When the proper reconstruction is done, the time boundaries for the dust event match in all parts of the figure. These adjustments also alter the magnitudes of the solar and thermal radiation perturbations for 22 February, and these alterations are incorporated into the new evaluation of the data described below.

Their second major point, concerning the factor cos θ, is correct. This adjustment should have been made in our report. Also, the original diffuse solar radiation data were not corrected for the portion of this radiation obscured by the shade band. When these changes are made, along with the changes for 22 February and some changes discussed below, our final result is such that the trace of our original figure 2 (not the individual data points) has its ordinate values reduced 60 percent; the abscissa values remain unchanged. Thus, the curve still starts at a diffuse/normal-incidence ratio of about 0.04, peaks at a ratio of about 0.1, and crosses to negative values at a ratio of 0.9. It remains conceptually unaltered.

The last major point of Herman *et al.* concerns the initial state of the earth's atmosphere. Before considering the earth as a whole, however, we must consider our data acquisition sites. For instance, the dust event on 11 January (figure 1C) was preceded by an initial diffuse/normal-incidence ratio of about 0.05, while on 22 February and 15 April the initial ratio was about 0.1. Since our other data allowed us to determine separately the dependence of solar and thermal radiation perturbations on this ratio from its base value of 0.04 to well past 0.1, we were able to deduce what changes in both solar and thermal radiation should have transpired on 22 February and 15 April in going from 0.04 to the initial value of 0.1. These increments were algebraically added to the measured radiation perturbations in deducing the revised form of figure 2 described above.

Finally, considering the earth itself, we did not deal in our report with clouds, nor do we know what effects variable dust concentrations beneath a cloud layer would have on the net radiation balance at the earth's surface. Assuming a null effect, we would have to admit a further 50 percent reduction in our calculated net climatological radiation balance. Again, however, it remains conceptually the same. We cannot make a precise estimate of the mean value of the diffuse/normal-incidence solar radiation ratio of the nonovercast portion of the world. However, this is a crucial point, for if the mean earth ratio were coincident with the value at which we observe the maximum alteration in net radiation, either addition or subtraction of particulates from the atmosphere would tend to initiate a cooling trend. Thus, the last point of Herman *et al.* is very well taken and indicates a need to experimentally determine this ratio in many different environments. We feel, however, that this ratio is less than 0.1, for we have measured much less than that at Phoenix, which has significant natural and anthropogenic aerosol pollution. Until a considerable body of new data indicates differently, we hold to our original assessment of the situation, that increased particulate pollution of earth's troposphere must tend to warm the planet's suface.

SHERWOOD B. IDSO
U.S. Water Conservation Laboratory, Phoenix, Arizona 85040
ANTHONY J. BRAZEL
Geography Department, Arizona State University, Tempe 85281

Subfornical Organ: A Dipsogenic Site of Action of Angiotensin II

Several years ago it was proposed that intracranially injected material may not act at the site of injection but may, in fact, spread via the ventricles (*1*) or the cerebral vasculature (*2*) to then act at some distant locus. We have indicated that one target for the spread of dipsogenic agents is the subfornical organ (SFO) (*3*), a position supported in part because localized SFO lesions reduced drinking induced by intrahypothalamic angiotensin II (AII) (*4*). The report by Buggy *et al.* (*5*) attributed to us the view that "the subfornical organ (SFO) contains the exclusive receptors for angiotensin-induced drinking" (*5*, p. 72). Rather, we stated, "It is tempting to speculate that the central dipsogenic receptors for circulating angiotensin II are within the SFO" (*4*, p. 1174). Despite their inaccurate portrayal of our position, we believe that there is sufficient interest in determining central AII sites of action to warrant discussion of their findings and interpretations.

