

Contralateral White Noise-Induced Enhancement in the Guinea Pig's MLR: A Possible Link to Directional Hearing*

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Abstract: The evoked potential components in a time window of 10-50 ms following an acoustic stimulus are called middle latency responses (MLRs). It is known that an amplitude enlargement occurs in guinea pig MLRs to monaural clicks when continuous white noise is applied to the other ear. This study was undertaken to see whether this enlargement is due simply to an overall, generalised effect of contralateral white noise (WN), or whether it may have some connection to directional hearing. Recordings were made from chronic guinea pig preparations with epidural electrodes in the temporal regions. Parallel to the results in the literature, an enlargement of the MLR to monaural clicks was seen when WN was at the

opposite ear relative to the condition with no WN. A decrease was the result when WN was applied to the same ear as the click. With WN delivered to both ears an increase was observed again. We suggest that these findings, which are not likely to result from a generalised effect of WN over the auditory system, could be explained by a contribution to the MLR from binaural mechanisms which are probably stimulated by the momentary shift of the intra-cranial sound image from the side of the ear receiving the WN to side of the ear receiving the click.

Key Words: Guinea Pig, Middle Latency Response, MLR, Directional Hearing, Contralateral White Noise Enhancement

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Introduction

Vertebrates use interaural intensity and time disparities to determine the lateral position of a sound source. These 2 cues to sound lateralisation are known to be encoded in the nuclei of the superior olivary complex (SOC) of both sides and there is also extensive exchange of binaural information between the bilateral afferent auditory centers, i.e., the inferior colliculus, the medial geniculate body and the auditory cortex (AC) (1).

Middle latency responses (MLRs) are the part of an auditory evoked potential in the 10-50 ms post-stimulus time window. Two different MLRs from the guinea pig's temporal and midline posterior regions can be recorded (2,3). The MLR recorded from the temporal region is composed of a positive wave A at 15 ms, a negative wave B at 25 ms and a positive wave C at 40 ms. These response waveforms can be recorded with highest stability and maximal amplitudes from the temporal region opposite the stimulated ear (4,5,6).

Some studies have shown that the guinea pig's temporal MLR is associated with primary AC, and its midline posterior MLR with non-primary auditory areas. The difference between the effects of binaural and monaural stimulation on midline and temporal MLRs, strengthens the hypothesis that they have different origins (2,7). Polarity reversal and lesion studies provide good evidence that AC is the source of temporal MLR (8) in guinea pigs.

In guinea pigs, the temporal MLR (especially waves A and B) evoked by a click in the contralateral ear, is enhanced in amplitude when there is continuous white noise (WN) in the other ear. This enhancement is thought to result from the suppression of an inhibitory mechanism by the WN (6).

The determination of the lateral position of a sound source is only possible by the interaction between two sides of the auditory system. If the sides of the auditory system were independent of each other, the binaural

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response would be equal to the sum of the left and right monaural ones as seen in the first 3 waves of auditory brainstem responses. However, the binaurally evoked response should not be equal to the sum of the responses to clicks in either ear. This inequality is quantified by subtracting the sum of the 2 monaural responses from the binaural one (9). The difference-potential so computed is called the binaural interaction component (BIC) and considered to be an indicator of such binaural interaction (BI). Although the phenomena of BIC and the enhancement in click-evoked MLR due to WN in the other ear, observed in the guinea pig's temporal MLR, are both products of binaural mechanisms, different mechanisms must be responsible for these 2 phenomena according to the results of a previous study performed by us (10).

The present study was conducted to see whether the enhancement, in click-evoked MLR due to WN in the other ear, is a general, nonspecific effect of the WN per se, or whether it may be associated with some binaural interaction related to directional hearing.

Materials and Methods

Recordings were made from 11 awake guinea pigs weighing between 300 and 725 grams after chronic epidural electrodes were implanted by using stereotaxic methods. In 5 of the animals the experiments were repeated for both hemispheres, so recordings were made from a total of 16 hemispheres.

