Autoregulation of cochlear blood flow in guinea pigs

Brown, J. Nadine, and Alfred L. Nuttall. Autoregulation of cochlear blood flow in guinea pigs. Am. J. Physiol. 266 (Heart Circ. Physiol. 35): H458-H467, 1994.—Autoregulation of blood flow in the inner ear following uncontrolled changes in systemic blood pressure (BP), which was induced by the application of pharmacological agents that cause local and/ or systemic vascular effects, has been reported in previous studies. In the current study, carotid BP was systematically manipulated without drugs, while the resulting cochlear blood flow (CBF) changes were measured using a laser Doppler flowmetry (LDF) Anesthetized guinea pigs were used, and the probe of a LDF was held against the ventral-posterior portion of the surgically exposed cochlea. A mechanical occluder was placed around the descending aorta or the inferior vena cava. BP could be elevated or lowered over a wide range and was held stable during 2-min occlusions. The mean level (±SD) of regulation (%ΔCBF/%ΔBP) for BP changes less than ±35% of preocclusion baseline was 0.24 ± 0.2 (or 0.18 ± 0.2 if BP is corrected by subtracting central venous pressure). Significant regulation occurred for BP between 20 and 70 mmHg. A demonstration of the cochlear origin of the regulatory response was obtained by “pharmacological blockade” following topical application of the vasodilator, sodium nitroprusside, to the cochlea. In this condition, CBF changed in nearly direct proportion to BP.

THE TERM AUTOREGULATION has been used by physiologists studying the cochlear blood flow without much regard to the type of stimulus that might evoke the regulation. Consequently, little is known about the capacity of the cochlear circulation to respond to its natural stimulus (sound) or to systemic blood pressure (BP) variations, whether static or dynamic. In a report by Dengerink (24) summa-

Preparation and materials. The 20 pigmented guinea pigs used in this study were housed in American Association for Accreditation of Laboratory Animal Care-approved facilities. Experimental protocols were reviewed and approved by the University of Michigan Committee on Use and Care of Animals. The animals weighed 250-400 g and were anesthetized with one of two protocols: pentobarbital sodium (15 mg/kg ip)/fentanyl droperidol (Innuvar-Vet, Pitman-Moore, Mundelein, IL) (0.4 ml/kg im) or diazepam (Valium, Roche Laboratories, Nutley, NJ) (0.5 mg/kg ip)/fentanyl (Janssen Pharmaceuticals, Piscataway, NJ) (0.32 mg/kg im). A heating pad maintained rectally measured body temperature at 38 ± 1°C. The right common carotid artery was cannulated for recording BP and for withdrawing blood samples for pH and blood gas.
determinations. The head was positioned in a headholder, and the left auditory bulla was exposed by a ventral surgical approach. Care was taken to avoid thermal cooling of the cochlea during anesthesia and surgery.

The animals were artificially resired (model 683, Harvard rodent ventilator), and a 2-mm silicone rubber inflatable vascular cuff (In Vivo Metric Systems, Healdsburg, CA) was placed around either the descending aorta or the inferior vena cava. To expose the aorta, a left anterior-posterior lateral incision was made, and the ribs were retracted. The vessel was isolated above the diaphragm with fine forceps, and the occluder's suture was passed around the vessel with blunt curved forceps. Tubing to a 1- or 3-ml syringe was exteriorized through the incision, which was then closed with surgical tape. The inferior vena cava was approached through an incision along the sternum, and the ribs were retracted. The occluder was placed around the vessel above the diaphragm and the wound closed as described above. Usually only one occluder was placed, but both arterial and venous occluders could be placed in some animals.

Two or more times during each experiment, 0.20-ml arterial blood samples were taken from the carotid cannula in heparinized glass syringes. Samples were kept on ice, and pH, Pco2, and Po2 values were determined within 30 min (Stat Profile 3 Blood Gas Analyzer, Nova Biomedical). Data from vascular occlusions (baselime, occlusion, and recovery data points) were used in this report if values from the relevant blood samples were within certain limits: Pco2 < 40 mmHg and Po2 > 60 mmHg. These values were within about one standard deviation of published mean blood gas values for awake and anesthetized guinea pigs (6).

