age number of intromissions per minute (Fig. 2) (*15*).

These data support our hypothesis. Eliminating the efferent control of the VNO pump produces deficits similar to those obtained after eliminating the afferent outflow from the VNO. There were differences, however, between the performance of the two groups in the estrous-female test. When compared with the sham group, both showed statistically significant deficits in this test, but the deficit in the VN + $ZnSO_4$ group was significantly more severe ($P < .001$) (*14*). Because the VN organ and nerves were intact in NP + $ZnSO_4$ animals, one or more of the following explanations may account for the difference between groups. (i) There may be some diffusion of small amounts of stimulus substances into the VNO during the course of the 10-minute estrous-female test. (ii) The stress of handling and encounters with other behaving animals may result in some activation of the vascular pump through fluctuations in systemic blood pressure. (iii) Changes in concentration of circulating epinephrine might also operate the pump directly (*16*), especially if the adrenergic target tissue in the VNO were subject to denervation hypersensitivity, as has been suggested for other tissues (*17*).

The deficits observed in NP + $ZnSO_4$ animals in the cycling female test are, in any case, unequivocal. In the scented male test, where many cues associated with receptive females are excluded, the results are even more striking. Here NP + $ZnSO_4$ and VN + $ZnSO_4$ animals showed almost identical deficits. Under these conditions any residual VN afferent input in the animals with NP nerve lesions seems to be insufficient to maintain the behavior. We interpret the results of these experiments as evidence that the VNO pumping mechanism previously demonstrated in anesthetized animals is necessary for normal stimulation of the VNO in behaving animals.

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7. The procedures of Powers and Winans (*2*) were used for cutting the VN nerves between the main olfactory bulbs and for administering $ZnSO_4$.
8. After being exposed through the palate, the NP nerves running along the free ventral border of the nasal septum were cauterized bilaterally.
9. Animals were tested once a day in 43 by 22 by 15 cm cages during the first 3 hours of the dark phase of a 14-hour light, 10-hour dark reversed light cycle. The two tests of sexual behavior were alternated with a test for attraction to the vaginal odor as part of a separate experiment. Animals from all four groups were divided into two sets, which received the three tests in a counterbalanced order. Tests were conducted during October.
10. The term vaginal discharge does not imply a pathological condition. It is used because the behavioral effects of the discharge may be due to chemicals that are not secreted but produced by microbial action [R. E. Johnston, *Behav. Biol.* **12**, 111 (1974); A. G. Singer, W. C. Agosta, R. J. O'Connell, C. Pfaffmann, D. V. Bowen, F. H. Field, *Science* **191**, 948 (1976); (*11*)].
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13. Animals were anesthetized and killed by cardiac perfusion with saline and 10 percent formalin. Heads were decalcified in 4.13 percent EDTA and embedded in paraffin. The VNO and the NP nerve regions were cut coronally at 12 to 14 μm; the bulbs were cut horizontally at 12 μm and stained with Kluver-Barrera stain. Small areas of near normal olfactory epithelium could be seen in most of our animals 9 to 10 days after $ZnSO_4$ infusion. At this time, some animals also exhibited behavioral evidence for returning olfactory function, but all of these continued to show deficits in sexual behavior. In the NP + $ZnSO_4$ group, all animals included in the analysis had no observable NP fibers remaining, but all showed intact blood vessels passing by the cauterized region to supply the VNO. In the VN + $ZnSO_4$ group, animals had complete cuts as judged by our inability to follow the remnants of the VN nerve through the region of the cut in serial 12-μm horizontal sections. We used Powers and Winans' procedure (*2*) but found that the glomeruli of the AOB had not entirely degenerated at 10- and 20-day survival times. In separate experiments with the same cutting procedure, horseradish peroxidase flushed into the nose was not transported to the AOB as it was in control animals. We therefore believe that we made complete cuts in our animals.
14. Results of all tests were analyzed by calculating the postoperative score as a percentage of the preoperative score for each animal. Each set of data was first subjected to Kruskal-Wallis analysis of variance to confirm differences between groups. Scores of different groups were then compared with Mann-Whitney U tests. Excluding those with incomplete lesions or incomplete data there were eight sham, nine $ZnSO_4$, seven VN + $ZnSO_4$, and six NP + $ZnSO_4$ animals.
15. This measure is a more accurate reflection of deficits since control animals reached five intromissions (the limit) in much less than the 10 minutes allowed.
16. Epinephrine injected into the carotid artery causes vasoconstriction in the blood vessels surrounding the VNO and results in the suction of mucus or air in through the VN duct (*6*).
17. V. B. Mountcastle Ed., *Medical Physiology* (Mosby, St. Louis, 1974), vol. 1, pp. 797–798.
18. We thank David Heath for excellent technical assistance. Supported in part by National Institute of Neurological and Communicative Diseases and Stroke fellowship NS05849 (to M.M.) and grant NS14453 (to R.J.O.).

