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Evolution of spatial cognition: Sex-specific patterns of spatial behavior predict hippocampal size

(sex differences/brain/mammal)

LUCIA F. JACOBS*†, STEVEN J. C. GAULIN*, DAVID F. SHERRY‡, AND GLORIA E. HOFFMAN§

*Department of Anthropology, University of Pittsburgh, Pittsburgh, PA 15260; ‡Department of Psychology, University of Toronto, Toronto, ON M5S 1A1, Canada; and §Department of Physiology, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261

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ABSTRACT **In a study of two congeneric rodent species, sex differences in hippocampal size were predicted by sex-specific patterns of spatial cognition. Hippocampal size is known to correlate positively with maze performance in laboratory mouse strains and with selective pressure for spatial memory among passerine bird species. In polygamous vole species (Rodentia: *Microtus*), males range more widely than females in the field and perform better on laboratory measures of spatial ability; both of these differences are absent in monogamous vole species. Ten females and males were taken from natural populations of two vole species, the polygamous meadow vole, *M. pennsylvanicus*, and the monogamous pine vole, *M. pinetorum*. Only in the polygamous species do males have larger hippocampi relative to the entire brain than do females. Two-way analysis of variance shows that the ratio of hippocampal volume to brain volume is differently related to sex in these two species. To our knowledge, no previous studies of hippocampal size have linked both evolutionary and psychometric data to hippocampal dimensions. Our controlled comparison suggests that evolution can produce adaptive sex differences in behavior and its neural substrate.**

The hippocampus, a large forebrain structure, plays an important role in spatial learning (1–3). Rodents given hippocampal lesions show impaired performance on spatial tasks (4–6), and spatial performance is positively correlated with certain hippocampal dimensions in inbred mouse strains (7–9). Hippocampal size also varies between males and females in laboratory rats (10) and across species (11, 12). Recent evidence suggests that variation in hippocampal size among species may be adaptively related to interspecific differences in the intensity of selection for spatial processing: the hippocampus is relatively larger in birds that hoard food items in scattered locations than it is in avian species that do not use this spatially demanding foraging tactic (13–15). In general, ecological pressures are known to shape brain evolution (16–18). In this paper, we integrate field and laboratory data on spatial behavior with measures of hippocampal size to show that evolution may produce adaptive sex differences in particular brain structures.

Likely candidates for neural sex differences are species known to exhibit adaptive sex differences in spatial ability. Spatial ability should evolve in proportion to the navigational demands that an individual faces in its natural environment. In most mammalian species, males and females exploit the same environment, but the patterns of competition for mates determine how the two sexes exploit this environment. In monogamous species, the sexes exhibit convergent reproductive strategies. They exploit the environment in similar ways and therefore are subject to similar selective pressures for spatial ability. Conversely, divergent reproductive strategies predominate in polygamous species. Here, range expansion is an important tactic used by polygamous males to maximize the number of potential mates (19). Thus, under polygamy, the two sexes experience divergent selective pressures for spatial ability.

The genus *Microtus* displays nearly the entire range of mammalian mating systems; some species are strongly polygamous and others are monogamous (20, 21). In the polygamous meadow vole (*M. pennsylvanicus*), breeding males have range sizes 4–5 times larger than those of females. This sex difference in range size is absent among immature meadow voles and among adults outside the breeding season, indicating that range expansion is a sexually selected male reproductive tactic (22). Monogamous vole species, such as pine (*M. pinetorum*) and prairie voles (*M. ochrogaster*), lack such sex differences in ranging behavior, regardless of age or reproductive condition (22–24). These species- and sex-dependent patterns in ranging behavior probably constitute an important selective pressure for spatial ability.

Under laboratory conditions, voles of polygamous species exhibit strong sex differences in spatial ability; in contrast, monogamous vole species, tested under identical conditions, lack such sex differences (23, 24). The laboratory rat is a domesticate of polygamous ancestry (25), and its sex-related patterns of maze performance have been known for 75 years (26). Males make significantly fewer errors than females in a wide range of maze types (27–33). This sex difference seems to be less replicable in radial mazes (34–36), but it is by no means always absent (37–40), and its direction is never reversed in normal rats.

The sex difference in maze performance in rats is sometimes attributed to the fact that female rats are more active in open-field tests, and this difference has been suggested to explain their higher error rate in maze tests (41). No direct test of this hypothesis exists for rats, but it can be rejected for voles, where the more error-prone sex is less, not more, active during maze testing (42). Thus, the available data on rats and voles suggest that particular mating systems foster sexually dimorphic ranging patterns, whereas other mating systems foster monomorphism in both naturalistic behavior and psychometric performance.