Stereotaxic operations were conducted under 70 mg/kg ketamine and 7 mg/kg xylazine anaesthesia. Three holes were drilled through the skull: 2 in the bilateral temporal regions for the recording electrodes, and 1 in the frontal region (7-10 mm anterior to the bregma) for the grounding electrode, which also served as a reference. The holes in the temporal regions were carefully drilled in symmetry, on both sides, 7.5 to 9 mm lateral to the midline depending on the size of the animal's head (2,3,5,6).

A closed system consisting of a pair of earphones matched for their dynamic characteristics and 2 rubber tubes were used for sound delivery. Clicks were obtained by 100 μ s electric pulses with a 400 ms inter-stimulus interval and WN with a frequency spectrum of 100-14000 Hz was obtained from the output of a digital-to-analogue converter fed random numbers.

In the abbreviations for stimulation paradigms, the stimuli to the 2 ears are separated by a slash so that the letter(s) before the slash show(s) the stimulus to the ear contralateral to the temporal electrode, while the letter following the slash stands for the stimulus to the other ear. As for the stimuli, C indicates click, N indicates WN and \emptyset indicates nothing delivered.

The following 4 experiments (schematised in the left-hand column of Figure 1) were carried out on each of the animals:

Experiment C/ \emptyset : 55 dB clicks (re. auditory brainstem response threshold) were delivered to one ear and nothing was delivered to the other. MLRs were recorded from the temporal electrode contralateral to the ear receiving the clicks (see Figure 1A).

Experiment C/N: Experiment C/ \emptyset was repeated but with 55 dB WN (re. peak equivalent of 0 dB clicks) in the ear contralateral to that receiving the clicks (see Figure 1B).

Experiment (C+N)/ \emptyset : A mixed stimulus composed of 55 dB clicks and 55 dB WN was delivered to the contralateral ear and nothing to the ipsilateral one (see Figure 1C).

Experiment (C+N)/N: Experiment (C+N)/ \emptyset was repeated but with 55 dB WN in the ear contralateral to that receiving the clicks (see Figure 1D).

Because the WN in experiment C/N was delivered to the ear contralateral to that receiving the clicks, it was called contralateral white noise (CWN).

Amplifiers had a pass band between 10 and 1000 Hz. Because of the WN enhancement seen in especially waves A and B of the guinea pig's temporal MLR, we decided to use the amplitude between the peak points of waves A and B (A-B peak-to-peak amplitude) as the criterion. The t-test for matched pairs was used to compare the peak-to-peak (A-B) amplitudes of the MLRs recorded in these 4 experiments.

Results

A typical set of temporal MLR tracings recorded from a guinea pig under 4 stimulation conditions (the 4 experiments described above) is presented in the right-hand column of Figure 1. The statistics of the A-B amplitudes in similar MLRs recorded from the 16

hemispheres are also given in the Table for all 4 experiments.

As seen in Figure 1, a comparison of the results of experiments C/N and C/∅ shows that a WN at the opposite ear caused, on average, a 25% increase in A-B amplitude, and this increase was highly significant (t=9.38, p<0.0005). On the other hand, when WN

delivered to the same ear as the click [experiment (C+N)/∅] caused the A-B amplitude to decrease by 37% in comparison to experiment C/∅ (t=9.39, p<0.0005). When WN was also delivered to the other ear [experiment (C+N)/N], however, the A-B amplitude partially recovered (t=8.28, p<0.0005); when compared to experiment (C+N)/∅, an increase of 38%, on average, was noted.

