

Review

Prenatal Auditory Stimulation and Its Significance for Newborns

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The ability to recognize and process auditory stimuli plays a central role in human development, especially during the prenatal phase when the auditory system takes shape. Around the 27th week of pregnancy, the fetus becomes able to hear, initiating a complex process of auditory development.^[1]

The prenatal acoustic environment is characterized by a variety of internal and external sounds that contribute to the intrauterine auditory experience of the fetus.^[2] This scientific work explores the fascinating world of the detection of different sounds in the womb and sheds light on the mechanisms by which the fetus perceives and responds to acoustic stimuli. Comprehending these processes holds significance as they form the basis for sensory, language, and musical development in the later stages of life.^[3] Furthermore, studying the effects of pre- and postnatal sound exposure helps to identify potential developmental risks and implement necessary interventions for optimal fetal development.^[1]

We address various aspects of developmental biology and investigate how the brain structures and neural connections of the fetus develop during pregnancy, paving the way for auditory processing ability.^[4] In addition, we are investigating the influence

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ABSTRACT

Around the 27th week of pregnancy, the fetus begins to hear, initiating a complex auditory development process. The prenatal auditory environment involves internal and external sounds that shape the fetus's experience. Internally, sounds like the mother's heartbeat, breathing, and digestion create a complex auditory environment. Externally, the fetus perceives sounds such as the mother's voice, environmental noises, and music, with lower frequencies being better transmitted. Fetal responses to sounds are evidenced by physiological changes like heart rate variations and movements. Prenatal and postnatal sound exposure significantly impact auditory development. Loud sounds during pregnancy can strain the auditory system and potentially lead to hearing issues. Maintaining a low-noise environment in neonatal intensive care units is crucial for healthy hearing development in premature infants. Prenatal experiences greatly influence sensory, linguistic, and musical development. Developmental biology plays a vital role in auditory advancement. The prenatal environment and genetics impact deoxyribonucleic acid methylation, an epigenetic mechanism governing gene expression. Auditory structures and brain regions mature during pregnancy and infancy, with peripheral activities aiding subcortical circuits and functional maturation. Restricted fetal growth might lead to delayed auditory brain responses, serving as potential markers for developmental disorders. This review emphasizes the critical importance of detecting and processing auditory stimuli throughout human development, particularly prenatal.

Keywords: Auditory processing, auditory stimuli, fetal hearing, intrauterine auditory experience, postnatal sound exposure, prenatal acoustic environment

of environmental factors and genetics, which can affect deoxyribonucleic acid (DNA) methylation patterns and influence individual differences in neonatal development.^[5] Researchers have observed that the fetus responds to various acoustic stimuli, showing different physiological responses, such as changes in heart rate, respiratory activity, and even fetal movements (FM). Understanding these responses and how they relate to the neurological and sensory development of the fetus provides

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valuable insights into the overall well-being of the unborn child. $^{\scriptscriptstyle [6\mathchar]}$

This review seeks to unravel the intricacies of recognizing different sounds in the fetal environment. By exploring the effects of pre- and postnatal sound exposure, sensory, language, and musical development, and various aspects of developmental biology, we aim to contribute to a deeper understanding of human hearing development before birth. This knowledge has the potential to pave the way for improved prenatal care and interventions to promote healthy auditory processing and overall fetal development.

RECOGNIZING DIFFERENT SOUNDS

In humans, fetal hearing becomes possible shortly after the onset of auditory development in the 27th week of pregnancy (gestational age), when external sounds begin to reorganize the auditory cortex.^[1] The earliest detectable responses to auditory stimuli, called surface-negative auditory evoked potentials, occur between the 36th and 40th week of gestation and continue long after birth. These potentials show that the fetus already reacts to acoustic stimuli before birth and that these reactions continue to be detectable after pregnancy.^[9] During the prenatal phase, the acoustic environment is characterized by background noises with a level of about 30 dB(A). The primary sources of acoustic stimulation are endogenous sounds that originate within the maternal body. External sounds, on the other hand, are strongly attenuated, the exact attenuation depending on the spectral characteristics. Interestingly, the mother's voice is less attenuated, and some frequencies are even amplified.^[2]