Blood pressure. After the vascular occluder was secured around the vessel, BP could be elevated (aorta compression) or lowered (vena cava compression) and then held relatively stable at a predetermined level by slightly increasing or decreasing syringe pressure as necessary. Generally the measurement protocol was as follows: a baseline of 3 min of stable BP preceded each occlusion; occlusion duration was 2 min, during which syringe pressure was manipulated to retain a constant BP value (typically, 10-90% increase or decrease); the occluder syringe pressure was released. In some animals, occlusion times were extended to up to 5 min to demonstrate that a 2-min duration is sufficient for the completion of the regulatory response. Recovery time after an occlusion varied somewhat, so at least 5-6 min were allowed before another occlusion was initiated. BP values at 1.0, 1.5, and 2.0 min during occlusion were used to determine mean occlusion BP. The desired percent changes in BP were randomly selected before each experiment. The range of percent changes gave ~5 mmHg as the minimum pressure shift. It also ensured having a sufficient number of trials for analysis of small (i.e., <35%) pressure changes. Achieved mean percent changes were usually within ±5% of the predetermined values.

A second occlusion protocol was followed in five guinea pigs to measure the degree of autoregulation during a state of artificially induced "normal awake" blood pressure. The mean awake BP in our strain of pigmented guinea pigs has been shown to be 53.1 mmHg (6). A baseline level consisted of 5 min of partial occlusion of the descending aorta to elevate the mean systemic BP to or near the normal awake value. The occluder syringe pressure was then adjusted to give an additional 2-min increase or decrease in BP relative to the elevated baseline. Mean occlusion BP over 2 min was determined as above.

In six animals, ~1 μl of 3% sodium nitroprusside (SNP) in physiological saline was applied to the round window membrane (RWM) of the cochlea by microsyringe. This procedure causes local vasodilation of the cochlear vessels (29). After 15-20 min, additional occlusions were initiated. As a control study, in some animals, 1 μl of saline was applied to the RWM and effects observed before drug application.

Cochlear blood flow. To monitor CBF, the 0.8-mm diameter "needle" probe of a laser Doppler flowmeter (LDF) (Laserflo BPM403, TSI) was positioned against the lateral wall of the basal turn of the cochlea (a ventral-posterior location). The mucosal vessels on the surface of the cochlea were gently removed with a cotton pledget. A light petroleum jelly was used between the probe tip and the surface of the cochlea to assure a constant optical coupling of the laser light to the cochlea and to prevent the accumulation of fluid and extraneous blood cells beneath the probe tip. The probe was held securely in a micromanipulator, such that nonblood cell-related movement of the cochlea or probe (which could contribute an artifact velocity signal) was eliminated. Because these experiments did not use sound stimulation of the cochlea, sound-induced measured flow artifacts were not of concern (38). Both BP and CBF responses were recorded simultaneously on a strip-chart recorder. Baseline CBF and mean CBF during occlusions were calculated as for BP.

To determine the relationship of BP and CBF during occlusions, both measurements were normalized to their respective baselines and expressed as percent change (%Δ). A measure of autoregulation was calculated as %ΔCBF/%ΔBP.

Further details of animal preparation, round window drug administration, and laser Doppler flowmetry are given elsewhere (28).

RESULTS

BP could be manipulated over a wide range by means of the vascular compressions. Complete occlusion of the aorta could increase BP by 150% or more, but elevations most frequently used in this study ranged from 10 to 90% above preocclusion baseline. A marked depression of BP could also be achieved by compression of the inferior vena cava; total inferior vena cava occlusion could decrease BP to < 10 mmHg. As Fig. 1 shows, at the initiation of the occlusion, BP began to change immediately, and, after the desired pressure level had been achieved by manually manipulating syringe pressure, occlusion BP could usually be held quite stable. Measurement time points were begun at 1.0 min to avoid most of the dynamic phase of the manually induced changes. Return toward baseline at the termination of the occlusion was very abrupt, as shown in Fig. 1, for both arterial and venous occlusions. BP usually returned to the original level (the baseline) in ~1 min following aorta occlusion. The recovery from venous occlusion typically took somewhat longer and often included a brief "reactive" phase of slightly elevated BP.