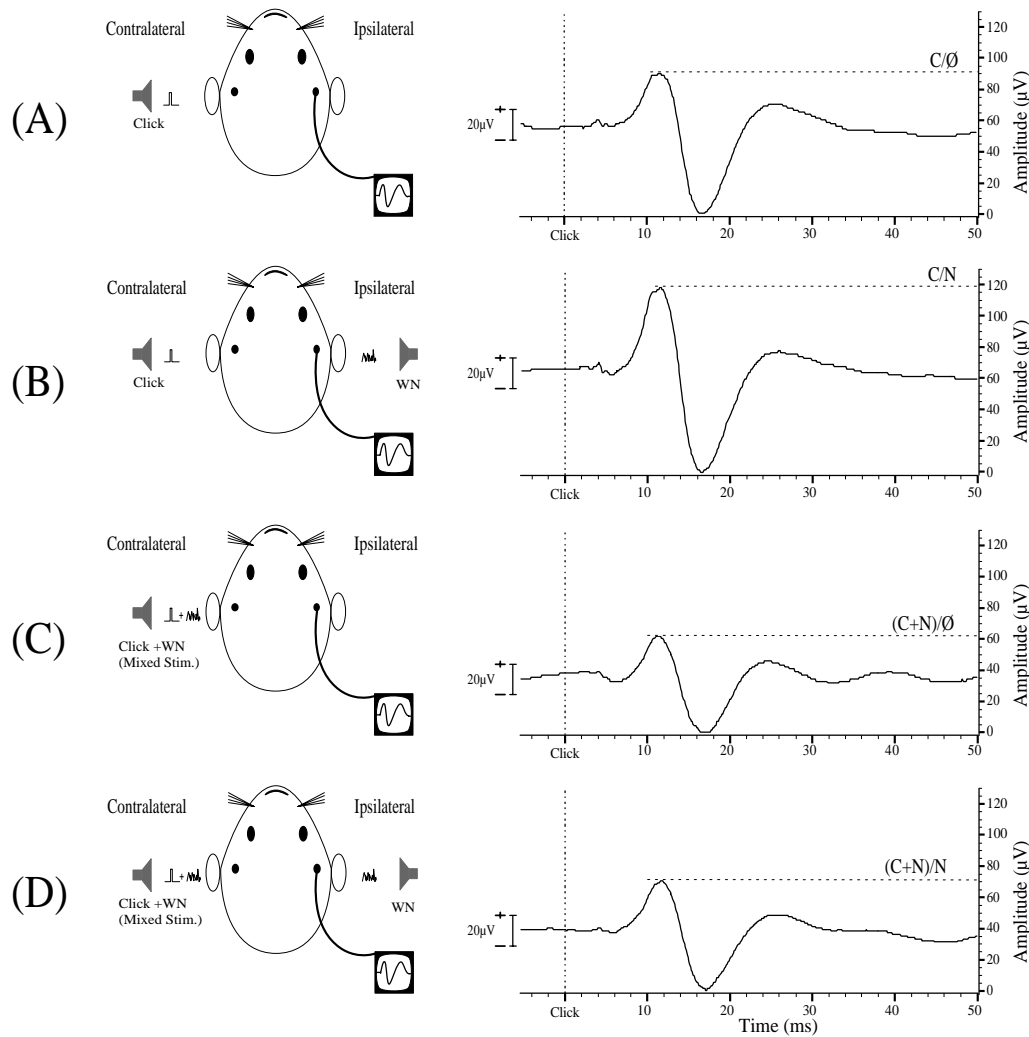


Figure 1. Recording methods schematised in the left-hand column and sample recordings of 4 experiments of guinea pig's temporal MLR for examining CWN enhancement, in the right-hand column.

Average Values of Recordings			
C/∅	C/N	(C+N)/∅	(C+N)/N
78.25 ± 6.62 µV	97.38 ± 8.12 µV > C/∅ (25%) *	49.38 ± 4.69 µV < C/∅ (37%) *	67.13 ± 5.78 µV > (C+N)/∅ (38%) *

* p<0.0005

Table.

Peak-to-peak amplitude averages, standard deviation values and statistical results of waves A-B in 16 temporal MLR recordings of guinea pigs in 4 different experiments.

In 5 of the animals we repeated the experiments for both hemispheres to see if there was any inter-hemispheric asymmetry. As seen in Figure 2, in none of

the 5 animals for which the experiments were repeated for both hemispheres was any significant inter-hemispheric asymmetry observed.