The specifics and new insights into the exposure of the fetus to internal and external noise are usually investigated through studies using a sheep model. Sheep are commonly selected as model organisms due to their physiological traits, which resemble those of humans, particularly in terms of sound transmission and reproductive system development. The researchers quantify the transmission of sound waves through the tissues and fluids in the womb across the entire human hearing range. This examines how well sound is transmitted to the fetus and the extent to which the fetus is exposed to external noise.^[7] Scientists have found surprising results in their experiments. The aim of the study is to determine what or how much the fetus actually hears. To do this, they implanted an electronic pickup in the inner ear of a fetal sheep. The intelligibility of the tones and

sounds was higher than expected. The reason for this assumption is that external sounds are usually interrupted by the internal sound environment in the womb. In addition, noise is more likely to be transmitted to your inner ear through vibrations in your skull. This explains why the mother's voice tends to be the most dominant and recurring sound in the womb. Another reason is that her ears are filled with water. Nevertheless, good and clear sound recordings were recorded. The study on the transmission of sound waves in the womb and the potential exposure of the fetus to external noise provides good data to

further investigate auditory development.^[10]

Internal Sounds

It is by no means quiet in the womb. To gain insight into the acoustic environment fetuses are exposed to during development, Parga et al.[11] examined externally recorded sounds from the womb in human subjects during pregnancy. To collect data, researchers recorded sounds from the womb of test subjects at different stages of pregnancy. The team used specialized equipment to record and analyze the sounds. The results of the study revealed several interesting observations. The researchers identified a range of sounds in the womb. The primary causes of internal murmurs in the womb are mainly cardiovascular, respiratory, and intestinal in the mother. These sounds are produced by the rhythmic beating of the mother's heart, the mother's respiratory movements, and the activity of the digestive system. Together they create a complex soundscape that surrounds the fetus and is part of its intrauterine auditory experience.^[6] However, the perception of the sounds changes in the course of pregnancy. Researchers revealed that the acoustic properties of womb sounds change during pregnancy. The volume and intensity of the sounds seemed to increase as the pregnancy progressed. This suggests that the acoustic environment for the fetus is dynamic and changes with growth and development.^[11]

External Sounds

In addition to internal sounds, external sounds such as the mother's voice, environmental sounds, and even music were occasionally recorded. This shows that fetuses can already come into contact with sounds from the outside world in the womb.^[11] The mother's voice has a special meaning for newborn babies, as they tend to pay more attention to it than to foreign voices. They recognize their mother's voice and even adjust their behavior to favor her. The ability to recognize voice, plays an important role in the development of the mother-child relationship.^[8]

Lower-frequency vowels have a greater ability to penetrate the inner ear. Human fetuses tend to show increased sensitivity to low-frequency sounds, making them more receptive to such sounds than to higher-frequency ones. Consequently, they prefer vowels to consonants and show greater sensitivity to the melodic components of speech than to the pitch of sounds.^[10] Another point made is that high-pitched sounds are muffled in the uterus.^[1] The uterus protects the fetus from excessive noise exposure and regulates the level of sound that reaches it. This allows for optimal development of the auditory system as the fetus grows in the womb. Even under extreme conditions, such as a rock concert, the noise level in the womb would probably not be high enough to jeopardize the hearing development of the fetus.^[10]

Overall, the uterus provides a protective environment for the hearing development of the fetus. While external sounds are muffled, the prenatal sound environment still allows for adequate stimulation of the auditory system to promote healthy development.