Changes in CBF during occlusions, as measured by LDF, are also illustrated in Fig. 1. Usually, particularly for occlusions elevating BP 40% or more, CBF declined toward baseline during the occlusion. This tendency was not so pronounced during venous occlusions. It is this adaptation phase of the CBF change that represents the autoregulatory capacity of the cochlea. Venous occlusions, reducing BP from the relatively low initial levels, tended to show less of this regulation.

Figure 2 shows the responses of a single guinea pig to 12 aorta occlusions producing BP increases of 13-88%.
BP as measured immediately before each occlusion is shown in Fig. 2 (mean ± SD = 40.1 ± 1.6 mmHg). The level of CBF regulation was < 0.50 for all occlusions and ~ 0.05 ± 0.2 for BP changes of <35%. In other words, regulation was nearly perfect for small increments in BP.

In two animals, a cannula was placed in the superior vena cava, and central venous pressure was measured during occlusions. For all occlusions (venous and arterial) in both animals, central venous pressure varied by 1 mmHg or less from an average pressure of 7 mmHg.

Four animals were anesthetized with Valium/fentanyl, the rest (n = 11) with pentobarbital/Innovar-Vet. Animals anesthetized with Valium/fentanyl tend to have somewhat higher BP than those with pentobarbital/
Innovar-Vet; however, the patterns of BP and CBF changes seen in the current study were similar to those of pentobarbital/Innovar-Vet animals. The reason why a Valium/fentanyl anesthesia protocol was used is the attempt to partially or fully offset the systemic BP reduction caused by artificial ventilation and placement of the occluders. Generally, normal BP was still not achieved, and it is not known if Valium/fentanyl is a better anesthetic choice (in the sense of microvascular regulation) because Brown et al. (6) have shown that with this anesthetic combination the anesthetized but surgically unoperated guinea pig has elevated (from normal awake) BP. This could be due to excessive sympathetic activity in the anesthetized animals.

Figure 3A shows the changes in BP and CBF for 76 occlusions in both of these groups of animals. A dashed line shows a third-order polynomial regression curve fit to the Valium/fentanyl data, whereas the solid curve is fitted to the pentobarbital/Innovar-Vet data. The polynomial functions are suggestive of the classical autoregulatory range curves. Using a random effects analysis of covariance on the polynomial regression, we did not reject the hypothesis that the slopes of the regression lines are the same ($P = 0.92$). Therefore, the data from both groups were combined in subsequent analyses.

Mean level of CBF regulation for BP changes up to ±35% of baseline from 38 occlusions in 15 animals (Fig. 3A, data between dashed lines) was 0.24 ± 0.2. Preocclusion BP for these 38 occlusions ranged from 18 to 53 mmHg, with a mean of 37.5 ± 8. Regulation calculated from venous occlusions was more variable than for arterial, particularly for decreases in BP greater than 35–40%. If the central venous pressure of 7 mmHg is subtracted from systemic pressure to give the net pressure across the cochlea, the mean level of regulation becomes 0.18 ± 0.2.

Also included in Fig. 3A are the data obtained from five guinea pigs (anesthetized with pentobarbital/Innovar Vet) in which BP was first elevated to the “normal awake” level by occlusion of the descending aorta (Fig. 3A, open triangles). The mean BP achieved in 13 occlusions was 52.4 ± 1.0 mmHg.) An additional 2-min occlusion further elevated BP by 14–29% ($n = 7$ occlusions). Slight release of the occluder syringe pressure gave decreases of 16–24% ($n = 6$ occlusions). A linear regression fit to these data shows the level of regulation to be 0.34 ± 0.20 (or 0.22 ± 0.08 after subtracting central venous pressure) ($n = 13$).

