike rate caused by the opposite-ear facilitator. Alternatively, facilitation could be defined as the percent increase in spike rate; this definition was not used because it exaggerates small changes in small responses that are typical of low main-ear levels. Described in this fashion, however, facilitation would be much greater at low main-ear levels because it caused a 65% increase in rate at 25 dB, a 49% increase at 65 dB, and a 14% increase at 105 dB SPL, when averaged over all neurons. By any measure, facilitation in most units declines at the highest sound levels. The small facilitation seen at high levels has implications for OC-mediated protection from overexposure to high-level sounds, a protection that reduces the threshold shifts caused by the overexposure (Cody and Johnstone 1982; Rajan 1995a; Rajan and Johnstone 1988b; Reiter and Liberman 1995). Protection is small when the OC system is stimulated with monaural sound but larger when stimulated with binaural sound (Rajan 1995b; Rajan and Johnstone 1988a). Of the units projecting to the exposed ear, monaural sound would activate mostly ipsi units (and the small number of either-ear units), whereas binaural sound would facilitate ipsi units and additionally recruit contra units. However, we now have shown that facilitation, at least as measured on the time scales used here (seconds), is small at the high sound levels used for overexposures. Thus protection is likely to result mainly from the recruitment of contra units. Possibly, contra units have more protective effects because of a difference in their peripheral action compared with ipsi units, but this has not been demonstrated.

Interestingly, contra units are facilitated more strongly than ipsi units by opposite-ear sound (Fig. 6B). All of these neurons project axons to the ipsilateral ear, thus contra units are facilitated strongly by the ear to which they project. The MOC reflex is consensual; it is activated by ipsilateral or contralateral sounds. However, the reflex is dominated by ipsilateral sound because ipsi units comprise about two-thirds of all MOC neurons. An even greater domination by ipsilateral sound is shown here by the stronger facilitation of contra units by ipsilateral sound. This stronger facilitation and the laterality of their main ear are the only known differences in response characteristics of ipsi and contra units; otherwise, these classes of units have very similar physiological properties (Brown 1989; Liberman 1988b; Robertson and Gummer 1985).

Rate increases with CF

MOC neuron firing rates increase with CF for high-level sound (Fig. 11B), but there is little CF dependency for moderate-level sound (Fig. 11A). We saw less CF dependence in our earlier study (Brown 1989), probably because moderate-level stimuli were used and fewer neurons were recorded. A different dependence was seen in an earlier study of cat MOC neurons (Liberman 1988b), in which rates were found to peak for middle CFs. There are multiple differences between this earlier study and the present study, including a different anesthetic, different surgical procedures, and a different species. The cat-guinea pig differences in MOC rate, though, may correlate with another measure of OC action: the effect of opposite-ear noise on amplitude of the otoacoustic emission, 2f1 − f2. In cat, the effect of opposite-ear noise on emissions peaks at mid-frequencies such as 2 and 4 kHz (Liberman et al. 1996), whereas in guinea pig, effects are greatest for higher frequencies (8–12 kHz range when tested between 2 and 12 kHz) (Kujawa and Liberman 1996). These data suggest that there are significant differences in these two preparations that have been used to study the MOC system.

Firing rate increases with CF are interesting in view of the CF dependence of shock rates necessary to produce effects on auditory-nerve response (Guinan 1997a,b). Shock rates must be more than doubled as frequency is changed from 5 to 20 kHz to obtain the same decrease in auditory nerve’s compound action potential. Apparently this arises in part because the synaptic targets of the MOC neurons, the outer hair cells, have membrane impedance made up of both capacitative and resistive portions, and the capacitative portion becomes much more important at high sound frequencies. The MOC synapses, however, primarily affect membrane resistance, according to the outer hair cell ‘‘shunt model’’ (reviewed by Geisler 1974b). So for MOC synapses to change membrane impedance at high frequencies, they must overcome membrane capacitance by producing a very
large change in resistance by being activated at high shock rates. The firing rates observed in the present study increase with CF, approximately doubling for a CF change from 1 to 20 kHz for monaural sound (Fig. 11B). This increase is nearly sufficient to accommodate the requirements of the shunt hypothesis. Interestingly, rate increases with CF were not observed for moderate-level stimuli (Fig. 11A). Perhaps at these moderate levels, the MOC system has little functional role and is only required to overcome shunting effects as sound levels become high.

When activated by electrical stimulation, the MOC neurons produce maximal effects at shock rates between 200 and 400 shocks/s (Brown and Nuttall 1984; Gifford and Guinan 1987). At rates between 60 and 110 shocks/s, equivalent to the firing rates observed in the present study, electrical stimulation produces substantial protection from overexposure (Rajan 1988; Rajan and Johnstone 1988b) but produces only about a 10% reduction in the compound action potential of the auditory nerve (Gifford and Guinan 1987; Guinan 1997a,b). Comparisons between firing rates and shock rates may be misleading though because other factors might influence firing rates (e.g., anesthesia) and electrical stimulation may activate only a portion of all MOC neurons (Guinan 1997a) and thus produce a small effect unless the portion activated is stimulated at artificially high rates. Although these effects would tend to underestimate the relative importance of the firing rates observed in the present study, the reconciliation of shock rates versus firing rates awaits future study.

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REFERENCES


RESPONSES OF OLIVOCOCHLEAR NEURONS TO BINAURAL NOISE


