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AUTOREGULATION OF COCHLEAR BLOOD FLOW

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ABSTRACT

We reviewed papers written about autoregulation of cochlear blood flow (CBF). In animals, autoregulation of CBF has been recognized not only by variations of systemic blood pressure (BP) but also by manipulations to the blood vessels, such as occlusion of the anterior inferior cerebellar artery, occlusion of the draining veins from the cochlea, and variations of the inner ear pressure. Recent reports have shown that autoregulation of CBF is not so different from that of cerebral blood flow in its strength, but it is disturbed in endolymphatic hydrops or aged animals. Since it became possible to measure CBF in humans, clinical investigation about autoregulation of CBF needs to be done in various inner ear diseases.

Key Words: cochlea, inner ear, blood flow, autoregulation

INTRODUCTION

Autoregulation of blood flow is a function that maintains blood flow within a physiological range regardless of changes in BP. It is important to keep homeostasis in various organs. Study of CBF is difficult because the cochlea is small and surrounded by bone. However, there have been many experiments regarding autoregulation of CBF conducted by changing BP with drugs or exsanguination, by occluding the supplying artery to the cochlea, by occluding blood vessels inside the cochlea with increased inner ear fluid pressure, and so on. This paper reviews the studies on autoregulation of CBF.

Occlusion of anterior inferior cerebellar artery (AICA)

The inner ear is supplied principally from the inner ear artery (labyrinthine artery) which is usually a branch of AICA, although it may arise directly from the basilar or even the vertebral arteries. The inner ear artery runs through the internal auditory meatus and nourishes the cochlea and vestibular apparatus. Various experiments to observe the effect of AICA (or inner ear artery) occlusion on CBF have been done in guinea pigs,^{1,2,3,4)} mice,⁵⁾ gerbils,⁶⁾ rats^{7,8)} and cats.⁹⁾ In these experiments, the closer the occlusion point is to the internal auditory meatus, the more severe the CBF reduction. Anastomoses between AICA and collateral blood vessels may not work for the inner ear if the occlusion point is very close to the internal auditory meatus. In humans also, many anastomoses between AICA and basilar artery pontine branches were reported.^{10,11)}

In experiments in which AICA was occluded, recovery of CBF even during the occlusion, and hyperemia after occlusion release were observed, indicative of CBF autoregulation (Fig. 1). In some experiments, however, recovery of CBF during occlusion was not observed,^{3,9)} although

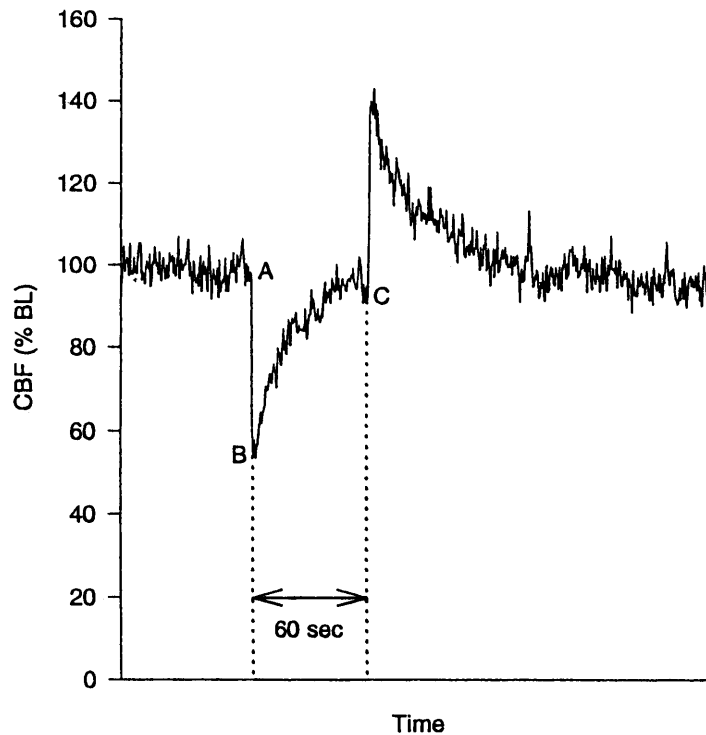


Fig. 1. An example of the cochlear blood flow (CBF) response during 60-second occlusion of AICA in young mouse. Between A and C, AICA was occluded. Immediately after the occlusion, CBF dropped from A to B. Recovery of CBF during the occlusion and hyperemia (rebound phenomenon) after the release are shown.⁵⁾

hyperemia after occlusion release was generally recognized.