We consider first the SFO lesions made by Buggy *et al.* (*5*), who report that intracranial AII-induced drinking recovered after 70 to 100 percent destruction of SFO. The SFO consists of rostral, central, and caudal zones (*6*), each of which possesses ultrastructurally identifiable neuronal perikarya. Because detailed description of the extent of the lesions is not provided, it is difficult to determine to what "70 to 100 percent destruction," used to denote SFO lesions (*5*), refers. It is also difficult to ascertain what adjacent tissues (for example, choroid plexus basal laminae) were damaged by these lesions. Sparing of portions of the SFO might be responsible for the drinking after lesions observed by these authors, a point previously indicated (*4*, *7*). In our study (*4*), animals were classified in terms of neural damage rather than in terms of behavioral performance (*5*). We have found that animals sustaining less than thorough SFO lesions are not reduced in AII-induced drinking (*4*, *7*). The absence of permanent deficits in AII drinking after SFO lesions (*5*) may be attributable, in part, to the methods of producing or of evaluating lesions, or both (*8*).

It was suggested (*5*) that blockade of the interventricular foramen ipsilateral to intracranial injections of AII, and not ablation of the SFO, produced deficits in elicited drinking consequent to SFO lesions. While reduced drinking could occur if the ipsilateral interventricular foramen were completely occluded, Buggy *et al.* have not demonstrated the complete occlusion of the foramen. In their radioactive tracing experiments, in fact, the blockage was not complete (*5*). Thus, as compared to recovered lesioned animals, 11 percent of the 100- or 500-ng intraventricular dose of AII passed into subarachnoid space, presumably via ventricular diffusion (*9*). The threshold for lateral ventricular AII-induced drinking is less than 1 ng of AII (*10*). Since these authors classified animals in terms of the reduction in elicited drinking and not in terms of extent of SFO damage, the relative contribution of ventricular occlusion versus SFO damage to the observed deficits in AII drinking remains uncertain.

We think there is some question as to the definition of recovery (*5*) used. In the Pittsburgh data, there is a persistent deficit in elicited drinking at 8 days after the lesion. Although a slight increase relative to the initial deficit exists, this ignores the persistent deficit. Since control water intake values (for example, injection of vehicle after the lesion) are not reported, the drinking observed may reflect recovery of response to AII per se, neurological recovery from surgical trauma, or changes in performance to repeated injections of AII (*2*). The failure of complete recovery of 1.8 percent saline intake is especially noteworthy, as it is suggested that AII acts specifically to

0036-8075/78/0728-0379$00.50/0

increase sodium intake (*11*). In the Iowa study, the recovery of drinking after the lesion is greater, albeit still incomplete. However, in this study, the 100- or 500-ng doses of AII are usually considered excessive (*12*). It is possible that portions of the injected dose interacted with residual SFO tissue to give rise to the observed drinking. If a true recovery had occurred, it could have resulted from AII interaction with remaining SFO tissue (*4*).

Buggy *et al.* report that 3 days after SFO lesions there is a deficit in lateral ventricular (LV), but not in third ventricular (III-V), AII-induced drinking (*5*). In our experience, III-V placements near the optic recess would be ideal for delivery, via cerebrospinal fluid diffusion, of AII to the remaining SFO tissue. Alternatively, partial occlusion of the interventricular foramen, as noted above, could be responsible for deficits in LV or preoptic AII drinking. If the quantities of AII reaching the SFO after III-V injection were larger than those reaching the SFO after LV delivery, then the differences in elicited drinking may reflect dose-response differences in AII drinking (*5, 12*). Until the amount of AII actually entering the SFO in the two cases is known, one cannot rule out its involvement on these grounds. In addition, the use of intraventricular injection (*5*), rather than intravenous (*7*) or direct SFO (*4*) application of AII, makes it difficult to compare the results of Buggy *et al.* with our findings.

Finally, the authors injected cold cream into the third ventricle to reproduce the effect of ventricular obstruction. We believe that this manipulation may obscure rather than clarify the difficult and subtle localization problems discussed here and in their report (*5*). Although a more detailed report has appeared (*13*), we are still concerned about the nonspecific damage resulting from these injection procedures, and the multiple cannulas in an individual animal's brain.