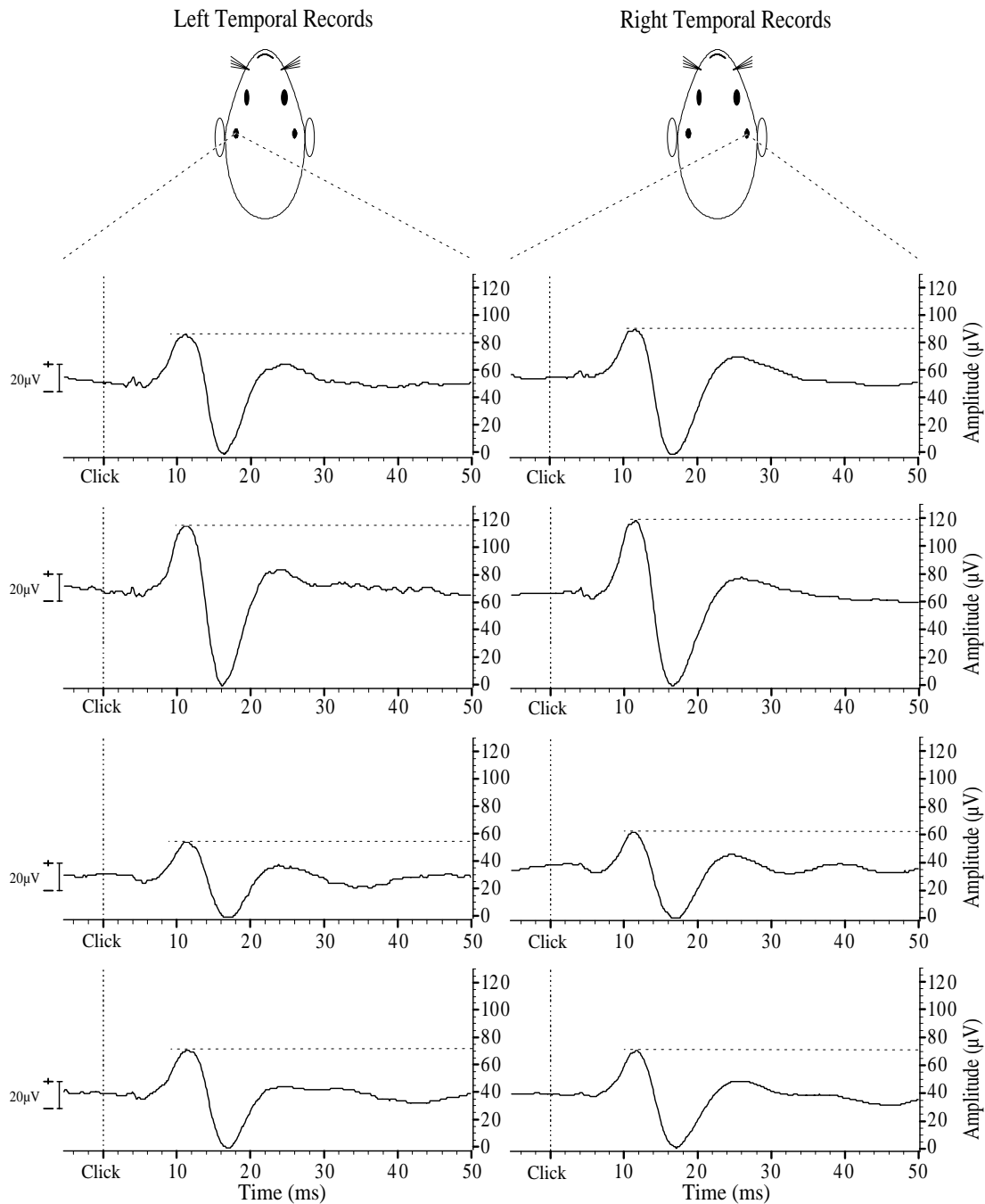


Figure 2. Sample bilateral temporal MLR recordings of the same guinea pig, in 4 experiments, conducted to see if there was any inter-hemispheric asymmetry.