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Differences in the Distribution of Gray and White Matter in Human Cerebral Hemispheres

Abstract. *The distribution of gray matter in the two cerebral hemispheres was determined by the xenon-133 inhalation method. There was more gray matter relative to white matter in the left hemisphere than in the right, particularly in the frontal and precentral regions. This finding suggests that the organization of the left hemisphere, relative to that of the right, emphasizes processing or transfer within regions, or both, rather than transfer across regions.*

No coherent body of data exists to explain why the left hemisphere specializes in analytic, logical, and verbal functions (*1*), whereas the right hemisphere subserves holistic, gestalt, spatial functions (*2*). Although the two hemispheres seem to contain equal amounts of neural tissue (*3*), a greater density of cells has been reported in the left than in the right hemisphere (*4*), the surface of the planum temporale is larger and the sylvian fissure is longer in the left hemisphere (*5*), and the left hemisphere is more extensively fissured than the right (*6*). These differences in themselves, however, do not give sufficient clues to the mechanisms responsible for functional differences between the hemispheres. We now present evidence, based on rates of isotopic clearance, for interhemispheric differences in amount and distribution of gray and white matter.

In a recently developed, noninvasive method for measuring regional cerebral blood flow, the subject inhales ^{133}Xe (*7*). Clearance of the xenon from the brain is measured by sodium iodide crystal detectors placed over the subject's head. We tested 36 right-handed male undergraduates who had no left-handed first-degree relatives. Eight detectors were placed over homologous regions of each hemisphere (Fig. 1). Using a two-compartmental analysis (*7*), we calculated the relative weight (w_1) of perfused gray matter, expressed as a percentage of the total weight (gray and white matter) of perfused tissue, for each location (*8*).

Values for w_1 were greater for the left than for the right hemisphere [F(1,

35) = 36.43, $P < .001$] (*9*); that is, the ratio of gray to white matter was greater in the left hemisphere than in the right. The differences among regions within a hemisphere were also significant [$F(7, 245) = 44.66, P < .001$], as was the interaction [$F(7, 245) = 11.17, P < .001$] (Fig. 1) (*10*).

The value of w_1 was greater for the left hemisphere than for the right in all but the parietal-central and one of the temporal areas. The proportion of gray matter was significantly greater in the left hemisphere for detectors 1, 3, 4, and 8 (all $P < .02$) and in the right hemisphere for detector 5 ($P < .02$). (The differences for the other three pairs were not significant.) Thus, the differences between the two hemispheres are particularly pronounced in the frontal and precentral regions, areas involved in speech production and abstract reasoning.

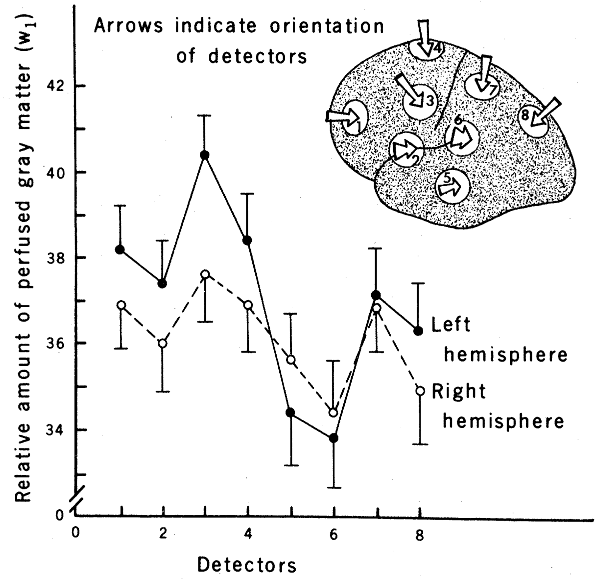

Fig. 1. Relative amount (± standard errors) of perfused gray matter (w_1) plotted separately for eight homologous regions in the left and right hemispheres.