Fetal Reactions to the Sounds

In the third trimester of pregnancy, hearing begins to develop progressively. The fetus becomes more sensitive to sounds and can perceive subtle differences in sound lengths. This phenomenon likely stems from the ongoing development of the fetus' auditory system and its progressing aptitude for sound perception. From the 22nd week of pregnancy, the fetus becomes increasingly active, and modern studies using three-dimensional ultrasound have shown that the complexity of both FM and behavior increases as the pregnancy progresses. It is fascinating to observe how the fetus moves more and more from this point on and how its behavior becomes more diverse. The reactions of the fetus to very loud noises have been noted from the 26th week of pregnancy. It seems that the fetus is able to react to strong acoustic stimuli and possibly respond with movements or other behaviors.^[9]

Research has shown that the mother's voice can cause a heart rate acceleration in fetuses. In contrast, the voice of a stranger has been found to cause a heart rate slowdown in fetuses. This response indicates that the fetus is able to distinguish between its mother's voice and a stranger's voice and respond to these differences with physiological changes.^[2] All cases studied showed an increased fetal heart rate (FHR) after sound stimulation at a volume of 70 dB compared to the situation before stimulation. These results indicate, as mentioned, that the fetus responds to acoustic stimuli and that sound stimulation leads to a change in heart rate.^[12] With regard to fetal responses to acoustic stimuli, it is important to introduce further terminology. In addition to FHR, FM is a term used to describe fetal responses to acoustic stimulation. The vibroacoustic stimuli (VAS) are stimuli to identify the acidotic fetus. The fetal heart rate response to VAS provides information about the condition of the fetus and can help to potentially identify potential health problems. Similarly, observation of FM can serve as an indication of the neurological development and well-being of the fetus. These findings emphasize the importance of the VAS as a diagnostic tool in prenatal medicine. When the fetus is repeatedly exposed to the same stimulus, habituation can be detected. Habituation refers to the process by which the fetus' response to the stimulus gradually decreases and eventually ceases when the stimulus is repeatedly presented. By monitoring FM and FHR responses and considering habituation to repeated stimulation, healthcare professionals can gain valuable insight to assess the health of the fetus and take appropriate action if needed.[13]

Observation of FHR acceleration in response to acoustic stimuli is an important diagnostic procedure to identify potential hearing difficulties in the fetus. In the absence of a normal response to sound, there is an increased risk of hearing loss or deafness in the newborn. Early diagnosis of prenatal deafness allows timely action to be taken for treatment, even before newborn hearing screening is performed.[12] Also of importance is the examination of fetal respiratory activity to assess the well-being and development of the fetus. In this case, a special stimulation with an artificial larynx was performed to test the reaction of the fetus. This stimulation was found to have immediate effects on respiratory activity. Changes in fetal respiratory activity were only observed in fetuses between 36 and 40 weeks of age. After stimulation, an immediate decrease in the frequency of fetal respiratory movements was observed. The decrease in respiratory movements after stimulation indicates that the fetus responds to the stimulus and temporarily changes its respiratory pattern. In addition, the breathing activity remained irregular for a period of up to one hour. This again indicates that the fetus needs time to recover from the stimulation and restore its normal breathing rate.^[6] In addition to the acceleration of the heart rate, the fetus reacts to the sound of the mother's voice in the last weeks

of pregnancy (from 36 weeks) with reflexive body movements and head turns.^[9] Another study, in the context of observations of auditory stimulation in the womb, looks at whether fetuses move their lips to the sounds they perceive. The researchers observed that fetal mouth movement tended to occur more frequently when sounds were presented to the fetuses. This suggests that fetuses may be able to respond to acoustic stimuli in the womb by moving their lips.^[14]

COMPARISON: EFFECT OF PRE- AND POSTNATAL EXPOSURE TO SOUNDS

In the womb, the fetus is protected by various mechanisms to minimize exposure to high-pitched sounds and other stimuli. One of these protective mechanisms is that sound is absorbed into the tissues and fluid around the fetus. This absorption process plays an important role in ensuring that the acoustic environment in utero does not become too loud or overwhelming for the fetus.^[3]

