plex changes in the conformation of the opiate receptor may result from the redox actions of Cu^{2+} and DTT, and the effects of these agents on nociperception may be due to alterations in receptor efficacy resulting from such conformational changes.

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6. Latency of tail flicking to the heat stimulus was measured [F. E. D'Amour and D. L. Smith, *J. Pharmacol. Exp. Ther.* **72**, 74 (1941)] (cutoff time, 10 seconds), and the percentage of analgesia was calculated [L. S. Harris and A. K. Pierson, *ibid.* **143**, 141 (1964)]. Saline or naloxone (10 mg/kg) was injected intraperitoneally 20 minutes before the intracerebroventricular injection of $CuCl_2$. Control latency was 3.2 ± 0.5 seconds ($N = 15$). Pretreatment with naloxone did not alter this latency significantly (2.8 ± 0.8 seconds, $N = 11$). Median effective dose values and confidence limits were calculated from log-probit plots [J. T. Litchfield and F. J. Wilcoxon, *ibid.* **96**, 99 (1948)]. The dose-response curves in Figs. 2B and 3B were parallel, and the ED_{50} values differed significantly in both cases.
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15. Since Cu^{2+} inhibits the binding of agonists, including endorphins, in vitro, the analgesic effects of this metal may seem paradoxical. However, narcotic agonists as well as antagonists block agonist binding, and this assay does not distinguish between the two classes of agents. C. B. Pert *et al.* [*Science* **182**, 1359 (1973)] proposed that the effects of added sodium in the binding assay may be used to distinguish narcotic agonists from antagonists. Our preliminary results with this test show a large "sodium shift" in the inhibition of binding by Cu^{2+}. This is consistent with a direct agonistlike action of the metal on the receptor. However, the agonistic effects of Cu^{2+} may also be explained in terms of an oxidation-induced enhancement in receptor efficacy.
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The Fetal Sound Environment of Sheep

Abstract. *Hydrophones implanted inside the intact amniotic sac recorded sounds available to fetal lambs. Unlike recordings made from outside the intact amnion in human subjects, sounds produced at levels similar to normal conversation from outside the ewe were picked up without masking by maternal cardiovascular sounds. Noises from inside the mother were intermittent and linked to her activity.*

In contrast to the rich and varied sound experience of birds before hatching (*1*), the predominating sounds available to the mammalian fetus are thought to come from the maternal cardiovascular system (*2–6*). These sounds are reported to be loud, 68 to 95 dB (*2, 3, 6, 7*); of low frequency, 20 to 700 Hz (*3, 4, 6*); in time with the maternal pulse (*2–4, 6*); and to provide a basis for prenatal conditioning (*5*). There is thought to be considerable attenuation of sounds arising from outside the mother, such attenuation varying from 19 to 90 dB (*2, 3, 6*). These results imply that fetal experience of sound is limited.

In one previous experiment (*7*), recordings were made from a hydrophone sutured to the outside of the uterine wall of a goat; most observations, however, have been made by inserting microphones into the uterine cavity (*3, 4, 6*) or against the cervix (*2*) of pregnant human subjects at term, before or after rupture of the fetal membranes, but never inside the intact amniotic sac. Therefore, sounds available to the fetus within the intact amnion have not, to our knowledge, been observed.

Through the use of hydrophones inside the amniotic sac of pregnant ewes, in the normal fluid environment of the fetus, we have found that the sounds of the mother's eating, drinking, rumination, breathing, and muscular movement were discernible, as also were sounds from outside the mother; external sounds were attenuated by 30 dB on average. Sounds from the maternal cardiovascular system were not perceptible, however.

Recordings were made within the amniotic sacs of two pregnant ewes. A hydrophone (Celesco LC-10) was sutured to the neck of the fetus on about day 120 of gestation. The ewes recovered rapidly from the implantation, behaved normally, and fed well. Neither animal had been shorn, although each had been shaved over the abdominal area before the operation.

For sounds generated from outside the ewe, attenuation was measured in two ways. First, a 100-mm loudspeaker was strapped to the shaven area of the ewe's flank, but separated from the skin by an annulus of foam rubber. The loudspeaker relayed patterned sound (bleats) from a tape recorder, and the sounds were then picked up by the implanted hydrophone and fed directly to a narrow band spectrum analyzer (Brüel and Kjaer No. 2031). The sound level outside the animal was measured with a probe microphone (Sennheiser), the tip of which was inserted between the loudspeaker and the skin. The output of this microphone was also fed directly to the spectrum analyzer. As the hydrophone and microphone systems were of equal sensitivity, attenuation could be measured by comparing the level of corresponding peaks from the record.

According to a second method, pure tones from a function generator were amplified and relayed by a loudspeaker about $1^1/_2$ m from and facing the sheep. The sound level outside the sheep's flank was measured by a sound level meter (Dawe) through the use of the "C" weighting. This level was then compared with that registered by the spectrum analyzer from the implanted hydrophone.

These two methods gave similar results (Fig. 1). Attenuation reached a maximum of 37 dB just below 1 kHz, but

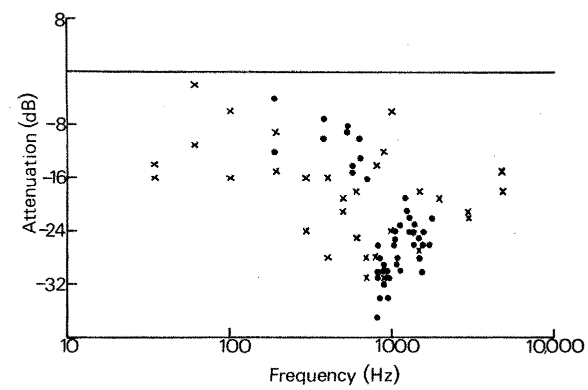

Fig. 1. Attentuation of sounds from outside the ewe. ×, Pure tones; ●, bleats.