Discussion

Noise is known to modulate the level of spontaneous activity in the cochlear nucleus (11) and 8th nerve (12), but this effect can have no relationship to CWN enhancement, because enlarged response amplitudes should result from increased synchronisation of unit firings and not from changes in their rates. Monaurally applied WN may affect the responses to click stimulation to the opposite ear via the following possible mechanisms.

Stapedius reflex

Özdamar et al., who were the first to observe CWN enhancement, tried to explain it first by the middle ear muscle reflex theory, the validity of which they themselves considered unlikely (6). The least WN intensity to cause stapedius muscle contraction in both ears is 90 dB and this WN causes a decrease of about 5 dB in hearing sensitivity (13,14). This is because decreased hearing sensitivity may only result in decreased response amplitude, so the stapedius reflex cannot explain CWN enhancement in MLR.

Cross-talk between the 2 ears

Although we cannot rule out the possibility of cross-talk in our experiments, this cannot be the reason for the enhancement in MLR. This is because, on the one hand, clicks which might leak to the other ear due to cross-talk would only cause a decrease in response amplitude in line with the fact that monaural MLRs are larger than the binaural one in guinea pigs. And, on the other hand, CWN which might leak to the other ear would only cause the response amplitude to decrease further, as indicated by the results of experiments C/N and (C+N)/N.

Central masking via inhibitory efferent mechanisms

SOC is the most important and most complicated component of the guinea pig's auditory system. This complex contains not only nuclei of the lateral and medial superior olives but also a number of periolivary nuclei consisting of small cell groups. All of these nuclei receive many descending inputs in addition to the ascending ones from other components of the auditory system, and send many outputs to other structures (15). This system, which is called the olivocochlear bundle (OCB), integrates the binaural information from superior brain regions and gives the output directly to the cochlea. The OCB's basic functions in the inner ear are the arrangement of dynamic

range, attenuation of the masking effect and protection of the inner ear from high-intensity sounds. The OCB innervates the outer hair cells in the cochlea and the dendrites of the auditory nerve. The trapezoid body is the most important point of crossing in the auditory system, and some neurons from its ventral nucleus join the olivocochlear system binaurally. One group of neurons from the OCB is called the crossed olivocochlear bundle (COCB) because of crossing in the trapezoid body.

Although we found some reports on the electrophysiologic effects of OCB and COCB in experimental animals, including the guinea pig, they imply a suppressive rather than an enhancing effect of WN on the click responses. Some authors have shown that electrical stimulation of OCB in the guinea pig stabilises the basal membrane in the basal turn of the cochlea and the efferent fibres terminating in outer hair cells, suppressing the cochlea's sensitivity and frequency selection (16). This suppression causes an evident decrease in response. Stimulation of the medial olivocochlear efferent fibres decreases the gain of the cochlear amplifier. According to data recorded from a chronic electrode implanted in the round window of an awake guinea pig, a significant decrease, on average, of the response amplitude is seen when the contralateral ear is stimulated with 55 dB WN (17). These findings show that OCB activity due to WN does not have any directional specificity and, therefore, cannot be the reason for the enhancement observed.

In the guinea pig, the COCB suppresses the depolarising and alternating components of the inner hair cells of the cochlea, and it also affects the auditory nerve fibres. Although the COCB effect sets in slowly, requiring 50 to 250 ms for the full effect (18), this was not an obstacle for this suppressive effect of the COCB in our experiments, because the WN was continuous. However, the effect is again a suppressive one and cannot lead to any response enhancement.

Although in the guinea pig a highly intense noise can cause suppression of both cochleas via a central inhibiting effect of cortical origin, it was shown that, following 1h of this noise, the auditory cortical evoked potentials were enlarged and this effect lasted for hours (19,20). However, this effect cannot explain the CWN enlargement because, firstly, this enlargement is a kind of rebound effect observable long after the termination of noise and, secondly, it is bilateral.