The prenatal listening environment is crucial for the development of the fetus and can have longterm effects on the hearing system. Exposure to loud noises during pregnancy, such as those encountered in noisy workplaces, can lead to excessive stimulation and stress on the developing auditory system. This can lead to impaired neural connections and possible hearing impairment later in life. Premature infants, especially those in neonatal intensive care units (NICUs), are particularly vulnerable to the negative effects of the prenatal noise environment. These environments often have high noise levels from medical equipment and staff conversations, which can put additional stress on premature babies' sensitive hearing systems and hinder their development. Therefore, it is important to create a conducive and low-noise environment for the development of the fetus and newborn.^[1]

From the 26th week of pregnancy, intense noise can cause a variety of physiological changes in fetuses. These include an adjustment in heart rate, blood pressure, respiratory rate as well and oxygen supply. There is also the possibility that noise affects sleep patterns. Excessive noise can also have a detrimental effect on neurological development, the neuroendocrine system, and the immune system of the fetus. Research in animals has shown that repeated exposure to high-frequency sounds can have significant effects on the formation of neural connections and structural and functional changes in the central auditory nervous system.^[15]

Premature birth can accelerate the maturation of some vital organ systems such as the intestines, gastrointestinal tract, lungs, and cardiovascular system. However, the order or timing of neurological developmentis not altered. Neurological development continues to follow a specific genetically determined program. While the basic physical structure of sensory receptors such as eyes and ears develops early in pregnancy, the crucial phase of neurosensory development occurs mainly in the last 16-20 weeks of pregnancy.^[3]

The recommendations for NICUs were updated in 2007 by the American Academy of Pediatrics. According to these standards, the maximum noise level inside the room but outside the incubator should be less than 45 dBA. An earlier study showed that sounds generated in the womb, such as maternal breathing or bowel activity, reach only 50 dB above 200 Hz (equivalent to 40 dBA) in the absence of external noise. This confirms the relevance of these recommendations. In one study, both the noise level generated by the delivery pump and the noise level recorded outside the incubator were measured. These are in the range of 55-63 dBA, which is above the recommended standards. In addition, the alarm triggered is a high-frequency sound with a frequency of 2450 Hz.[15]

In current research, it is possible to replicate the acoustic environment of the uterus and its variability using laboratory facilities. Replicating the auditory conditions within the uterus holds immense significance, given the constant exposure of the developing fetus to the sounds within this sheltered realm. By simulating these soundscapes, researchers can better understand the effects of sounds on the fetus and potentially take steps to promote optimal development.^[2]

Implementing this research is possible with the help of technologies such as micro-audio systems. Here, this auditory intervention, maternal sound stimulation, was installed in the infant's incubator throughout the hospital stay in the NICU. In addition, the loss of exposure effects of maternal sounds, such as the maternal voice and the heart, can be compensated for during hospitalization. These also play a major role in the development of the autonomic nervous system in preterm infants.^[16]

SENSORY, LINGUISTIC, AND MUSICAL DEVELOPMENT

The current state of research provides expanded knowledge about early sensory processing in newborns. Studies show how newborns perceive and process different sensory stimuli, such as auditory stimuli. The results of this research report that newborns are able to recognize and learn multimodal sensory stimuli. The cortical processing of these stimuli shows specific activation in the sensory regions of the brain involved.^[17]

The cores and pathways of the brainstem exhibit remarkable synaptic plasticity, which means that they are receptive to external auditory experiences and are capable of synaptic learning. This means that repeated auditory stimulation, or the lack of it, causes these networks and pathways to form and respond, selectively to the stimuli that have shaped them. In other words, the brain structures responsible for hearing can adapt and learn by responding to repeated auditory stimuli or to those that are absent. This capacity for synaptic plasticity plays an important role in the development of hearing and the processing of sounds.^[9] In this context, there is a study by scientists that focuses on the question of whether infants have the ability to perceive and learn embeddings. Embeddings refer to the ability to recognize and process complex relationships between elements of a sequence or hierarchy. They investigate this using experimental paradigms in which infants are exposed, for example, to auditory stimuli that have an embedding structure. The study shows that infants are indeed able to encode and learn embeddings. They can recognize and process complex relationships between elements of a sequence. This capability is deemed potentially distinctively human, as it demands cognitive exertion surpassing mere associations and holds a pivotal function in fostering language development, rule acquisition, and cognitive adaptability.^[18]