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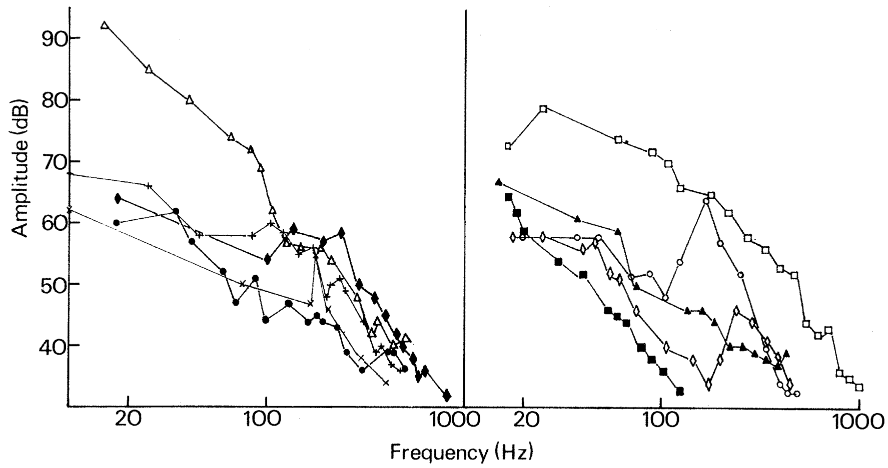

Fig. 2. Root mean square values at peaks from spectrum analyses for different types of internal sound: ○, gurgle; ●, swallow; △, blowing; ▲, chewing cud; □, rushing noise; ■, quiet ewe; ×, intestinal noise; +, eating hay; ◇, drinking; ◆, eating nuts.

it was reduced below and above this frequency and at higher frequencies remained at about 20 dB up to the highest recorded, 5 kHz. The amount of attenuation fluctuated, however: conversation at normal levels outside the animal could often, but not always, be understood when transmitted from inside. Raised voices were almost always distinct.

Sounds generated within the ewe herself were picked up by the implanted hydrophone, amplified, and recorded by a tape recorder or fed directly to the spectrum analyzer (as the amplifier had two outputs we were able to listen while analyzing the sounds). In the main, sounds heard were characteristic and identifiable: drinking, eating, swallowing, rumination, and sometimes heavy breathing could be heard. Rumination, unexpectedly, was rather quiet. A rushing sound sometimes accompanied movement by the ewe and irregular gurgles, probably of digestive origin, occurred frequently. Periods of quiet were not unusual. Figure 2 shows root mean square values at peaks taken from spectrum analyses, for different types of internal sound. These were of low frequency, tailing off above 500 Hz.

Although we found attenuation of external sounds to be less than in other species (*2, 3, 6*), the loudness peaks and frequency of internal sounds were similar to those recorded by others (*3, 6*). However, average sound levels were lower than those previously reported (*2, 3, 6, 7*), especially as we often observed periods of quiet. In one particular our results were at variance with those of other workers: we were not able to hear sounds from the maternal cardiovascular system. By holding a hydrophone firmly against the ewe's skin in the brachial area we were able to pick up heart sounds from outside the animal without being able to hear the reported pulsations from inside. It is possible, and consistent with spectrum analyses, that these sounds occur at very low frequencies and, when attenuated, are below the human threshold for sound.

Our results suggest that sounds available to the sheep fetus, within its normal fluid environment, are varied and of rather low frequency when they are generated by, or within, the mother. External sounds are attenuated by about 16 to 37 dB, most attenuation occurring at frequencies around 1 kHz. In the sheep, external sounds of above 65 dB at the body wall should often penetrate to the uterus.

The extent to which sound signals inside the amniotic sac are heard by the fetus is another question currently being explored; in precocial mammals, the auditory system is believed to become functional well before birth, and there is evidence for this in the sheep after day 100 of gestation (*8, 9*). A further question concerns the efficiency of the hearing mechanism within a totally fluid environment; the mammalian fetus is known to move in response to sound from outside the mother (*10*), and in the guinea pig, prenatal exposure to a specific sound changes the neonate's response to the sound (*11*).

Implications for the human fetus are not clear because of postural, placental, and other anatomical differences. The main difference between results of research with the goat (*7*) and ours can be attributed to our use of a method of greater physiological validity, namely, recording from inside the intact amnion in the fetus's normal fluid environment. We suggest that the auditory experience of the fetal mammal may be considerably more extensive, more varied, and, as in birds, possibly of greater postnatal significance than has been believed.

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Of Human Bonding: Newborns Prefer Their Mothers' Voices

Abstract. *By sucking on a nonnutritive nipple in different ways, a newborn human could produce either its mother's voice or the voice of another female. Infants learned how to produce the mother's voice and produced it more often than the other voice. The neonate's preference for the maternal voice suggests that the period shortly after birth may be important for initiating infant bonding to the mother.*

Human responsiveness to sound begins in the third trimester of life and by birth reaches sophisticated levels (*1*), especially with respect to speech (*2*). Early auditory competency probably subserves a variety of developmental functions such as language acquisition (*1, 3*) and mother-infant bonding (*4, 5*). Mother-infant bonding would best be served by (and may even require) the ability of a newborn to discriminate its mother's voice from that of other females. However, evidence for differential sensitivity to or discrimination of the maternal voice is available only for older infants for whom the bonding process is well advanced (*6*). Therefore, the role of maternal voice discrimination in formation of the mother-infant bond is unclear. If the newborn's sensitivities to