The influence of noise on blood flow in the basilar artery (BA) – measurements with transcranial color-coded duplex sonography (TCCD)

J. Zenk [a,*], D. Scheffler [a], P. Scheffler [b], W. Delb [a], H. Iro [a]

[a] *Department of Otorhinolaryngology – Head and Neck Surgery, Saarland University, D-66424 Homburg, Germany*
[b] *Department of Cardiology and Angiology, Saarland University, Homburg, Germany*

1. Introduction

Both its anatomic topography and its vulnerability complicate the direct examination of the inner ear. Laser Doppler flowmetry is the current method used which is only to a minor degree invasive and which allows measurement of changes in the cochlear blood flow even for humans (Miller et al., 1995).

At present, mainly two hypotheses on the generation of cochlear damage are discussed. To a large extent, both are based on findings from animal experiments:

1. A direct effect of traumatic factors in the cochlea, causing structural damage to the organ of Corti, can lead to acute hearing loss or impaired hearing (Libermann and Mulroy, 1983).
2. An overuse of metabolically dependent processes in the inner ear. One suggested mechanism for this is the generation of reactive oxygen species (ROS) in the cochlea, based on reports that cochlea blood flow is affected during intense sound exposure and that ROS are generated in response to prolonged hypoxia followed by reperfusion (Yamasoba et al., 1999).

Especially for the second mechanism, blood circulation in the cochlea is of essential importance.

Taking this mechanism into account, the study of cochlear microcirculation has a long history and different direct techniques have been applied to date (Sillman et al., 1988):

1. Intravital microscopy: this allows visualization of the major vascular beds of the lateral wall and the

* Corresponding author. Present address: Department of Otorhinolaryngology, Head and Neck Surgery, University of Erlangen-Nuremberg, Waldstr. 1, D-91054 Erlangen, Germany.
Tel.: +49 (9131) 853 3156; Fax: +49 (9131) 853 6857.

basilar membrane in living animals, but it is an invasive technique (Weille et al., 1954).
2. Microsphere measurement (Angelborg et al., 1977): this allows the evaluation of regional as well as whole organ blood flow in combination with histology in animals.
3. Laser Doppler flowmetry: this relatively non-invasive procedure provides real time assessment of cochlear blood flow (CBF) in animals and patients. The disadvantages are that the blood vessels cannot be specified during the measurement and that it is not possible to provide a physical reference (Miller et al., 1983).

Indirect measurements related to CBF include measurements of oxygen tension in animals and humans, of perilymph production and of hydrogen clearance (Thorne and Nuttall, 1989).

It has been reported that visual stimulation can evoke a reflex-like response in specific vessels supplying the visual cortex (Aaslid, 1987; Sturzenegger, 1996; Gomez et al., 1990). It was demonstrated that this also has an effect on the hemodynamics in the areas perfused by these vessels (Niehaus, 1994; Mueck-Weymann and Schweitzer, 1996).

Similar to this, noise can induce a decrease in the flow velocity detectable in the basilar artery (BA) and hence an increase in resistance in its circulation area (Schweitzer et al., 1996).

It is well known that high intensities of sound exposure lead to temporary or permanent threshold shifts through hypoxia and following generation of ROS. Therefore the aim of this study was to investigate the degree of changes in the BA blood flow and resistance during noise exposure. On the one hand previously published data (Mueck-Weymann and Schweitzer, 1996) was to be scrutinized. On the other hand the issue whether changes in resistance of the BA could be suggestive to changes in CBF and/or in higher centers of the auditory pathway should be discussed.

The examination of the BA through a nuchal window by means of transcranial color-coded Doppler sonography (TCCD) is a routine examination in humans and can be carried out non-invasively (Fig. 1).

The inner ear is supplied with blood by the BA via the anterior inferior cerebellar artery (AICA) and the labyrinthine artery (66%) or directly via the labyrinthine artery (33%) (Palchun et al., 1992). According to current literature (Ren et al., 1993), approximately 45% of the blood flow in the cochlea of guinea pigs originates from these vessels. But the proportion of the BA flow volume supplied to either the AICA or the labyrinthine artery is not known. The BA supplies not only the cochlea but also higher neuronal centers related to hearing. Furthermore, there is a variable connection to the arterial circle of Willis with participation in blood flow of cortical area 43 together with the medial cerebral artery.