We wish to emphasize that considerable evidence indicates that the SFO is a receptor for AII (*10*). Some of the most important data supporting this viewpoint are: (i) Specific SFO application of the physiologically meaningful dose of 1 pg of AII elicits drinking (*12*). This sensitivity is greater than for other cerebral loci (*14*), including the optic recess (*5*) and hypothalamus (*15*). (ii) Selective destruction of SFO permanently and specifically decreased drinking induced by intravenous AII (*7, 10, 16, 17*). Destruction of tissue dorsal, lateral (including the ependyma lining the interventricular foramina), and/or ventral to SFO is without effect (*10, 17*). (iii) Application of low doses of the competitive AII antagonist, Saralasin, to the SFO but not the adjacent tissue or ventricles reversibly and specifically blocks systemic AII drinking (*14, 17*).

In summary, the report of Buggy *et al.* (*5*) is subject to alternative interpretation. That SFO lesions prevent AII-induced drinking by causing occlusion of the interventricular foramina is not adequately demonstrated. Indeed, perusal of our SFO lesions that prevented AII drinking suggests quite the opposite; an enlarged space exists in the interventricular foramina of SFO-lesioned animals [for example, figure 2 in (*4*)]. The implication should not be drawn, then, that these authors have ruled out the involvement of the SFO in AII drinking. Rather, the hypothesis that the SFO contains dipsogenic receptors for circulating AII (*4*) is supported by considerable evidence and, indeed, by several recent reports (*13, 15*). Whether the SFO is the exclusive dipsogenic receptor for AII has not been determined.

JOHN B. SIMPSON
Department of Psychology, University of Washington, Seattle 98195
ARYEH ROUTTENBERG
Cresap Neuroscience Laboratory, Department of Psychology, Northwestern University, Evanston, Illinois 60201

References and Notes

1. A. Routtenberg, *Science* **157**, 838 (1967).
2. ———, *Behav. Biol.* **1**, 601 (1972).
3. ——— and J. B. Simpson, *Life Sci.* **10**, 481 (1971); J. B. Simpson and A. Routtenberg, *Brain Res.* **45**, 135 (1972).
4. J. B. Simpson and A. Routtenberg, *Science* **181**, 1172 (1973).
5. J. Buggy *et al.*, *ibid.* **190**, 72 (1975).
6. H.-D. Dellmann and J. B. Simpson, *Brain Res.* **116**, 389 (1976).
7. J. B. Simpson and A. Routtenberg, *ibid.* **88**, 154 (1975).
8. Buggy *et al.* (*5*) used either three penetrations of steel insect pin electrodes, with 1.5 mA for 15 seconds per penetration, or one penetration of Nichrome wire electrode with 2 mA for 30 seconds. Stereotaxic coordinates are not indicated. Simpson and Routtenberg (*4*) used three penetrations of a 127-μm tungsten wire electrode, with 1.0 mA anodal current for 20 seconds per penetration. In the absence of accurate anatomical documentation of the lesions in the report by Buggy *et al.* (*5*), comparison between experiments (*4, 5*) is impossible. Further, the difficulties inherent in stereotaxically manipulating the SFO in the rat have been discussed (*3, 4, 7*).
9. Buggy *et al.* (*5*) indicate cisternal recovery, following lateral ventricular injection, of 4.0 count/min of [^{14}C]angiotensin II in lesioned rats with drinking deficit versus 37.7 count/min in lesioned rats without drinking deficit and 85.8 count/min in nonlesioned controls. Comparisons between lesioned-deficit rats and either control group indicates measurable percentage of the label fluxed from site of injection to site of collection. Hence, complete obstruction of the interventricular foramen does not result from SFO lesions in (*5*), and initial cessation of AII drinking cannot be totally attributed to ventricular occlusion.
10. J. B. Simpson, *Central Actions of Angiotensin and Related Hormones*, J. P. Buckley and C. W. Ferraria, Eds. (Pergamon, New York, 1977), p. 439.
11. J. Buggy and A. E. Fisher, *Nature (London)* **250**, 733 (1974).
12. J. B. Simpson, A. N. Epstein, J. S. Camardo, Jr., *Physiologist* **18**, 391 (1975).
13. W. E. Hoffman and M. I. Phillips, *Brain Res.* **108**, 59 (1976); J. Buggy and A. E. Fisher, *Pharmacol. Biochem. Behav.* **4**, 651 (1976).
14. The lowest reported threshold doses of intracranially injected AII at loci other than the SFO are 1.0 ng applied to preoptic area or lateral ventricle [A. K. Johnson and A. N. Epstein, *Brain Res.* **86**, 399 (1975)], or to lateral or dorsal third ventricle (*10*).
15. J. Kucharczyk, S. Y. Assaf, G. J. Mogenson, *ibid.* **108**, 327 (1976).
16. A. E. Abdelaal, S. Y. Assaf, J. Kucharczyk, G. J. Mogenson, *Can. J. Physiol. Pharmacol.* **52**, 1217 (1974).
17. J. B. Simpson, A. N. Epstein, J. S. Camardo, Jr., *Fed. Am. Soc. Exp. Biol.* **34**, 374 (1975).
18. Supported by NS 10768 to A.R.