Although our detectors sampled fairly large and representative regions of the brain, there were areas, particularly in the occipital and some of the temporal regions, that we did not sample (*11*). The ratio of gray to white matter in these areas is conceivably different from what we have observed. In particular, our detectors did not adequately sample temporal regions generally assumed to subserve language processing. However, McHenry *et al.* (*12*) sampled both the anterior and the posterior temporal regions and found that these regions contained the largest ratios of gray to white matter and that the ratios were higher in the left than in the right hemisphere. In general, the ratio of gray to white matter was greater in the left for five of their seven detectors (*13*). Meyer *et al.* (*14*) used different detector locations in which occipital and a number of temporal regions were sampled. In all of the seven homologous pairs of detectors, w_1 was greater for the left hemisphere than for the right. Blauenstein *et al.* (*15*) found approximately equal values for w_1 in the two hemispheres for the regions sampled. If all four studies thus far reported are considered jointly, w_1 values were larger for the left than the right hemisphere in 21 of 28 homologous pairs of detectors that showed interhemispheric differences ($P < .001$). Thus, it is unlikely that our findings of an interhemispheric difference in w_1 were an artifact of our sampling of brain regions.

Our results could also be stated as showing a higher ratio of white matter to gray matter in the right hemisphere than in the left. Given Connolly's (*6*) report of greater fissuration in the left hemisphere, LeMay's finding (*16*) that the right frontal lobe and the left parieto-occipital regions tend to be wider in humans, and Berger's report (*4*) of greater cell density in the left hemisphere, it is reasonable to suspect that, at least in the precentral regions sampled in our study, there is more white matter in the right hemisphere and more gray matter in the left in absolute terms. Gray matter consists of nerve cells and nonmyelinated fibers, whereas white matter consists primarily of myelinated fibers. Thus, our results suggest that verbal-analytic functions are subserved by an organization that emphasizes processing or transfer within regions, whereas spatial-gestalt functions are subserved by an organization that optimizes transfer across regions.

The greatest amount of w_1, as well as the greatest interhemispheric difference in the relative amount of gray matter, was recorded in region 3. These homologous detectors were positioned over the region that includes the basal ganglia—structures associated with fine sensorimotor control (*17*). As Semmes (*18*) pointed out, it is probably not a coincidence that the dominant hemisphere for language also has sensorimotor control over the better-coordinated hand. Rather, this fact suggests that "differences at these simpler levels [that is, sensorimotor control] are indicative of a contrast in neural organization which favors hemispheric specialization" (p. 12). Discrete lesions in the left hemisphere produce specific sensorimotor deficits, whereas similar deficits resulting from damage to the right hemisphere depend less specifically on locus (*18*). Semmes concluded that the left hemisphere is heterogeneously or focally organized, favoring integration of similar units of information, while the right hemisphere contains more homogeneous or diffuse representation of elementary functions, favoring integration of dissimilar units. The focal organization of the left hemisphere may underlie "specialization for behaviors that demand fine sensorimotor control, such as manual skills and speech" (p. 11), while the diffuse organization of the right hemisphere underlies "specialization for behaviors requiring multimodal coordination, such as various spatial abilities" (p. 11). Semmes did not suggest neurophysiological substrates for these asymmetries. However, there is greater variability across regions in the left than in the right hemisphere (Fig. 1). We determined, for each subject, the variance of w_1 across regions for the left and right hemispheres. Homogeneous distribution of w_1 should produce a lower variance. Conversely, focal or-

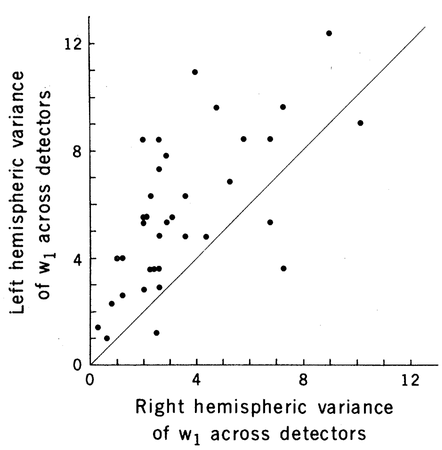

Fig. 2. The variance of w_1 across eight regions in the left and right hemispheres for individual subjects. Each subject is represented by a dot; a dot above the diagonal indicates greater left than right hemispheric variance.

ganization should be associated with greater variability.

Variation across regions in the left hemisphere was greater than in the right hemisphere [$t(35) = 6.30$, $P < .001$)] (Fig. 2). The variances in the two hemispheres positively correlated ($r = .64$), and the variability of w_1 in the left hemisphere was greater than that in the right hemisphere for 32 out of the 36 subjects (*19*).