The resistance in the BA – measured by duplex sonography – is a measure of the overall resistance of the flow area which is supplied by this vessel. A change in resistance or blood flow in this artery can be caused by changes in only one or in multiple areas of blood supply. In the case of CBF, only very small changes would be detectable in the BA, if at all.

2. Materials and methods

2.1. Transcranial color-coded duplex sonography and noise stimulation

TCCD was performed using the instrument version Ultramark 9 HDI supplied by Advanced Technology Laboratories. The implemented transcranial probe was a 20 mm phased-array (P3-2) model from the same supplier, with an operating frequency of 2–2.5 MHz and a Doppler frequency of 2 MHz. The system was equipped with an additional video documentation unit which allowed all cardiac cycles relevant to the period of investigation to be evaluated later.

Pink noise was applied to the subjects through fully sound-insulated headphones. The unit, which comprised a CD player, amplifier and headphone, was calibrated for the noise levels to be applied using an artificial ear.

Blood pressure and pulse rate were monitored at closely spaced time intervals (1/min) and recorded.

2.2. Subjects

Twenty volunteers aged 15–35 (14 male, 6 female) were selected. All of them were healthy and were not under the influence of any medication at the time of the investigation. Through the use of a pure tone audiogram, no hearing loss was found to exist before, or to have been incurred directly after the investigation had been carried out. On the day of the investigation and immediately before the tests the subjects were not allowed to smoke, to consume coffee or alcohol, or to do any type of physical exercise.

2.3. Measurements

The investigations were conducted in a quiet and darkened room. Acoustic stimulation was performed – with the subjects in the ventral position – from dorsal via the transnuchal (transoccipital) access to the basilar artery (Fig. 1) with the head maintained in a maximally anteclined position. To make the investigation as com-

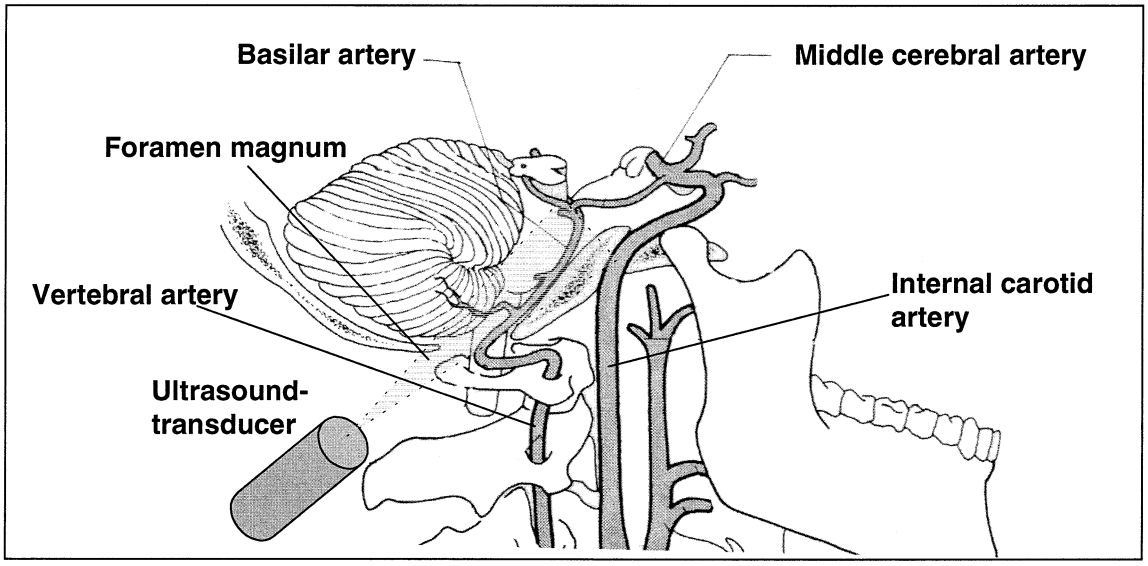

Fig. 1. Anatomy of the vertebral arteries and BA during transcranial Doppler sonography with the transoccipital approach through the foramen magnum (modified from Widder, 1995).

fortable as possible for the subject and the investigator, the position of the subject, and especially that of his head, was individually adapted using exchangeable padding. During measurement the subjects wore the sound-insulated headphones. The eyes of the subjects had to be kept closed during the tests to exclude artifacts caused by visual stimuli.