1 February 1977; revised 9 August 1977

In addition to the well-known peripheral actions of vasoconstriction and stimulation of aldosterone release, the hormone angiotensin (AII) also contributes to regulation of blood volume and blood pressure by a direct action on the central nervous system to increase antidiuretic hormone release and blood pressure, and to arouse thirst (*1*). To better understand the functional significance of these AII-sensitive central mechanisms, we have attempted to localize the central site or sites of action of this hormone. The subfornical organ (SFO) was proposed as the central dipsogenic site of action for angiotensin by Simpson and co-workers (*2*). Our experimental results (*3*), however, demonstrated that dipsogenic responses normally elicited by intracerebroventricular (ICVT) administration of AII could still be obtained when the hormone was prevented from acting on SFO by either restriction of AII access to SFO or by ablation of SFO. These data led us to conclude that "SFO cannot be the exclusive dipsogenic receptor site for AII," and implicated preoptic-hypothalamic periventricular tissue bordering the anteroventral third ventricle (AV3V) "as a likely site for angiotensin receptors" (*3*, pp. 72 and 74). Rather than debating whether we have, as Simpson and Routtenberg (*4*) suggest, inaccurately portrayed their position (*2*), we elect to review here the data that prompted our conclusion (*3*) and to summarize more recent data that demonstrate the functional significance of the AV3V for not only AII-induced thirst but also pressor and antidiuretic responses.

In agreement with Simpson and Routtenberg (*2*), we found that an SFO lesion in the rat could under certain conditions block drinking induced by intracranial injections of AII (*3*). However, we also observed that the blockade of AII-induced drinking by an SFO lesion was not uniform since, at a time when drinking induced by injection into the lateral ventricle (LV) was blocked, the drinking response induced by injection of AII into

AV3V was unaltered in the same animals. Moreover, the selective reduction in drinking induced by LV injections after SFO ablation was only temporary, with significant recovery of drinking over time. Simpson and Routtenberg argue that our description of the extent of SFO damage is insufficiently detailed and that residual SFO tissue might have accounted for our observations. Although limited space prevented our giving a detailed description (*3*), histological documentation of extent and completeness of our SFO ablations and correlation to drinking deficits and recovery is provided in later full-length articles (*5, 6*), which Simpson and Routtenberg do site but in a different context [reference 13 in (*4*)].