Chronic effects of AICA occlusion or occluding the arteries which supply the cochlea have not been investigated well. Afzelius & Aursnes¹²⁾ described that damage to the upper turns was stronger than that to the lower turns after chronic obstruction of AICA in guinea pigs, and hypothesized that one of the causes of Meniere's disease was an interference with the inner ear circulation. On the contrary, Jiang & Umemura¹³⁾ did not observe such differential damage among the cochlear turns after AICA thrombosis was induced by a photochemical reaction between green light and a systemic injection of Rose Bengal.

Occlusion of venous drainage

Compared to the number of experiments investigating the effect of occluding arteries to the cochlea, there are far fewer experiments involving the occlusion of the draining vein. As for the draining vein of the cochlea, the vein of the cochlear aqueduct (VCAQ),^{14,15)} the vein of the vestibular aqueduct,¹⁶⁾ and the internal auditory vein are listed.¹⁷⁾ Among these, VCAQ is the main drainage vein of the cochlea in the guinea pig.

The VCAQ runs linear and parallel to the cochlear aqueduct by the side of the middle ear. The VCAQ receives communicating veins from the mucoperiosteum of the middle ear. Perlman

AUTOREGULATION OF COCHLEAR BLOOD FLOW

and Kimura^{15,16)} destroyed the VCAQ (which is synonymous with the inferior cochlear vein) almost totally and observed histological changes in the cochlea in guinea pigs. In their studies, extensive damage appeared in the stria vascularis and spiral ligament, being most evident in the basal turn of the cochlea. Watanabe et al.^{14,18)} occluded the point at which the VCAQ joined the dural sinus and observed the change in CBF and endocochlear potential (EP) in guinea pigs. Obviously, the effect of the vein occlusion by this method was less extreme compared to Perlman and Kimura. This difference can be explained by the function of the communicating veins between the VCAQ and the mucoperiosteum veins: Watanabe et al. did not destroy the communicating veins. Following occlusion of the VCAQ at the point where the VCAQ joined the dural sinus, CBF was reduced to various degrees but the distribution of blood flow in each cochlear turn was similar. In some animals, transient decreases in EP, which may be associated with autoregulation of CBF, were observed.¹⁸⁾

Elevation of inner ear pressure

Increased fluid pressure or increased fluid volume in the inner ear lowered CBF.^{19,20,21)} When perilymphatic pressure was raised by inserting a glass capillary tube into the perilymphatic space, endolymphatic pressure increased to match perilymphatic pressure.²²⁾ Accordingly perilymphatic and endolymphatic pressures can be considered as the inner ear pressure. When the inner ear pressure was raised to a relatively high level, EP decreased to a negative value, in a similar way to the response to anoxia, because of the CBF reduction.^{19,22)} The phenomenon whereby the lowest pressure which could reduce EP to a negative value increased gradually may be associated with CBF autoregulation. The elevation of the inner ear pressure stopped CBF except for blood flow in the modiolus. Since the modiolus is surrounded by bone, it was considered that the increased inner ear pressure did not transmit directly to the blood vessels in the modiolus.