If sexual selection for ranging behavior has influenced the evolution of cognitive skills, then the consequences of selection for spatial processing should be evident not only in maze performance but also in the hippocampus of wild voles. To test this hypothesis, we measured sex differences in hippocampal size in two vole species whose mating systems differ markedly: polygamous meadow voles and monogamous pine voles. These measurements allowed us to compare the magnitude and direction of hippocampal sex differences within each species. As we had no *a priori* hypotheses about the presence or absence of morphological sex differences elsewhere in the brain, we did not examine other structures.

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†To whom reprint requests should be addressed.

Moreover, the hypothesis predicts the presence or absence of differences in hippocampal size between males and females, not between species. Cross-species comparisons are subject to more confounding influences than is the present design of within-species, between-sex comparisons. For example, some vole species are more fossorial than others, and thus species may differ in the three-dimensionality of their ranges, whereas males and females of a single species do not.

Because our hypothesis predicts an adaptive pattern occurring under natural conditions, we used wild-caught rather than lab-reared subjects. There is an effect of rearing conditions on the structure of the hippocampus in the laboratory rat (43, 44). Our hypothesis predicts the outcome of selection on the adult male and female phenotypes, but makes no predictions about the ontogenetic pathway leading to such phenotypic differences. Whether an adult's hippocampal size is determined solely by gender, as suggested by the persistent behavioral sex differences seen in laboratory rat strains (26–33, 37–40), or by spatial experience, is an important question. If sex differences in hippocampal size were shown to be entirely dependent on sex differences in experience, the developmental basis of these neuroanatomical sex differences would be clarified. In fact, maze performance seems largely independent of spatial experience in voles (45). But neither the presence nor the absence of experiential effects would preclude an evolutionary analysis of adult sex differences.

METHODS

We had previously assessed ranging behavior and spatial ability in meadow voles and pine voles, so we returned to our former study sites to collect the subjects for this study. During the breeding season, we trapped 10 adult females and males of each species. The process of trapping in the wild might bias the choice of subjects; however, any biases should have had similar consequences in the two species. After pentobarbitol anesthesia (dosage, 40 mg/kg of body weight), gross body measures were taken, including body weight and body length. Voles were then transcardially perfused with physiological saline followed by Perfix (Fisher). Perfused brains were uniformly trimmed caudal to cerebellum, weighed to the nearest 0.001 g, and embedded in 0.05% gelatin and 30% egg albumin. The tissue was postfixed in Perfix before being transferred first to 15% and then to 30% sucrose in phosphate buffer before sectioning. Frozen sections were cut in the coronal plane at 40-μm intervals; every fourth section was mounted and stained for Nissl substance with cresyl violet.

Hippocampal area (the summed areas of dentate gyrus and Ammon's horn) was determined with the aid of an image-analyzing system. Boundaries were determined at $\times 1$ to $\times 10$ with a Nikon Optiphot microscope; sections were projected at $\times 0.75$ onto a high resolution video monitor and analyzed with IMAGEPRO II software (Media Cybernetics). An average ($\pm$SE) of 24.6 ± 0.4 sections (range, 19–31) was measured for each individual. To eliminate experimenter bias, we used the following design: all sections were prepared by the senior author, assigned random labels by another experimenter, and traced by a supervised technician who was therefore unaware of the sex and species of the animal whose hippocampus was being measured. The formula for the volume of a truncated cone (15) was used to calculate the volume between sequential sections, and these volumes were summed to calculate absolute hippocampal size. Total brain volume was calculated from brain weight by using an established constant (46). The ratio of hippocampal volume to brain volume yielded a measure of relative hippocampal size. The sex-by-species interaction term from two-way analysis of variance was used to test whether the pattern of sex differences differed between species. In each such test, an appropriate exponential transformation of the raw data was used to eliminate a strong correlation between cell means and cell standard deviations (47).

RESULTS

Based on sex-by-species patterns of range size and maze performance, we predicted that there would be a sex difference in hippocampal size in the polygamous species but no such difference in the monogamous species. Fig. 1 shows the observed differences in absolute and relative hippocampal sizes. In the polygamous species (meadow voles), male hippocampi averaged 3.2 mm^3 (11.3%) larger than female hippocampi. The monogamous species (pine voles) exhibited a different pattern: male hippocampi were only 0.5 mm^3 (2.1%) larger than female hippocampi. Two-way analysis of variance shows the sex-by-species interaction to be marginally significant ($F = 3.07$, $P = 0.088$). This comparison of absolute hippocampal size is misleading because it does not take account of differences in overall brain size between males and females. The appropriate test of the hypothesis would compare relative, not absolute, size of the hippocampus and thus would focus on the proportion of the brain tissue allocated to hippocampus in each group. Thus we analyzed the ratio of hippocampal volume to total brain volume in a similarly structured two-way analysis of variance: the sex-by-species interaction was significant ($F = 4.61$, $P = 0.039$). Furthermore, both P-values reported above underestimate the predictive power of our hypothesis because they are based on two-tailed tests. Our hypothesis is strongly directional, predicting larger male hippocampi in the polygamous species and no sex difference in the monogamous species.