Figure 3B shows the data for the ±35% changes in pressure (i.e., from Fig. 3A, between the dashed vertical lines) plotted as absolute LDF voltage units versus absolute BP. Open symbols indicate baseline pressure values; filled symbols indicate the corresponding occlusion pressure value. Filled symbols to the left of open symbols are venous occlusions, whereas symbols to the right are arterial occlusions. The triangle symbols represent the same animals as noted in Fig. 3A. Inspection of the data in the graph reveals several relevant facts. 1) The x-axis length of the connecting lines is the absolute BP change. Most changes are 5–10 mmHg. One can also see that, while our constant percentage change protocol could bias the regulation index (by giving smaller pressure shifts for lower initial BP) there is, in fact, a similar BP shift in absolute units across the data set. 2) The slope of the lines is the regulation index. Most slopes are very shallow, indicative of the high degree of regulation. 3) There is a wide distribution of absolute LDF voltage units. This is an expected property of the LDF method in which the absolute voltage is not calibrated as absolute flow. The voltage is a function of thickness of the bone of the cochlea and of the placement and orientation of the probe and thus is the vascular volume measured by the instrument. The LDF scale does, however, have a true zero, and this allows percentage measurements.

Figure 4 depicts the level of regulation as a function of actual preocclusion systemic BP for BP changes up to ±35% of preocclusion baseline. The level of regulation was < 0.50 for most of the 38 occlusions, and the group mean was 0.24 ± 0.2 (or 0.18 ± 0.2 after central venous pressure was subtracted). It is clear that the limits of regulation, i.e., a tendency toward no regulation in the very low and very high BP ranges, is not evident in the group data of this study.

In three animals in this group (i.e., animals with BP change of up to ±35% of baseline), BP was lowered to 22 mmHg or less, and regulation was still maintained below 0.50 for four of six occlusions (2 animals). Preocclusion BP for the six occlusions ranged from 18 to 33 mmHg.

Effect of local vasodilation. SNP (1 μl, 3%) topically applied to the RWM in six animals increased CBF by 16–50% (mean 31.5 ± 13) in 20 min, while BP decreased 2.0 ± 7.5%. After 60 min following the RWM application, CBF in five animals remained 10–79% above...
pre-SNP baseline. At 120 min, CBF in three animals was still >35% of baseline; experiments in the other three animals were terminated at <120 min. CBF and BP responses before and after topical SNP in two animals are given in Fig. 5. Initially a 34% elevation of BP in one animal was accompanied by only a 6% change in CBF, but after local application of SNP, a similar BP manipulation produced a 53% change in CBF. In another animal, decreasing BP by 39% resulted in a 12% decrease in CBF. After SNP, CBF decreased 28% for a 38% decrease in BP.

Figure 6 shows the effect of SNP on the regulation of CBF. Pre- and post-SNP responses are given; all measurements of post-SNP regulation were obtained within 120 min after RWM application of SNP. Linear regression lines are fitted to the data for BP up to ±35% of preocclusion baseline. The solid line (pre-SNP) has a slope of 0.30 ± 0.2, whereas the dashed line (post-SNP)
1.5 regulation

is 0.87 ± 0.5. A random effects covariance on all of the data in the two groups of Fig. 6 indicates that we reject the hypothesis that the slopes of the regression lines are equal \((P = 0.001)\).

No significant changes in BP or CBF were induced by application of ~1 μl of saline to the RWM as a control for later drug application.