In experiments in which the relationship between the inner ear pressure and CBF was investigated, gradual recovery of CBF even during a certain level of inner ear pressure, or rebound phenomenon of CBF after releasing the increased inner ear pressure, was observed as shown in the response to AICA occlusion (Fig. 2).²⁰⁾ These CBF responses to variations in the inner ear pressure, associated with autoregulation, seemed to be weak, compared to those related to AICA occlusion. This difference may suggest that the modiolar artery plays an important role in CBF autoregulation. However, in experiments in which the inner ear pressure was manipu-

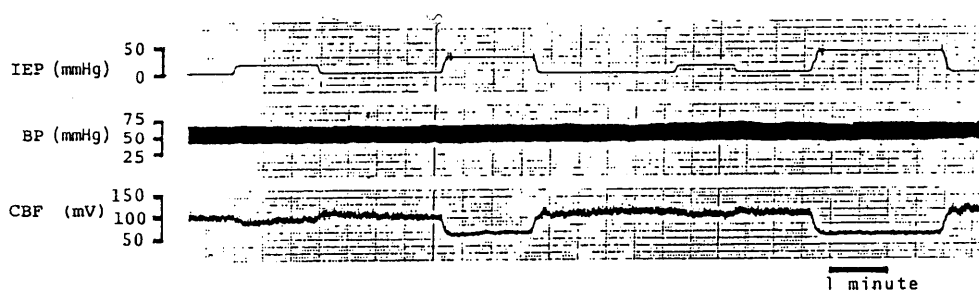


Fig. 2. Effect of changes of inner ear pressure (IEP) on cochlear blood flow (CBF) in guinea pig. Blood pressure (BP) did not change significantly, but CBF decreased because of IEP elevation. In this figure, IEP was raised four times. Gradual recovery of CBF during the raised IEP, and hyperemia after the release, are evident.²⁰⁾

lated, the environmental changes in the inner ear fluid, especially its temperature and chemical composition, might have disturbed CBF autoregulation because saline was injected into the perilymphatic space through the glass capillary tube to raise the inner ear pressure.^{19,20)}

CBF in hydropic ear

Endolymphatic hydrops is a situation where too much endolymph exists. In Meniere's disease, this endolymphatic hydrops exists and the degree of hydrops fluctuates with the severity of hearing loss. Larsen et al.²³⁾ measured CBF in guinea pigs with endolymphatic hydrops using the microsphere technique and reported that there was no significant difference in CBF between normal and hydropic ears. Baldwin et al.²⁴⁾ investigated the effect of hyperosmotic agents on CBF in guinea pigs with normal and hydropic ears. They could not observe a difference between the responses of CBF in hydropic and normal cochleas.

However, autoregulation of CBF may be abnormal in hydropic ears.^{25,26,27)} Yamamoto et al.²⁵⁾ measured CBF in guinea pigs with unilateral endolymphatic hydrops while systemic BP was lowered by removal of whole blood. The decrease in CBF was larger on the hydropic ear side than on the intact side. Brechtelsbauer et al.²⁷⁾ occluded AICA and reported reduced autoregulation of CBF in guinea pigs with endolymphatic hydrops.

Zhou et al.²⁸⁾ observed microcirculation of the lateral wall in the hydropic cochlea and reported that hydrops elicited different changes in spiral ligament vessels and stria vascularis capillaries. According to them, the diameter of spiral ligament blood vessels decreased and the diameter of stria vascularis capillaries increased following formation of endolymphatic hydrops. Michel et al.,²⁹⁾ however, using histological methods, described that spiral ligament blood vessels dilated in hydropic cochlea. The distribution of nitric oxide-synthases (NOS) in the cochlea may be different between normal and hydropic cochleas,²⁹⁾ although there was no difference in basal nitric oxide production in normal versus hydropic cochleas.²⁷⁾

Autoregulation in disease model animals

Quirk et al.³⁰⁾ investigated autoregulation of CBF in spontaneously hypertensive rats (SHR) and normotensive Wistar-Kyoto rats (WKY). Since initial BP baselines were higher in SHR than in WKY, they adjusted baseline BP through intra-cerebroventricular infusions of sarthran in SHR and angiotensin II in WKY. Following the adjustment of the baseline BP, the effect of intra-arterial angiotensin II injection on systemic BP and CBF was investigated. They observed significantly impaired elevation in CBF in the SHR as compared with the WKY, despite similar increases in systemic BP. They interpreted that CBF autoregulation was more evident in the SHR than in the normotensive WKY.