These patterns of hippocampal size are not a reflection of gross sexual dimorphisms in these species. None of the gross brain or body measurements (volume, weight, and length) show significant sex differences in either species ($0.20 < F < 2.8$; $0.11 < P < 0.65$). The sex difference in absolute hippocampal size in the polygamous species does not necessarily imply a reallocation of brain space; in meadow voles, male brains are on average 10.3 mm^3 (1.6%) larger than female brains. Although this overall brain difference does not approach statistical significance ($F = 0.34$, $P = 0.567$), it could accommodate the observed 3.2-mm^3 difference in hippocampal size.

DISCUSSION

An important assumption underlying studies of brain evolution is Jerison's principle of proper mass: "The mass of neural tissue controlling a particular function is appropriate to the amount of information processing involved in performing the function" (48). Although this principle is appealing, only a few studies have tested it directly (14, 49) because of the inherent difficulty of isolating and assessing the function of discrete brain structures. Our result illustrates the principle of proper mass at the level of an individual brain structure, the hippocampus, among whose various functions (50–53) spatial processing has been repeatedly demonstrated with a variety of independent techniques (4–6).

The finding that sex-specific patterns of hippocampal size vary with range size and maze performance does not rule out the possibility that there are other, more microscopic, sex differences in hippocampal anatomy, as have been described for laboratory rats (54, 55). However, hippocampal size has been shown to be related to behavior (56), and the measurement of size is traditionally the first stage of research in comparative studies (11, 12, 14, 49).

A variety of behavioral differences between monogamous and polygamous rodent species has been catalogued (25).

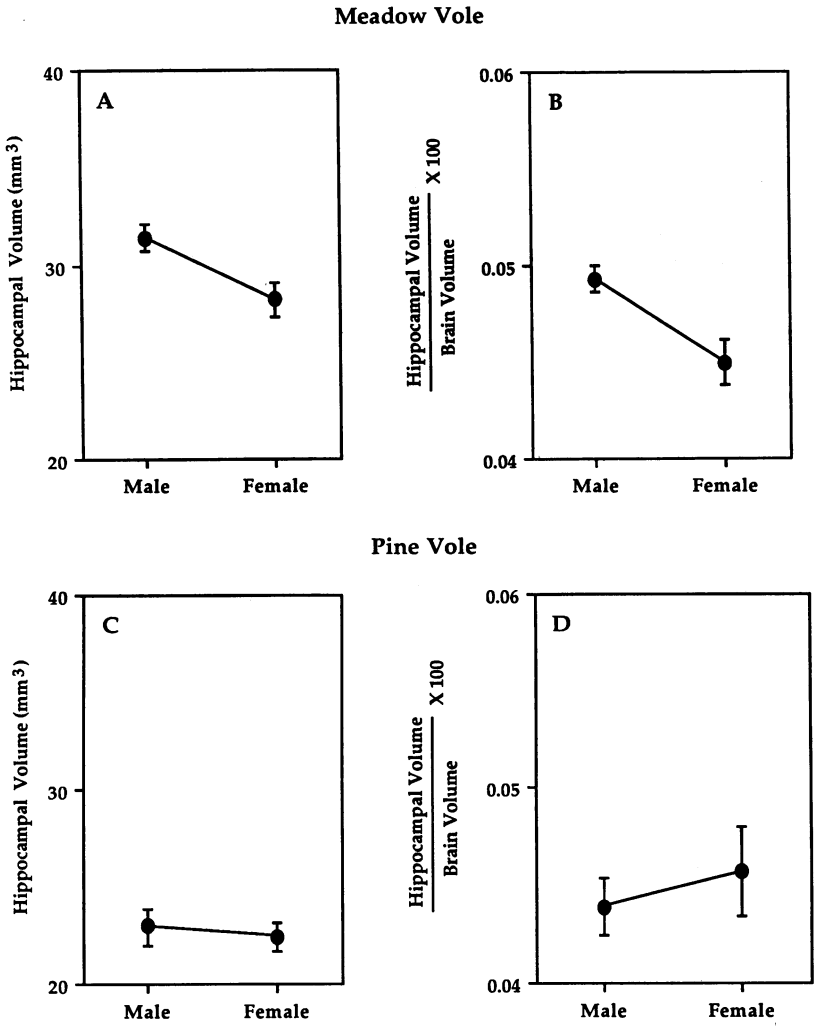

FIG. 1. Comparisons of absolute and relative hippocampal size by sex for meadow voles (*A* and *B*) and pine voles (*C* and *D*). Points represent means ± SE; sample size is 10 for each species and sex.