During measurements the BA was probed for through the foramen magnum. It could be visualized in the posterior cranial fossa at a depth of 60–90 mm as the confluence of the vertebral arteries (Becker et al., 1993) and could be readily identified in the color-coded duplex image (Fig. 2).

The BA together with the two vertebral arteries form

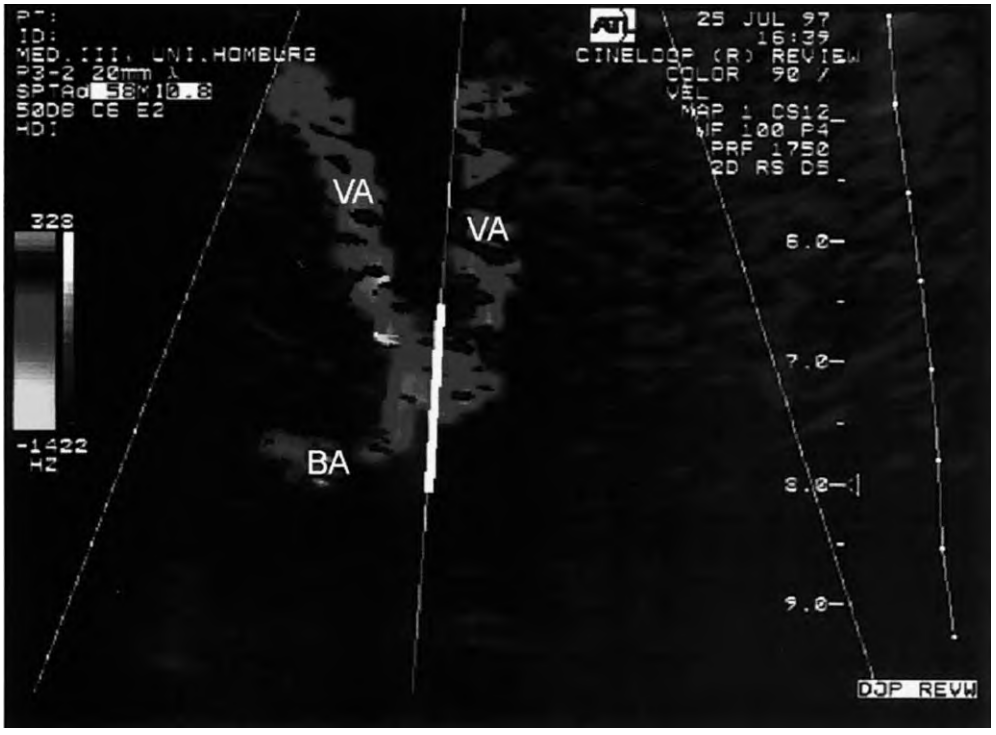

Fig. 2. Representation of the characteristic 'Y'-shaped junction formed by the BA and the vertebral arteries (VA) in TCCD. The Doppler volume has been placed in maximum size directly above the confluence of the vertebral arteries into the basilar artery (image in black and white).

a very prominent vascular junction which appears as a 'Y' in the color image. The lowest lying branch represents the BA. Aided by the color coding, the Doppler volume was placed over a preferably extended section of the vessel and the spectrum then recorded (Figs. 2 and 3).

The ultramark 9 HDI modality offers the option of automatic Doppler analysis (HighQ technique). The following parameters were determined for each cardiac cycle: systolic maximum of velocity (V_{max} syst), diastolic maximum velocity (V_{max} diast), and the time-averaged maximum velocity (TAV_{max}) for that particular cardiac cycle (Fig. 3).