Autoregulation of cerebral blood flow, however, was significantly weaker in SHR than in WKY.³¹⁾ Since antihypertensive treatment almost restored autoregulation in SHR to normal, impairment of the autoregulation was not considered to be caused simply by genetic differences between SHR and WKY. Because CBF is similar to cerebral blood flow, further study needs to be done regarding CBF autoregulation in SHR and normotensive WKY.

Autoregulation of CBF in aged animals

Human temporal studies^{32,33)} and experimental animal models^{34,35)} have demonstrated age-related histopathologic changes in the cochlear vasculature, and alteration in CBF has been considered one of the etiologic factors related to presbycusis. Prazma et al.³⁶⁾ reported that CBF in old gerbils was less than in young animals and used these findings to support a vascular theory of presbycusis. However, other studies have shown that there is no significant difference in the cochlear vasculature between young and old guinea pigs,³⁷⁾ and that CBF does not vary be-

AUTOREGULATION OF COCHLEAR BLOOD FLOW

tween young and aged normotensive rats.³⁸⁾ These conflicting results may reflect a difference in the species studied or the ages at which animals were selected for investigation.

The mouse is a suitable animal for aged-related studies because of its short life span and its previous use in investigations of aged-related hearing loss. It was shown to be possible to measure CBF in mice in spite of their small size.³⁹⁾ Nakashima et al.⁴⁰⁾ investigated the effect of age on CBF autoregulation in 2-month-old, 10-month-old and 18-month-old CBA mice by investigating CBF and BP during angiotensin II injection and exsanguination, and suggested that autoregulation changed with maturation and age. Brown et al.⁴¹⁾ investigated changes in CBF following topical application of nitroprusside, a vasodilating agent, onto the round window membrane in young and old mice (from 2 to 21-months-old). They observed that cochlear vascular reactivity was less in old mice than in young mice. Suzuki et al.⁵⁾ also observed a CBF change during and after AICA occlusion in 6-month-old and 21-month-old mice, and reported that CBF autoregulation was significantly reduced, and that collateral vascular functions supplying CBF were lower in the aged group (Fig. 3).

Comparison of autoregulation between the cochlea and brain

Blood flow in the cochlea generally comes from AICA which is a branch of the vertebral arterial system in the brain. It was presumed that the brain and cochlea are similar from a functional standpoint and that the cochlear circulatory system is one branch of the brain's cir-

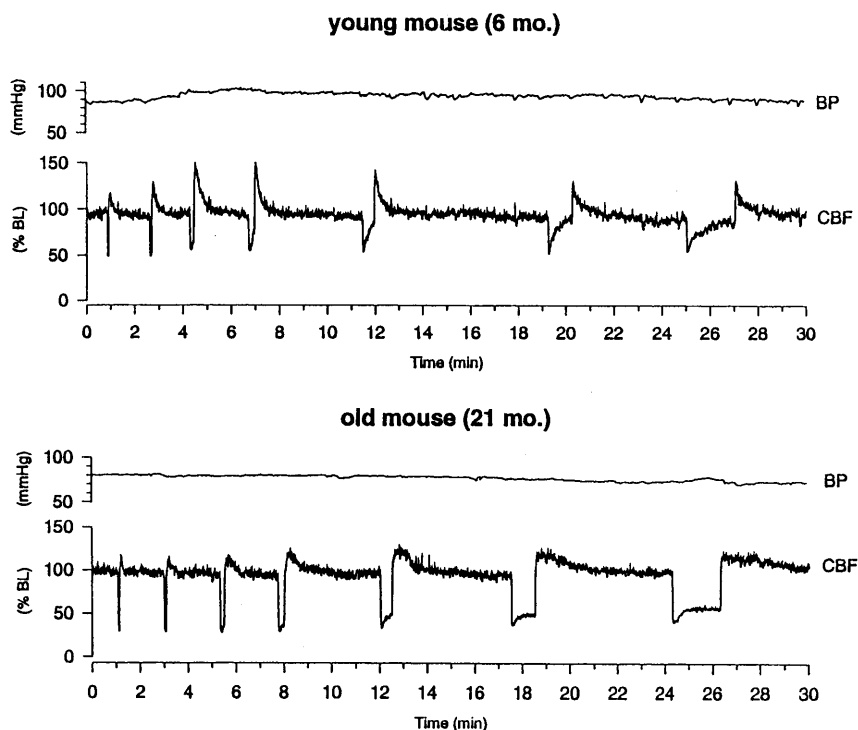


Fig. 3. Response of blood pressure (BP) and cochlear blood flow (CBF) to 3-, 5-, 10-, 15-, 30-, 60-, and 120-second AICA clamping in young and aged mice. Decrease amplitude is larger and recovery amplitude is smaller in aged mice.⁵⁾