Any of these behaviors may have neuroanatomical correlates and some may be partially mediated by the hippocampus. However, the evidence that other sexually dimorphic behaviors, such as parental care, are mediated by the hippocampus is conflicting (1). Moreover, the hippocampus clearly plays an important role in spatial processing (1–3). Thus, while other brain structures could be examined for sex and species differences, any observed correlations between behavior and anatomy could only be treated as *post hoc* findings. The present study tests an *a priori* hypothesis that rests on established ethological, psychometric, and neurological linkages.

Our hypothesis predicts that sex differences in hippocampal size should also be found in other polygamous mammal species. Indeed, because most mammals are polygamous (57), sex differences in hippocampal volume should be the dominant mammalian pattern, if our hypothesis is correct. Unfortunately, there are no published data on sex differences in hippocampal volume in other mammals. Unpublished data on laboratory rats, a rodent of polygamous ancestry (25), indicate that the absolute size of the hippocampus is significantly greater in males than females (G. F. Sherman, personal communication), a result which supports our hypothesis.

Across species, the form of the mating system represents an important selective pressure shaping sex-specific ranging patterns. These ranging patterns, in turn, require various commitments to cognitive processing of spatial information that must be mediated by the brain. Our results suggest that sexual selection, arising from social ecology, can produce adaptive sex differences in behavior via modifications in the underlying neuroanatomical substrate.

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1. O'Keefe, J. & Nadel, L. (1978) *The Hippocampus as a Cognitive Map* (Oxford Univ. Press, Oxford, UK).
2. Olton, D. S. (1987) in *Cognitive Processes and Spatial Orientation in Animals and Man*, eds. Ellen, P. & Thinus-Blanc, C. (Kluwer, Boston), Vol. 2, pp. 16–27.
3. Olton, D. S., Wible, C. G. & Shapiro, M. L. (1986) *Behav. Neurosci.* **100**, 852–855.
4. O'Keefe, J., Nadel, L., Keightley, S. & Kill, D. (1975) *Exp. Neurol.* **48**, 152–166.