Exposure of the fetus to melodic sound patterns can form neural representations that persist over a period of several months. The effects of prenatal exposure without additional stimulation show a minimum duration of four months.^[1] This is also confirmed by other studies on the effect of environmental language on the cry of the newborn. Studies have shown that newborns and infants have a preference for the language of their environment and are able to distinguish between different languages. Even infants' vocalizations are influenced by the acoustic features of the surrounding language. Researchers have found from a detailed acoustic analysis of cry melody patterns that newborns not only learn the characteristic variations of their mother tongue but also seem to be able to reproduce them in their own vocal production.^[19]

Already in the prenatal stage, certain brain regions are active and can react to auditory stimuli, especially speech. This indicates that the brain of the fetus is already prepared for language processing before birth. The development of primordial linguistic networks is the basic element for later language processing. The prenatal environment and exposure to language play an important role in the development of the brain in relation to language processing.^[20] For example, another study shows that the brain is particularly adaptable and plastic in the early stages of life. Prenatal experiences, such as hearing the mother's voice, can influence brain development and linguistic abilities.^[21]

Changes in the processing of complex sounds such as music also show that the hearing system of the fetus develops and adapts during pregnancy. At 33 weeks of pregnancy, an interesting change in the way fetuses process complex sounds such as music was noted. However, in younger fetuses, their response to music tends to be limited to basic acoustic properties, such as pitch, rhythm, and volume.In contrast, in older fetuses, attention plays a greater role. This suggests that they are beginning to respond consciously to musical stimuli and may have developed some form of perception and processing beyond simply reacting to the acoustic properties.^[9]

Ullal-Gupta et al.^[22] investigate the relationship between prenatal experiences and the development of musical understanding in infants. They investigate how prenatal experiences can influence the brain of the fetus and have long-term effects on musical development. The study shows that infants who were repeatedly exposed to musical sounds in the womb show increased attention to musical stimuli after birth. This suggests that prenatal experiences can influence the neural processing of music. They suggest that targeted exposure to musical sounds during pregnancy may have positive effects on infants' musical perception and preferences.

ASPECTS OF DEVELOPMENTAL BIOLOGY

For development in the womb, all sensory systems except vision require external influences or exogenous factors.^[3] Thus, the prenatal environment and genotype have a significant influence on the individual variation of DNA methylation in newborns, an epigenetic mechanism that regulates gene expression. The results show that certain genetic variants are associated with different patterns of DNA methylation. In addition, the findings show that environmental factors during prenatal development may also be associated with changes in DNA methylation. These findings provide an understanding of individual variation in neonatal development and health. They suggest that both genetic and environmental factors should be considered to understand the complex interaction between genotype and environment in the development of phenotypes.^[5]

In studies of the effects of the acoustic environment on the fetus and its physiological responses, scientists find that the primary pathway by which the fetus perceives sound is through vibrations in the tissues of the mother and the fetus itself. These vibrations are then interpreted as sound waves. When the fetus responds to sound, changes in behavior, blood flow, auditory nerve response, and pupillary response along the auditory pathway are evident. For the fetus to perceive an acoustic stimulus from outside the womb, certain conditions must be met. First, the inner ear (cochlea) and the nerve pathways must be functional. In the human fetus, this generally happens at the beginning of the third trimester.^[6] This means that the basic structural components of the inner ear are already present from the 15th week of pregnancy. However, the function of the cochlea, also the hearing organ, only becomes effective after the 24th week of pregnancy.[15] The stimulus must have energy in frequency bands that are above the background noise in the same frequency range. The intensity of the external stimulus must be strong enough to produce sufficient sound pressure to penetrate the uterus. The energy at the head of the fetus must then lead to mechanical movements of the basilar membrane in the organ of Corti to activate the hair cells and the associated sensory neurons.^[6]

The findings can be explained by the tonotopic organization of the cochlear nuclei and the maturation of the brainstem during pregnancy. At the time of birth, the subcortical brain structures are well-matured, with high activity in the primary cortex areas and lower activity in the association areas.^[9]