**DISCUSSION**

In the examples of raw data shown in Fig. 1, the relative stability of the arterial BP is typical. Variations represent a possible physiological response to pressure change (e.g., vasomotion) and variations due to efforts to manually stabilize the pressure. In Fig. 1, A and C, the increase and decrease in pressure are moderate (42 and 30%, respectively). The much smaller change in LDF units makes the high level of regulation obvious. Measurements of regulation taken from the tracings were at the 1.0-, 1.5-, and 2.0-min time points following the pressure step. One can see that most or all of the dynamic phase of CBF change is over by these times.

The absolute BP values seen in the tracings shown in Fig. 1 are quite low. This is because of the fact that the mean systemic arterial BP in the awake guinea pig is only ~53 ± 4 mmHg (6) or 64 mmHg (9). Many anesthetics tend to lower BP, and in this study BP was unavoidably lowered even further by open-chest surgery and artificial ventilation.

Because of its low BP, one is justified in asking if the guinea pig is a valid model to use for studies of whole organ regulation and microcirculation physiology. We submit that it is justified, based on two issues. The first issue is that the guinea pig is the most common animal model used for studies of cochlear physiology and the pathophysiology of certain types of auditory dysfunction. Cochlear blood circulation is an essential but little understood component of such dysfunction. Second, the relatively low awake mean systemic BP of this rodent suggests that it is an interesting model in a comparative sense. The autoregulatory range seems to be shifted to one that is centered about the mean pressure that is appropriate for this animal. The mechanisms that allow this should ultimately be interesting in comparison to the rat and other mammals used for circulatory studies. However, one must still exercise care in the interpretation of these results in comparison to other mammals as well as the extension to the human.

Preocclusion BP values in the animals of this study ranged from 18 to 60 mmHg (37.8 ± 9). Figure 4 indicates that the strength of the regulation is relatively unaffected by preocclusion BP values ranging from 53 mmHg to the exceptionally low level of <20 mmHg. We have not explored regulation in animals with BP > 70 mmHg, which is about the highest “normal” anesthetized BP we see. Such elevated BP values are more frequently noted in animals anesthetized with Valium/fentanyl (6). One can also see in Fig. 4 that there is no clear trend that suggests the limits of regulation in the guinea pig. Perhaps this is due, in this experimental population, to variability introduced by level of anesthesia. The low end of the regulation can also be extended somewhat by the slightly smaller absolute pressure shifts used when systemic pressure is low. Figure 3B shows that such biasing of the data is small.

We were concerned that the already low BP in the guinea pig, upon further reduction by surgery and
Fig. 5. BP and CBF responses before (A and C) and after (B and D) application of 3% sodium nitroprusside on round window membrane of cochlea (2 animals). Arrows indicate initiation and release of occluder syringe pressure. A: occlusion BP is increased 34% above preocclusion baseline; CBF, 6%. B: BP is increased 35%; CBF, 53%. C: occlusion BP is decreased 39% below baseline; CBF, 12%. D: BP is decreased 38%; CBF, 28%.

artificial ventilation, would move the cochlea out of its autoregulatory range or would provoke regulatory mechanisms that would interfere with the intrinsic whole organ regulation in the cochlea. To address this problem, an additional five animals were tested following a step elevation in systemic BP by aorta occlusion to the "normal awake" level. Results (Fig. 3, open triangles) show that the high level of regulation was evident but significantly less strong than that of the other animals analyzed in Fig. 3. We attribute this finding to incomplete compensation during the 5-min BP elevation of the control baseline period. In these animals, this is a much larger step increase than that used to test regulation, and 2 min was sufficient for the
The mean %ΔCBF/%ΔBP for BP changes of up to ±35%, which can be derived from the “flow-pressure” curve, is 0.24 (or 0.18 when corrected for central venous pressure). This metric can be converted to the closed-loop gain factor, similar to that of Norris et al. (27), by the relationship: $G = 1 - (\% \Delta \text{CBF}/\% \Delta \text{BP})$. A gain (or autoregulatory index, $G$) of 1 then represents perfect regulation, and 0 represents no autoregulation. Thus, in the current study, $G = 0.76$ (or 0.82). It is important to note that we have selected animals to include in the analyzed data based on arterial blood gas values as noted above (and not on BP). Morff and Grainger (26) have shown that mild hypoxia can enhance the autoregulatory response, so it is possible that some guinea pigs have contributed to inflating the resulting value of $G$.