culatory system.^{42,43)}

Autoregulation of CBF was stronger than that of middle ear blood flow which belongs to the external carotid artery system.⁴⁴⁾ It is interesting that the behavior of blood flow was significantly different between the middle ear and inner ear in spite of their close anatomical relationship. Actually, there is no functional anastomosis of blood vessels between the middle ear and the inner ear.

Several investigators have compared CBF autoregulation to autoregulation of cerebral blood flow. Yamamoto et al.²⁵⁾ measured inner ear and brainstem blood circulation while systemic BP was modulated by norepinephrine infusion or exsanguination in guinea pigs. They described that blood flow in the brainstem remained constant in the BP range of 35 to 80 mmHg, but that inner ear blood flow showed a poor autoregulatory systemic function relative to the BP change. Kawakami et al.⁴⁵⁾ also described that CBF was considered to have some autoregulation but this autoregulation was less than brain blood flow in guinea pigs.

Some studies in the guinea pig, however, have shown strong intrinsic autoregulation in the cochlea.^{46,47)} Suzuki et al.⁴⁷⁾ investigated the effect of increased cerebrospinal fluid pressure on CBF and cerebral blood flow in guinea pigs in which cerebrospinal fluid pressure was transmitted directly to the inner ear through the patent cochlear aqueduct. They reported that CBF was not decreased by the fluid pressure elevation as much as was cerebral blood flow. These differences in results regarding the strength of autoregulation in comparison with CBF and cerebral blood flow may depend on the differences between the experimental conditions.

Autoregulation of CBF in various parts

Comparison of autoregulation of blood flow in various parts of the cochlea has not been well investigated. Nakashima et al.²⁰⁾ observed that CBF decreased more strongly in the upper turn than in the basal turn following the elevation of the inner ear pressure. Tyagi et al.⁴⁸⁾ also reported that the reduction of blood flow due to hemorrhagic hypotension was more remarkable in the upper turns than in the basal turn in guinea pigs. These results may be related to the fact that blood flow volume in the upper turns is less than that in the lower turns in connection with the direction of blood flow from the basal turn to the apex.

It is interesting to investigate the difference in autoregulation of blood flow between the stria vascularis and spiral ligament because blood vessels in the spiral ligament are considered as arteriovenous anastomoses running outside of the capillary vessels in the stria vascularis. Not only anatomical differences but also functional or behavioral differences may exist between these blood vessels in normal and diseased ears such as hydroptic ears.^{27,28,29)}

CBF in humans (clinical application)

There have been various reports describing CBF measured by laser-Doppler flowmetry in humans.⁴⁹⁻⁵⁴⁾ In humans, it is difficult to observe how large BP variations influence on CBF. Degoute et al.⁵⁵⁾ investigated the effect of BP changes on CBF in eight anesthetized patients undergoing tympanoplasty. They reported that sympathetic nerve regulation via its vasomotor tone at the level of cochlear microcirculation occurred markedly when BP was above 160 mmHg and that the autonomic nervous system appeared to control CBF against large variations in blood flow in response to hypertensive phenomena.

Fisch et al.^{56,57)} described that the response of oxygen tension in the perilymph to inhalation of carbogen was impaired in some patients with sudden deafness. Autoregulation of CBF may be impaired in sudden deafness or Meniere's disease. However, direct evidence of the impaired autoregulation in clinical inner ear diseases is still lacking. Further study about clinical CBF in various inner ear diseases needs to be done.

AUTOREGULATION OF COCHLEAR BLOOD FLOW

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AUTOREGULATION OF COCHLEAR BLOOD FLOW

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