Convinced of the completeness of our SFO ablations, we proposed (*3*) that edema or debris after SFO lesions might have blocked the interventricular foramen and retarded cerebrospinal fluid (CSF) circulation from LV to the rest of the ventricular system, including the AV3V. Radioactive tracing experiments in rats with SFO lesions qualitatively demonstrated such an obstruction but could not quantify the amount of intact hormone reaching the receptors (*3, 5, 6*). In rats with intact SFO, simulation of interventricular foramen obstruction by controlled placement of plugs that blocked CSF flow duplicated the effects of SFO lesions on drinking induced by ICVT injection of AII.

Although Simpson and Routtenberg "believe that this manipulation may obscure rather than clarify the difficult and subtle localization problems" (*4*), we contend that the results from ventricular obstruction experiments cannot be dismissed without cause. The selective disruption of drinking is due not to the obstruction by plugs or multiple cannulas per se since each animal served as his own control; the rat with a plug obstructing the interventricular foramen no longer drank in response to LV injections but did continue drinking normally in response to AV3V injections of AII. By varying ventricular injection and plug sites, AII-induced pressor and antidiuretic responses, as well as drinking, are undiminished when hormone access to SFO is prevented, but abolished when hormone access to AV3V is prevented, even if the hormone has unimpeded access to SFO (*5–8*). Furthermore, converging results were produced with a different method, since ablation of the AV3V region in rats with intact SFO also abolished drinking, pressor, and antidiuretic responses to ICVT injections of AII (*9–11*). Taken together, results of the plug and lesion experiments implicate AV3V as a necessary central site of action but indicate that the SFO is neither necessary nor sufficient for responses elicited by ICVT injections of AII.

Simpson has also reported dipsogenic sensitivity of SFO to AII doses as low as 1 pg (*12*). While acknowledging this exceptional sensitivity, it should be recognized that the SFO is not uniquely sensitive since injections into AV3V of 50 fg of AII have recently been reported to elicit pressor and drinking responses (*8*). These demonstrations of unusual sensitivity are of interest because the organum vasculosum of the lamina terminalis, a structure within the AV3V region, and the SFO are highly vascularized circumventricular organs lacking a blood-brain barrier and are thus possible ports of entry to the brain for circulating AII. Simpson and co-workers (*12, 13*) have reported that, after SFO lesions, drinking induced by intravenously administered AII was abolished for infusion of near threshold dose but only attenuated after near maximally effective doses. Other investigators have also noted that drinking following peripheral administration of AII or renin is reduced but not abolished in rats with SFO ablation (*5, 14*). Ventricular obstruction after SFO lesions is unlikely to account for these effects since, in contrast to ICVT administration, ventricular obstruction with plugs did not reduce drinking induced by peripheral administration of AII (*10*). Thus, the SFO appears to play at least a partial role in mediating drinking induced by AII circulating in blood.

Ablation of AV3V, on the other hand, both abolished drinking induced by peripheral administration of AII and reduced by about 40 percent the overall (60 percent direct peripheral plus 40 percent central component) pressor response to intravenous infusion of 100 to 900 ng of AII per kilogram per minute (*15*). Therefore, the evidence suggests that the SFO and AV3V are both involved in mediation of central responses to blood-borne AII. We have noted (*5*) that the SFO and the organum vasculosum of the lamina terminalis have common vascular and neural connections (*16*) and proposed (*17*) that they may function as an access system for blood-borne AII to central receptors. A more detailed account of the means by which AII circulating in blood affects the brain is lacking. The functional relation between the SFO and AV3V in monitoring AII levels in blood remains an unresolved matter for study; our working hypothesis is that the SFO contribution depends on its vascular or neural connections with AV3V.

Available data indicate that centrally mediated responses to AII in the rat do not require the SFO after ICVT administration, but are partially dependent on the SFO after peripheral administration; the AV3V region appears essential for centrally mediated drinking, antidiuretic, and pressor responses to AII circulating in either CSF or blood.