It is also important to note that a gain value, as defined, is subject to variable amount of “error,” depending on whether the line fitted to the data passes through the origin, i.e., zero flow for zero pressure (17, 19). In the current study we calculate and give the regulation values corrected by the central venous measure. This calculation tends to make regulation appear stronger so, in the interest of completeness, both values are given in the RESULTS. We have not, however, attempted to estimate the zero-flow pressure to use it as an additional correction factor in the regulation value calculation. Again, this correcting factor would be subtracted from each arterial BP value, under the assumption that the difference is a better estimate of the true BP across an organ system, and regulation would be stronger still. There is controversy about this type of correlation because of the highly nonlinear nature of flow at low shear rates and pressures.

Figure 3B is provided to allow the reader to inspect the “raw data.” As mentioned earlier, the absolute millivolt values of the LDF measure of CBF are meaningless for the cochlea. They are shown here to emphasize that the millivolt values vary because of uncontrolled factors such as the exact system of cochlear vessels analyzed by the instrument. There is a true zero reading for zero flux, and therefore relative measurements are valid. One can see in Fig. 3B that the slope of each line is shallow (good regulation) and that the absolute pressure change is similar across the data set.

In their study of isolated rabbit ear, Griffith and Edwards (14) found gain values ranging from 0.3 to 0.5. Values for hindlimb vary from 0.61 in rat (16) to 0.46 in cat (5). The highest levels of gain seem to occur for the coronary arteries (~0.7) (37) and kidney (0.81) (16). In contrast, Osol and Halpern (30) found in vitro cerebral blood vessels in normal rats had gain values of 0.38 for increasing BP values and 0.14 for decreases in BP, substantially worse than an earlier study of the rat where nearly perfect regulation was found (15). By comparison, the regulation of cochlear vessels seems quite strong. Bearing in mind the following caveats concerning the interpretation of LDF, we would certainly be safe in the conclusion that regulation to systemic BP change exists and is very strong in the guinea pig cochlea.

Most previous studies of whole organ regulation apply more direct measures of blood flow than LDF, such as microsphere trapping or intravital microscopic observations of the velocity of red blood cells. Recently, LDF has been coming into greater usage in various organ systems, e.g., (1-3, 20), and it is quite convenient for cochlear measurements because of the difficult anatomy of the inner ear as well as the small size of the cochlea (see Miller and Nuttall, in Ref. 25 for a review of LDF in relation to CBF studies). One must keep in mind, however, that LDF is a complex measurement (of red cell flux) dependent on the relatively unknown optical characteristics of the tissue/LDF probe configuration. This means that the exact analysis volume of tissue penetrated by laser light of LDF is unknown. Considering the complex vascular anatomy of the cochlea, this would imply sampling from inhomogeneous vascular beds which, along with physiological manipulations that

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**Fig. 6.** Response to application of 3% sodium nitroprusside (SNP) to round window membrane; $n=6$. Filled circles, pre-SNP occlusion BP response; $n=25$. Open circles, post-SNP occlusion BP response; $n=42$. Vertical dashed lines, ±35% change in BP; autoregulation slopes are calculated from data between these lines by linear regression. For solid and dashed lines, see text.
alter the volume fraction or number of red cells in the analysis volume, can affect the signal. In our experiments, systemic BP changes could be altering the microhematocrit by redistributing blood within the network (23, 34) or by venous congestion. The possibility for microhematocrit change to influence the LDF reading is also predicated on the assumption that the instrument is measuring chiefly from capillaries. If a significant portion of the signal comes from venules or veins where microhematocrit shifts are not possible, then the influence of redistribution is lessened. Although these caveats need to be enumerated, we believe that their effects will be secondary and not change the substance of this report.