From these parameters the angle-independent resistance index (RI) (Pourcelot, 1974) and pulsatility index (PI) (Gosling and King 1974) are calculated in real time according to the following formulas:

$$\text{Resistance index} = \frac{V_{max}\ \text{syst} - V_{max}\ \text{diast}}{V_{max}\ \text{syst}}$$

$$\text{Pulsatility index} = \frac{V_{max}\ \text{syst} - V_{max}\ \text{diast}}{\text{TA}V_{max}}$$

These indices provide a measure of the resistance in the vessel measured. The higher this value, the higher the resistance in the area which is supplied by this vessel. An increase in resistance occurs for example when diameters of the supplied vessels are reduced by vasoconstriction.

The values of PI and RI were displayed in the monitor together with the whole Doppler frequency spectrum for each cardiac cycle (Fig. 3).

2.4. Investigation procedure

Prior to noise exposure, the subjects had to lie in a state of rest with their eyes closed for at least 20 min. In this rest phase headphones screened the subjects against noise. During the last 2 min of the rest phase, directly before the ensuing application of noise, the Doppler spectra together with RI and PI were continuously monitored and recorded.

Then, retaining the ultrasound probe in position, sound with an intensity level of 75 dB(A) was applied via the headphones (the noise level was slowly increased over a period of 5 s so as to avoid startling the subject). The noise was discontinued after 2 min, and 1 min later the flow measurement was terminated. A rest period of 10 min followed. This measurement pattern was successively repeated in the same manner, first at 85 dB(A) and second at 95 dB(A).

The studies were performed in accordance with the guidelines of the Declaration of Helsinki.

2.5. Evaluation and statistics

The data stored on video documentation tape were reviewed at a video editing desk and the RI and PI for each cardiac cycle transferred to a chart calculation program (Microsoft EXCEL). An individual arithmetic mean was calculated for each subject for every noise level and rest period. From these values arithmetic means and simple standard deviations were derived for each measurement phase for the overall series of 20 subjects. The values for the noise phases thus obtained were then compared with those obtained from the first rest phase (base value). Significant values were

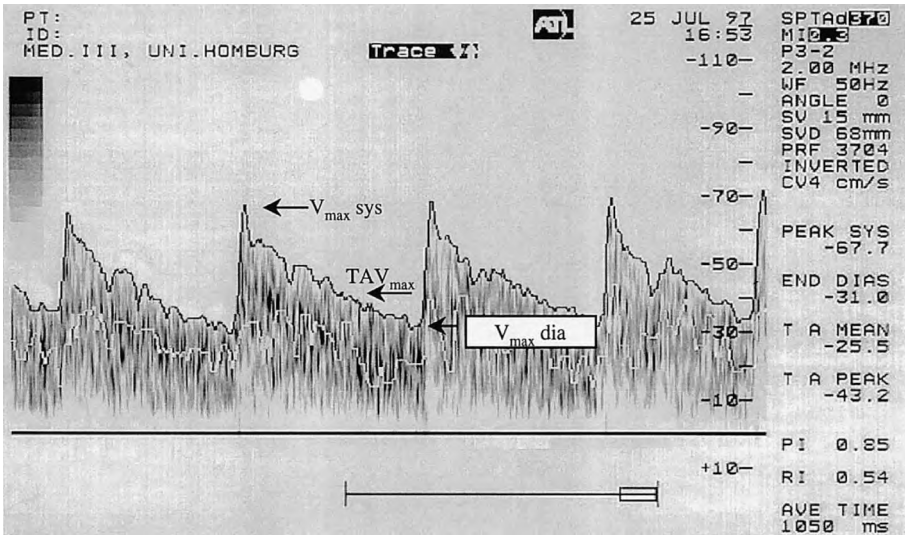

Fig. 3. Doppler spectrum of the BA. Using the maximum-flow curve the following parameters are determined for each cardiac cycle: systolic maximum (V_{max} sys), diastolic maximum (V_{max} dia) and the time averaged maximum velocity (TAV_{max}) for that particular cardiac cycle. From these parameters the angle-independent indices RI and PI are calculated and printed on the monitor (right).