5. Morris, R. G. M., Garrud, P., Rawlins, J. N. P. & O'Keefe, J. (1982) *Nature (London)* **297,** 681–683.
6. Sutherland, R. J., Whishaw, I. Q. & Kolb, B. (1983) *Behav. Brain Res.* **7,** 133–153.
7. Crusio, W. E. & Schwegler, H. (1987) *Behav. Brain Res.* **26,** 153–158.
8. Crusio, W. E., Schwegler, H. & Lipp, H.-P. (1987) *Brain Res.* **425,** 182–185.
9. Lipp, H.-P., Schwegler, H., Heimrich, B., Cerbone, A. & Sadile, A. G. (1987) *Behav. Brain Res.* **24,** 111–123.
10. Diamond, M. C. (1987) *Brain Res. Rev.* **12,** 235–240.
11. Stephan, H., Frahm, H. & Baron, G. (1981) *Folia Primatol.* **35,** 1–29.
12. West, M. & Schwerdtfeger, W. K. (1985) *Brain Behav. Evol.* **27,** 93–105.
13. Sherry, D. F., Vaccarino, A. L., Buckenham, K. & Herz, R. (1988) *Soc. Neurosci. Abstr.* **14,** 235.
14. Krebs, J. R., Sherry, D. F., Healey, S. D., Perry, V. H. & Vaccarino, A. L. (1989) *Proc. Natl. Acad. Sci. USA* **86,** 1388–1392.
15. Sherry, D. F., Vaccarino, A. L., Buckenham, K. & Herz, R. (1989) *Brain Behav. Evol.* **34,** 308–317.
16. Pagel, M. D. & Harvey, P. H. (1989) *Science* **244,** 1589–1593.
17. Clutton-Brock, T. H. & Harvey, P. H. (1980) *J. Zool.* **190,** 309–323.
18. Mace, G. M., Harvey, P. H. & Clutton-Brock, T. H. (1981) *J. Zool.* **193,** 333–354.
19. Trivers, R. L. (1972) in *Sexual Selection and the Descent of Man, 1871–1971,* ed. Campbell, B. G. (Aldine, Chicago), pp. 136–179.
20. Wolff, J. O. (1985) in *Biology of New World Microtus,* ed. Tamarin, R. H. (Am. Soc. Mammalogists, Provo UT), pp. 340–372.
21. Ostfeld, R. S. (1985) *Am. Nat.* **126,** 1–15.
22. Gaulin, S. J. C. & FitzGerald, R. W. (1988) *J. Mammal.* **69,** 311–319.
23. Gaulin, S. J. C. & FitzGerald, R. W. (1986) *Am. Nat.* **127,** 74–88.
24. Gaulin, S. J. C. & FitzGerald, R. W. (1989) *Anim. Behav.* **37,** 322–331.
25. Dewsbury, D. A. (1981) *Biologist* **63,** 138–162.
26. Hubbert, H. B. (1915) *Behav. Monogr.* **2,** 1–55.
27. Sadownikova-Koltzova, M. P. (1926) *J. Exp. Zool.* **45,** 301–318.
28. McNemar, Q. & Stone, C. P. (1932) *J. Comp. Psychol.* **14,** 171–180.
29. Barnett, R. J. & Ray, O. S. (1970) *Dev. Psychol.* **3,** 73–77.
30. Davenport, J. W., Hagquist, W. W. & Rankin, G. R. (1970) *Behav. Res. Methods Instrum.* **2,** 112–118.
31. Dawson, J. L. M. (1972) *Behav. Genet.* **2,** 21–42.
32. Stewart, J., Skvarenina, A. & Pottier, J. (1975) *Physiol. Behav.* **14,** 291–295.
33. Joseph, R., Hess, S. & Birecree, E. (1978) *Behav. Biol.* **24,** 364–377.
34. Juraska, J. M., Henderson, C. & Muller, J. (1984) *Dev. Psychol.* **17,** 209–215.
35. Maier, D. M. & Pohorecky, L. A. (1986) *Pharmacol. Biochem. Behav.* **25,** 703–709.
36. van Haaren, F., Wouters, M. & van De Poll, N. E. (1987) *Physiol. Behav.* **39,** 409–412.
37. Joseph, R. (1979) *J. Psychol.* **101,** 37–43.
38. Joseph, R. & Gallagher, R. E. (1980) *Dev. Psychobiol.* **13,** 527–544.
39. Tees, R. C., Midgley, G. & Nesbit, J. C. (1981) *Dev. Psychobiol.* **14,** 425–438.
40. Williams, C. L., Barnett, A. M. & Meck, W. H. (1990) *Behav. Neurosci.* **104,** 84–97.
41. Beatty, W. W. (1979) *Horm. Behav.* **12,** 112–163.
42. Gaulin, S. J. C., FitzGerald, R. W. & Wartell, M. (1990) *J. Comp. Psychol.* **104,** 88–93.
43. Walsh, R. N., Budtz-Olsen, O. E., Penny, J. E. & Cummins, R. A. (1969) *J. Comp. Neurol.* **137,** 361–366.
44. Juraska, J. M. (1984) *Prog. Brain Res.* **61,** 205–214.
45. Gaulin, S. J. C. & Wartell, M. S. (1990) *J. Comp. Psychol.* **104,** 183–189.
46. Stephan, H. (1960) *Z. Wiss. Zool. Abt. A* **164,** 143–172.
47. Box, G. E. P. & Cox, D. R. (1964) *J. R. Statis. Soc. Ser. B.* **26,** 211–252.
48. Jerison, H. J. (1973) *Evolution of the Brain and Intelligence* (Academic, New York).
49. Nottebohm, F. (1981) *Science* **214,** 1368–1370.
50. Olton, D. S., Becker, J. T. & Handelman, G. E. (1979) *Behav. Brain Sci.* **2,** 313–365.
51. Rawlins, J. N. P. (1985) *Behav. Brain Sci.* **8,** 479–496.
52. Teyler, T. J. & DiSenna, P. (1986) *Behav. Neurosci.* **100,** 147–154.
53. Berger, T. J. & Orr, W. B. (1983) *Behav. Brain Res.* **8,** 49–68.
54. Loy, R. & Milner, T. A. (1980) *Science* **208,** 1282–1284.
55. Juraska, J. M., Fitch, J. M., Henderson, C. & Rivers, N. (1985) *Brain Res.* **333,** 73–80.
56. Wimer, C. C., Wimer, R. E. & Roderick, T. H. (1971) *J. Comp. Physiol. Psychol.* **76,** 57–65.
57. Daly, M. & Wilson, M. (1983) *Sex, Evolution, and Behavior* (Wadsworth, Belmont, CA), 2nd Ed.