It is also important to take note of the technique we used to manipulate BP in this study. The restriction of flow to the lower body (by descending aorta constriction) raises total peripheral resistance, whereas cardiac output remains relatively high; BP is thus elevated. The restriction of venous return from the inferior vena cava reduces cardiac output, whereas total peripheral resistance remains relatively unchanged; BP is thus reduced. Neither procedure changed the central venous pressure significantly in our measurement, although one would expect a decrease during venous occlusion. Therefore we make the assumption that the change of the differential BP between the input (or supply side) of the cochlea and the output (or drain side) of the cochlea is proportional to the systemic BP. The process of BP manipulation essentially incorporated the investigator into a “feedback loop” controlling BP. That is, we attempted to set BP change to predetermined values by continuous adjustment of the syringe pressure that affected the vessel clamp. This approach was taken to minimize the number of guinea pigs in the study. If the alternative procedure had been used (i.e., apply constant pressure to the syringe and let BP be what it will), then animal and experimental variability could result in a wide range for the independent variable. Our approach could give information about the dynamic change in CBF much like a step response of a mechanical system. Indeed, in Fig. 1, the dynamic changes of CBF are easily seen, but they are not the subject of this report.

It is also beyond the scope of the present study to explore how closely the observed autoregulation is due to a myogenic response. One confounding factor is the potential role of the sympathetic reflex in influencing the results of this study. A complex sympathetic innervation of the cochlea exists (35), and recent work in our laboratory has indicated that LDF-measured flow can be reduced by ~15% with electric stimulation of the cervical ganglia (22, 33). The systemic pressure changes of the present study may also affect a change in circulating catecholamines. Thus it is not practical to eliminate sympathetic activity, although a local a-receptor blockade could be one approach to reduce the effects, because a-receptors appear to be present on cochlear blood vessels (28). If there is a sympathetic component of the autoregulation data, it would act counter to regulatory response. For example, increased systemic BP would result in peripheral vasodilation, while autoregulation would cause vasoconstriction.

Clearly, in animals having such low BP as the guinea pig, the system may also be subject to metabolic influences, particularly during the 2-min BP decreases imposed by our method. We do, however, address the question of the origin of the regulatory response. Is it from the vessels within the cochlea or partly or wholly due to the main feeder artery (the labyrinthine artery) and its first-order branch (the spiral modiolar artery)? To address this question we applied a 3% solution of SNP onto the RWM of the cochlea. We have shown in previous studies that the application of vasoactive agents to the round window is equivalent to topical treatment of the inner ear (28). Other work has demonstrated that SNP is a long-lasting and powerful vasodilator agent in the cochlea, increasing the LDF-measured flow (29).

Figure 6 shows that SNP reduced the amount of regulation significantly. The \( \% \Delta \text{CBF}/\% \Delta \text{BP} \) value of 0.87 ± 0.5 is much closer to 1, the slope representing no regulation. Because of the complex vascular anatomy of the cochlea and the unknown diffusion pattern of the drug applied to the RWM, the interpretation of this slope value is made difficult. That complete loss of regulation was not found could be interpreted to mean that vessels more central from the cochlea possess some of the regulatory capacity (i.e., the feeding arteries), because the vasodilator would be unlikely to diffuse to these vessels. However, it is possible that incomplete vasodilation was effected in the arterioles and venules within the cochlea because the SNP did not diffuse to the locations of these vessels or did not achieve sufficient concentration. We also observed some instances of excessive CBF percent change for a given BP percent change, an example of which is shown in Fig. 5D. Such responses are not expected in a “passive” system but could be due to properties of the LDF metric (i.e., hemoconcentration and velocity) as discussed above.

To our knowledge, the data presented here represent the first systematic quantitative evaluation of blood flow regulation in the cochlea. The evidence points to a strong autoregulatory capability of the inner ear. Further studies could investigate the dynamic components of the regulation and important issues such as the role of the sympathetic tone in the strength of the autoregulatory response [see Ping and Johnson (31)].

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