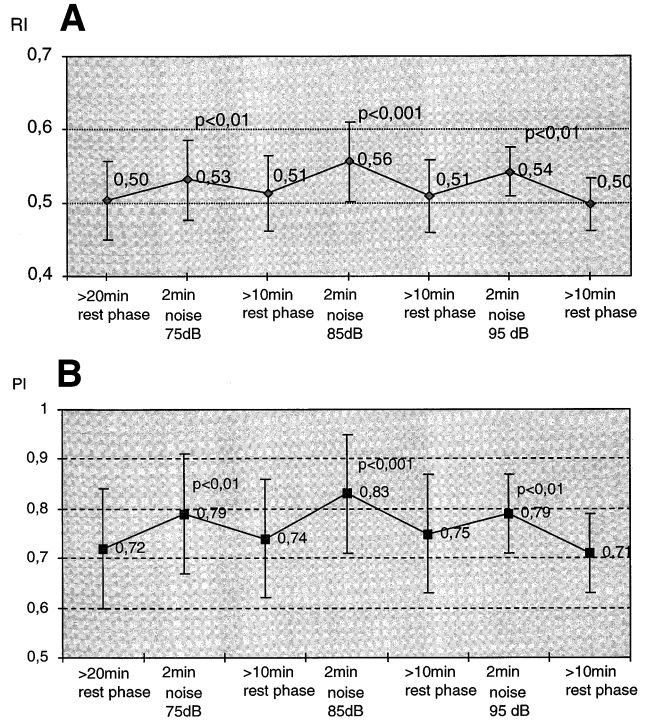

Fig. 4. (A) RI of the 20 healthy subjects during noise exposure. Noise exposure leads to a significant increase in resistance in the BA. (B) PI of the 20 healthy subjects during noise exposure. Noise exposure leads to a significant increase in resistance in the BA.

calculated according to the non-parametric Wilcoxon test using a statistical evaluation program (SPSS).

3. Results

The basilar artery could be identified and investigated by TCCD in all subjects. Blood pressure and pulse rate showed no remarkable changes during the measurements. Fig. 4A,B shows the course of the PI and RI throughout the investigation as a result of the varying sound intensity.

In the figures the first values represent the arithmetic means of the indices (with simple standard deviation) after a 20 min rest phase. These initial values were defined as base values (RI base value = 0.50; PI base value = 0.72).

At a noise level of 75 dB(A) lasting 2 min the RI and PI increased significantly to RI = 0.53 and PI = 0.79 ($P < 0.01$). At a noise level of 85 dB the reaction was the most pronounced. Here resistance values reached their maxima (RI = 0.56 and PI = 0.83), with $P < 0.001$.

At an exposure level of 95 dB(A) the increase in the resistance index was no longer as pronounced as at 85 dB(A), despite the higher sound level. Here the RI was 0.54 and the PI 0.79 ($P < 0.01$).

Increases in the resistance values were reversible during each rest phase. They returned to base level values after only 10 min rest between the individual noise phases. Twenty minutes after the last measurements were taken the base level with an RI of 0.50 and a PI of 0.71 was reached again.

4. Discussion

The exposure to noise of the human and the animal organism has a multitude of possible consequences. They are relatively complex and can affect almost all organ systems (Algers et al., 1978). According to Borg and Møller (1973), noise can be regarded as a stressor and thus causes a general stress effect: the auditory nerve paths influence the activity in the formatio reticularis, which in turn affects both the sympathetic and the parasympathetic nervous systems together with all the organs they innervate, i.e. pupils, heart, digestive system, adrenal medulla, blood vessels and body musculature.

Also, the changing levels of hormones regulated by the hypothalamus have an influence on metabolic pathways (Cransac et al., 1998). For our investigations two effects of noise are of importance and need further consideration. On the one hand there are the different effects on the circulatory system and on the other hand there are the effects on different parts of the auditory pathway.

The influence of noise on the circulatory system can principally be divided into the influence of a short and acute noise exposure and a chronic noise exposure. For our examinations the change in the vessel resistance in the BA under acute noise exposure is of interest.

Lehmann and Tamm (1956) reported an acute influence of noise from 70 dB (SPL), mainly a peripheral vasoconstriction of non brain-supplying vessels with a lowered stroke volume. This occurred without a significant rise in heart rate or blood pressure. Rosen (1970) observed an increase in blood pressure under noise exposure. Animal experiments have shown both an increase and a decrease in the heart rate under acute noise exposure, thus both sympathetic and parasympathetic effects (Ames and Arehart, 1972).