Studies on the development of the auditory cortex are recorded in the perinatal period. This period covers the time before and after birth and is crucial for the development of the auditory system and the formation of auditory processing skills. Research has shown that the primary auditory cortex shows advanced maturation before birth, while the non-primary auditory cortex takes a longer time to fully develop. The primary auditory cortex is responsible for processing basic auditory information, whereas the non-primary auditory cortex performs more complex auditory processing functions. This is being investigated using imaging techniques such as magnetic resonance imaging and diffusion tensor imaging.^[4]

The development of the brain and the specialization of different brain areas are dynamic processes that take place continuously. During pregnancy, neurons are formed and eliminated, and complex neuronal connections are formed. Especially during this time, neuronal connections in the brain are highly variable. To study the maturation of the auditory cortex, researchers make non-invasive recordings of human auditory evoked magnetic fields with magnetoencephalography (MEG). The MEG technique makes it possible to follow the development of auditory responses both in the womb and in newborns. In a longitudinal study using MEG, an age-related shortening of reaction time was found in fetuses and newborns. This means that the latency decreases between the 29th week of pregnancy and a few weeks after birth. This gradual decrease clearly indicates a continuous further development of the auditory system and the associated brain processes.^[23]

Focusing on the early development of the auditory system, analysis reveals that early peripheral activity plays a significant role in shaping the subcortical circuits in the auditory cortex. Experiments with mice show that a change in peripheral activity leads to structural and functional changes in the subcortical circuits. This suggests that peripheral activity plays an important role in shaping the neural connections and functional maturation of the auditory system.^[24,25]

In view of the topic of brain development, further considerations about growth restrictions should also be taken into account. The study of fetal growth restriction and its effects on the development of auditory brain responses also uses MEG to measure electrical activity in the fetus's brain. Studies show that in fetuses with growth restriction, there is a delay in the maturation of auditory brain responses. This is evident from the MEG recordings, which show a delayed and attenuated response to auditory stimuli. The clinical relevance of these findings should be emphasized, as the delay in auditory maturation could be a potential marker for fetal developmental disorders. Early identification of such changes may lead to improved prenatal diagnosis and treatment.^[26]

In conclusion, future research should further investigate the mechanisms of auditory development during the prenatal period to gain a comprehensive understanding of how the fetus perceives and responds to sounds. Advanced technologies such as 3D ultrasound and MEG could help to further detail and analyze the physiological responses of the fetus to acoustic stimuli. Furthermore, future studies should examine more closely the long-term effects of prenatal sound exposure on the hearing development and behavior of newborns and infants. A special focus should be placed on premature infants in NICUs in order to develop appropriate intervention measures to promote healthy hearing development. Research into the neurobiological basis of auditory processing during pregnancy and after birth should be continued to gain insights into the development and maturation of the auditory system. New imaging techniques and neuroscientific approaches could help to better understand the links between the maturation of brain structures and the development of auditory skills. In addition, the importance of prenatal experiences for sensory, linguistic, and musical development should be further investigated. Long-term studies could show how prenatal representations influence children's behavior, skills, and abilities later in life. Integrating genetic and environmental factors into research on DNA methylation and its influence on hearing development may help to better understand individual variation in neonatal growth and identify possible prenatal risk factors. Overall, research into the processing of sounds in the womb and its effects on babies should continue to advance in order to recognize the importance of the prenatal environment for healthy hearing development and to develop appropriate interventions to promote auditory processing and overall fetal growth. This knowledge could help improve prenatal care and promote the well-being and development of the unborn child. In summary, research on the processing of sounds in the womb and their effects on babies has already provided important insights, but there are still many open questions that need to be further investigated. Clinically relevant data on the cognitive functions of the fetus may be of importance in the treatment of fetal pain, in the care of premature births, but also to improve the further neurobiological development of the fetus in high-risk pregnancies. After all, brain development, including cognitive functions, continues just as rapidly in the postnatal period as before.

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