The relative weight of gray matter was greater in the left hemisphere than in the right for 31 subjects. In the five other subjects, the variance of w_1 was greater in the left hemisphere. Conversely, the four subjects with more variable w_1 in the right hemisphere had a higher w_1 in the left hemisphere. Three quarters of the subjects had both greater w_1 and greater variance in w_1 in the left hemisphere. Since all subjects were right-handed males, with no left-handed first-degree relatives, we can assume language dominance in the left hemisphere. All subjects had either greater relative amount or more variation of gray matter in the left than in the right hemisphere. Therefore, hemispheric differences in magnitude and variability of w_1 may be potential markers of language dominance. To validate these markers, however, they must be studied in subjects with right-hemispheric dominance for language (*20*). Further, subjects who differ in degree of hemispheric specialization (*21*) should be studied in order to determine the extent to which our measures reflect individual differences in the degree as well as the direction of functional cerebral asymmetry.

Our findings suggest a further line of investigation centering on the relation between the distribution of the two types of neural tissue in the cerebral hemispheres and the morphological and cytoarchitectonic asymmetries discovered earlier (*5*). It would be of interest, for example, to find out whether the larger planum temporale in the left hemisphere reflects an increase in the amount of gray matter, white matter, or both types of neural tissue. A more complete understanding of structural and functional asymmetries in the human brain could also be obtained by three-dimensional histological and tomographic studies. Such research will not only help identify the areas in which the most pronounced differences between the two hemispheres occur, but can also suggest more detailed mechanisms to account for the functional differences among those regions.

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8. The relative tissue weights are derived from the coefficients of the biexponential equation used to represent clearance of ^{133}Xe from the brain. Given the exponential decay constants, which are obtained by an iterative least-squares curve-fitting procedure, we solved for the coefficients, w_i (i = 1,2), by linear regression. For details of the method, see [(*7*); J. Risberg, A. Ali, E. M. Wilson, *Stroke* **6**, 142 (1975)]. In the normal brain, w_1 is assumed to represent gray matter, which has a perfusion rate approximately four times that of white matter.
9. Inspection of the distribution of w_1 values revealed no significant deviations from normality, which justified the use of parametric statistics.
10. Each subject was also tested during the performance of a verbal task (analogies taken from the Miller Analogies Test) and during the performance of a spatial task [R. B. Ekstrom, J. W. French, H. H. Harman, D. Dermen, *Gestalt Completion Test: Manual for Kit of Factor Referenced Cognitive Tests* (Educational Testing Service, Princeton, New Jersey, 1976)]. The results for w_1 in these conditions duplicated the results presented here. For the verbal task, the effect of hemispheres was significant [$F(1, 35) = 4.80, P < .05$], as were the effect for detectors [$F(7, 245) = 41.16, P < .001$] and the interaction [$F(7, 245) = 15.50, P < .001$]. For the spatial task, the effect of hemispheres was also significant [$F(1, 35) = 13.52, P < .002$], as were the effect of detectors [$F(7,245) = 43.12, P < .001$] and the interaction [$F(7, 245) = 12.31, P < .001$]. There was no effect of task on w_1.
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19. We assumed that variations in the tissue-blood partition coefficients of Xe for gray and white matter, if they exist, are the same for the two hemispheres. Given that our subjects were normal young college students, this seems to be a reasonable assumption. A question can also be raised with regard to the validity of comparing w_1 across different regions, since w_1 is calculated from a two-compartmental analysis when a third compartment, extra cerebral tissue, contributes a small number of counts. However, D. H. Ingvar, F. Philipson, P. Torlof, and A. Anders [in *Cerebral Function, Metabolism and Circulation*, D. H. Ingvar and N. A. Lassen, Eds. (Munksgaard, Copenhagen, 1977)], using the intracarotid technique that greatly reduces the influence of this compartment, found a distribution of gray matter within a hemisphere that is similar to ours. Furthermore, Meyer *et al.* (*14*) subtracted the radiation emanating principally from the third compartment and found that the differences in w_1 between the left and the right hemispheres were in fact accentuated by this procedure. Finally, the distribution as determined by our technique is congruent with the distribution of perfused gray matter obtained by measuring cerebral blood volume with emission tomography [R. L. Grubb, M. E. Raichle, C. S. Higgins, J. O. Eichling, *Ann. Neurol.* **4**, 322 (1978)].
20. For example, right-handed persons who use the inverted writing posture and left-handed persons who use the noninverted writing posture [J. Levy and M. Reid, *Science* **194**, 337 (1976)].
21. For example, females and left-handed persons who use the inverted writing posture [S. F. Witelson, *Science* **193**, 425 (1976); (*20*)].
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