During recent research it was found that after exposure to 104 dB, 16 volunteers showed a temporary threshold shift but neither heart rate nor mean blood pressure changed significantly (Allessio and Hutchinson, 1992). These results are in accordance with the present examinations on the reaction of blood pressure and pulse rate.

The current knowledge on the reaction of the peripheral vessel system under noise exposure is not directly applicable to brain-supplying vessels, like vessels such

as the internal carotid arteries, the vertebral arteries and the basilar artery. Due to the fact that they supply succeeding cranial circulation areas those vessels are subject to auto-regulation. The flow behavior depends on local factors, for example p_{CO_2}, and on the activity of neuronal structures (Widder, 1995).

Measurement of flow and resistance in these vessels by means of duplex sonography reflects an overall picture or the sum of the blood flow, respectively, in the following areas of supply to the brain (Widder, 1995). Thus, a change in resistance in the preceding vessels such as the BA is not necessarily responsible for the changes in the terminal organ but for the variation of resistance in the whole succeeding circulation area (redistribution).

Changes not only depend upon the noise stimulus but also on the anatomic circumstances, i.e. the anastomoses in the arterial circle of Willis.

At the end of the last century the physiologists Roy and Sherrington (1890) published the basic models describing the regulation of cerebral circulation. Their notion was that activation of the brain leads to an enhanced metabolic activity in the activated neuronal centers and thus to an increase in oxygen uptake and in consequence to an increase in the perfusion of these centers.

Recent developments in medical diagnostics allowed these model concepts to be tested in animals and also increasingly in humans by means of minimally invasive or non-invasive techniques.

Over the last few years non-invasive transcranial Doppler sonography has positively asserted itself in this context. With the assistance of this method it was demonstrated that short light stimuli evoke a simultaneous increase in blood flow in the respective supply vessels (A. cerebri posterior) of the visual cortex (Aaslid, 1987). This investigation was corroborated in a more selective study in which series of flashlight pulses with varying frequencies were employed as a source of stimulation (Gomez et al., 1990). It had already been discovered before that visual stimulation provoked an increase in blood flow and metabolic demand on the optic area (area 17) and its adjacent area (Cooper et al., 1966).

Similar investigations concerning acoustic stimuli have been carried out. Miyazaki (1971) examined the effect of random noise by means of Doppler sonography at '100 phon' on the blood flow in the internal carotid artery and the cerebral artery of 10 volunteers (six of them over 60 years of age). He reported an increase in cerebral blood flow in all cases in either the vertebral artery or the internal carotid artery. Contrary to other authors (Allessio and Hutchinson, 1992), he found an increase of heart rate in all cases. In his opinion, the change of cerebral blood flow was due to the activation of cerebral metabolism and not to direct vasodilatation.

With regard to the anatomic region being supplied by the BA, especially under consideration of the influence of different acoustic stimuli, the change in the activities in different hearing centers and consequently in blood flow are described in the literature in dependence on the kind and the intensity of the stimuli:

Cochlea and lower auditory centers. In investigations of glucose uptake in the cochlea and dorsal cochlear nucleus in mice, using a radioactively labeled substrate, it was shown that moderate acoustic stimulation (broadband noise below 85 dB) induces an increase in metabolic activity. But high-intensity noise exposure (broadband noise above 100 dB) evokes a decrease in metabolic activity in these structures (Canlon et al., 1984; Mandal et al., 1997). In an extended animal experiment it was demonstrated by laser Doppler flowmetry that this activity decrease in glucose metabolism affects the regional blood flow in the same way (Mandal et al., 1997). A distinct decrease in blood flow in the supply vessels was identified upon exposure to high-intensity noise (110 dB broadband noise) (Lonsbury-Martin and Martin, 1981; Libermann and Mulroy, 1983; Nakai and Masutani, 1988).