JAMES BUGGY
Department of Physiology, University of South Carolina School of Medicine, Columbia 29208
ALAN E. FISHER
Department of Psychology, University of Pittsburgh, Pittsburgh, Pennsylvania 15213
WILLIAM E. HOFFMAN
Department of Physiology, Texas A & M University School of Medicine, College Station 77843
A. KIM JOHNSON
Department of Psychology, University of Iowa, Iowa City 52242
M. IAN PHILLIPS
Department of Physiology and Biophysics, University of Iowa

References and Notes

1. R. K. Bickerton and J. P. Buckley, *Proc. Soc. Exp. Biol. Med.* **106**, 834 (1961); A. N. Epstein, J. T. Fitzsimmons, B. J. Rolls, *J. Physiol. (London)* **210**, 457 (1970); W. B. Severs, J. Summy-Long, J. S. Taylor, J. D. Connor, *J. Pharmacol. Exp. Ther.* **174**, 27 (1970).
2. J. B. Simpson and A. Routtenberg, *Science* **181**, 1172 (1973); A. N. Epstein and J. B. Simpson, *Acta Physiol. Lat. Am.* **24**, 405 (1974).
3. J. Buggy, A. E. Fisher, W. E. Hoffman, A. K. Johnson, M. I. Phillips, *Science* **190**, 72 (1975).
4. J. B. Simpson and A. Routtenberg, *ibid.* **201**, 379 (1978).
5. J. Buggy and A. E. Fisher, *Pharmacol. Biochem. Behav.* **4**, 651 (1976).
6. W. E. Hoffman and M. I. Phillips, *Brain Res.* **108**, 59 (1976).
7. ———, *ibid.* **110**, 313 (1976).
8. M. I. Phillips, J. Quinlin, C. Keyser, J. Phipps, *Fed. Proc. Fed. Am. Soc. Exp. Biol.* **38**, 438 (1978).
9. J. Buggy, W. E. Hoffman, A. K. Johnson, *Soc. Neurosci. Abst.* **3**, 340 (1977).
10. J. Buggy and A. K. Johnson, *Brain Res.*, in press.
11. M. I. Phillips and W. E. Hoffman, in *Central Actions of Angiotensin and Related Hormones*, J. P. Buckley and C. M. Ferrario, Eds. (Pergamon, New York, 1977), p. 325; also see B. Andersson, G. Leksell, F. Lishajko, *Brain Res.* **99**, 261 (1975).
12. J. B. Simpson, in *Central Actions of Angiotensin and Related Hormones*, J. P. Buckley and C. M. Ferrario, Eds. (Pergamon, New York, 1977), p. 439.
13. J. B. Simpson and A. Routtenberg, *Brain Res.* **88**, 154 (1975).
14. A. E. Abdelaal, S. Y. Assaf, J. Kucharczyk, G. S. Mogenson, *Can. J. Physiol. Pharmacol.* **52**, 1217 (1977); J. Kucharczyk, S. Y. Assaf, G. J. Mogenson, *Brain Res.* **108**, 327 (1976).
15. J. Buggy and A. K. Johnson, *Am. J. Physiol.* **233**, R44 (1977); J. Buggy, G. D. Fink, A. K. Johnson, M. J. Brody, *Circ. Res.* **40**, (Suppl. I), I-110 (1977).
16. J. Hernesniemi, E. Kawans, H. Bruppacher, C. Sandri, *Acta Anat.* **81**, 321 (1972); P. R. Lewis and C. C. D. Shute, *Brain* **90**, 521 (1967); V. Spoerri, *Acta Anat.* **54**, 333 (1963).
17. A. K. Johnson and J. Buggy, in *Central Actions of Angiotensin and Related Hormones*, J. P. Buckley and C. M. Ferrario, Eds. (Pergamon, New York, 1977), p. 357.

17 February 1978