Özdamar et al., who were the first to observe CWN enhancement, suggested the hypothesis of the suppression of an existing inhibitory mechanism to explain this phenomenon (6). Although there are inhibiting mechanisms which may produce contralateral masking through OCB, as briefly mentioned above, no mechanism which may suppress such masking is known.

We nonetheless found a study which might indicate facilitation via efferent fibres. It was found in a cat study that, although the effect of ventral lateral lemniscus stimulation was inhibitory in the dorsal cochlear nucleus (CN), it was facilitatory in the ventral CN (21). Because in this study the S-segment or the lateral lemniscal nuclei was directly stimulated by electric current, it is not known if it would simulate the effect of ipsilateral, contralateral or binaural noise. Therefore, we cannot discuss whether this would explain the CWN enhancement observed.

Proposed hypothesis for CWN enhancement based on directional hearing

If a non-specific auditory mechanism with no direct relationship to directional hearing is responsible for CWN enhancement, this effect should be independent of the side of the noise. However, not an increase such as that in experiment C/N but a decrease was observed in experiment (C+N)/∅, although in both cases a WN was applied to the auditory system (albeit through different ears). Although this decrease is probably due to the cochlear masking effect of the noise in the stimulated ear, there is certainly no enhancement.

Furthermore, if CWN enhancement is due to a non-directional mechanism, there would not be any difference between the results of experiments (C+N)/∅ and (C+N)/N, because in both cases noise is applied to the overall auditory system. However, response amplitudes in experiment (C+N)/N were evidently greater than those in experiment (C+N)/∅ and, therefore, the hypothesis of non-directional effect must be rejected.

The enhancement studied seems to result from a sort of binaural interaction and we can therefore hypothesize that this phenomenon is related to some directional hearing mechanism. The following hypothesis can be put forward: WN in one ear creates an intra-cranial sound image on the side of that ear, and with every click to the other ear this sound image shifts temporarily towards this ear. This constitutes a directional stimulus for some spatial hearing mechanism, which in turn produces a

response in addition to the MLR evoked normally by the click alone. It is this additional directional response that makes the observed enhancement in A-B amplitude.

According to this hypothesis an enhancement must not be expected in experiment (C+N)/∅ relative to experiment C/∅, because under these conditions, WN produces a sound image on the same side as the clicks, and the clicks will not therefore cause any lateral shifting of the image. On the contrary, in experiment (C+N)/∅ a decrease must be expected because of the well-known ipsilateral masking effect of WN on clicks. In fact, this was exactly what we observed: a decrease, not an enhancement.

If directional hearing mechanisms underlie the CWN enhancement, in experiment (C+N)/N an enhancement was also to be seen relative to (C+N)/∅, because the intra-cranial sound image would occur then in the midline and this image would shift to the contralateral side with each click. Indeed, a significant enhancement was recorded.

The question as to why this enhancement only happens in guinea pigs although binaural interaction is a specialty of all vertebrates can be answered by the fact that the guinea pig has many other unique features in the electrophysiology of its hearing system. Some of the features which have only been observed in this animal are as follows:

- a) Two types of MLRs probably with different neural generators are recorded from the midline posterior and temporal region (2,3)
- b) There is a clear inter-hemispheric asymmetry in the temporal MLRs (4,5,6)
- c) The temporal MLR to contralateral clicks has larger amplitudes than that to binaural clicks (6).

Thus, CWN enhancement in MLR may be considered another interesting peculiarity of the guinea pig.

However, we do not have any conclusive evidence for the involvement of directional hearing mechanisms in CWN enhancement. Certainly, further research is necessary to test this hypothesis.

These findings lead us to conclude that the enhancement in click-evoked MLR due to CWN in the other ear is not likely a generalised (non-directional) effect of WN on the auditory system. We can speculate, therefore, that it results from an inter-cellular synchronisation produced by temporary shifting of the

intra-cranial sound image from the side of the WN to the side of the click, thus implying a connection to the mechanisms of directional hearing.

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