The autoregulation of the CBF also depends on age (Miller and Dengerink, 1988; Suzuki et al., 1998), and the likely role of circulating hormones, i.e. angiotensin IV, (Coleman et al., 1998) and also nitric oxide (Brechtelsbauer et al., 1994) in blood flow regulation of the inner ear are further influencing factors.

Furthermore the neuronal effect on circulation in the cochlea must not be neglected. It is well known that the centrifugal neuronal input to the cochlea enters through the perivascular sympathetic plexus from the cervical sympathetic chain and along the vestibular nerve from the periolivary area of the brainstem. Both of these systems are distributed topographically in the cochlea. In guinea pigs electric stimulation of the sympathetic ganglion stellatum produced a 10–15% decrease of CBF and a 20–35% increase in blood pressure (Laurikainen et al., 1993, 1997). The decrease in CBF was interpreted as the net result of perfusion pressure, local autoregulatory mechanisms and a direct sympathetically induced vasoconstriction. A bilateral chemical sympathectomy of the stellate ganglia led to 20–35% increase of CBF.

In other auditory centers Galin (1964) showed that in cats white noise produced a marked increase in activity in the inferior colliculus while pure tone stimuli produced a marked decrease below the spontaneous level. Jensen and Rasmussen, 1970 recognized that the oxygen consumption in different parts of the brain decreased in proportion to the exposure time to noise.

Auditory cortex. In the available investigations in which positron emission tomography and functional magnetic resonance imaging have been applied it was more the higher centers of the auditory cortex that formed the focus of attention. An activity increase in the investigated areas was noted upon stimulation with moderately intense sound and various other acoustic stimuli (speech, pure tones, noises) (Millen et al., 1995).

The BA mainly supplies the basal cerebral structures, but less the auditory cortex (see above). A change in the blood flow in the BA could be interpreted as the overall sum of changes in activity occurring in all of the areas supplied by this vessel. Therefore, alterations in basilar blood flow should be largely – but not only – attributed to changes in the activity of basal structures or even the CBF. Our measurements have shown an increase in the resistance of the basilar artery during noise exposure, returning to baseline shortly after exposure. This increase was independent of the varying noise volume. Thus, alterations in flow in the neuronal centers supplied by this artery, and accordingly changes in the different sections of the auditory pathway and the inner ear, could be postulated. The unchanged heart rate and blood pressure which were measured during noise exposure and time of rest do not indicate an increase in sympathetic activity.

Our findings are supported by very similar experimental results reported by Schweitzer et al. (1996), who measured the same rise in resistance during exposure to music.

As even from animal experiments so far no data are available on the changes of flow resistance in the BA during noise exposure, it remains doubtful if and to what extent the inner ear participates in this change. Other authors' results could probably indicate such a connection. Patients with severe unilateral hearing loss showed significantly higher resistance indices in the BA in comparison with a control group (Schweitzer et al., 1995). Individual cases and clinical features could not be taken into consideration in this study.

In contrast to other authors (Canlon et al., 1984; Mandal et al., 1997) we note, however, that in humans already far lower levels of acoustic stimulation than those used in animal experiments and measurements of CBF lead to an increase in basilar artery resistance.

In an animal model it was shown that vasoactive hormones are produced or activated in the inner ear (Cransac et al., 1998). An enhanced release of such hormones in response to acoustic stress would also be a feasible mechanism.

Ultimately, our examinations confirm that a connection between noise exposure and resistance in the BA and resistance could be established. Because of the above mentioned variety of influencing factors, a standardized examination in animal experiments should clarify how far these changes occur because of variations of the CBF or other mechanisms. These still to be considered alterations in regional blood flow in the area of basilar circulation may be an important, but yet unaccounted for, co-determining factor in the pathogenesis of acute idiopathic disorders of the inner ear.

In particular, measurements in patients with sudden hearing loss and patients with labyrinthine trauma can be expected to provide interesting and possibly also diagnostically or prognostically relevant new insights, with the transcranial Doppler providing a new indirect device for measuring both blood flow and hearing activity.

Acknowledgements

We would like to thank Professor M. Grade and Stuart Irwin for revising the English translation of our manuscript. This study was supported by the Johannes and Frieda Marohn Foundation in Erlangen, Germany.

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