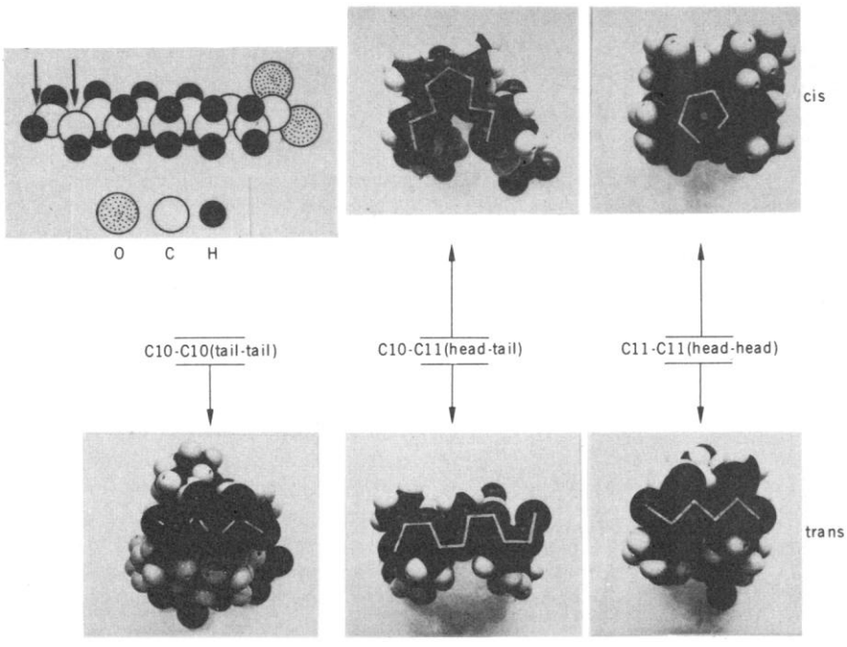

Fig. 2. Polyethylene backbone structure may accommodate head-to-head and head-to-tail conformations, with the exception of the tail-to-tail *cis* structure.

weight) at 60°C, at which temperature the polymerization took place in an N_2 atmosphere of degassed components.

The optical pattern (Fig. 1A) and low-angle x-ray reflections with radius ratios 1 : 1.71 : 2.03 indicated that the liquid crystalline structure before polymerization was a hexagonal array of close-packed cylinders (*17*). The pattern (Fig. 1A) was identical over the temperature range 20° to 75°C, leaving no doubt about the structure at 60°C before polymerization.

Structural changes during polymerization were followed at 60°C by direct microscopic observation of a sample sealed between two microscopy slides glued to spacers. Weighing of the sample during the process showed that no evaporation took place. After polymerization for 24 hours, no optical anisotropy was found; the polymerization was complete. Infrared spectra showed no double bonds in the structure. When the temperature was reduced to 20°C the optical pattern of a lamellar liquid crystalline phase appeared (Fig. 1B), and low-angle x-ray reflections of a powder from the polymerization in a sealed ampul showed distance ratios of 1 : 1/2 : 1/3 characteristic of a lamellar structure.

These results show that a lamellar structure was formed. Evidence for a lamellar liquid crystalline structure as distinguished from a crystalline structure of lamellae was the observation of one diffuse reflection at 4.5 Å characteristic of liquid hydrocarbon chains. A crystalline structure would display a series of sharp reflections in the range 3 to 4.5 Å, showing the crystalline packing of the methylene groups of the hydrocarbon chains.

The structure of the lamellar phase must be related to the fact that the molecular weight is medium; high-pressure liquid chromatography showed an average size with 270 amphiphilic units in each molecule. The backbone of the polymer is the polyethylene chain "substituted" with the remaining parts of the amphiphile chain. Molecular models showed that such a structure accommodates all head-to-tail and head-to-head configurations in the *cis* and *trans* conformations (Fig. 2) with exception of tail-to-tail in the *cis* conformation. The structure necessitates considerable bending of the hydrocarbon chains; a formal calculation of the thickness of the amphiphilic layer supports this suggestion. An expected hydrocarbon length for a normal liquid crystalline packing chain (*18*) of 14.15 Å would mean an angle of 29.4° for the hydrocarbon chain axis against the layers. There appears to be little basis for accepting such a structure. The suggested structure of a polyethylene backbone appears reasonable.

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References and Notes

1. G. H. Brown and W. G. Shaw, *Chem. Rev.* **57**, 1049 (1957).
2. G. H. Brown, Ed., *Advances in Liquid Crystals* (Academic Press, New York, 1974–1977), vols. 1–3.
3. G. W. Gray, *Molecular Structure and the Properties of Liquid Crystals* (Academic Press, New York, 1962).
4. P. G. de Gennes, *The Physics of Liquid Crystals* (Oxford Univ. Press, London, 1974).
5. S. L. Kwolek, U.S. Patent 3,671,542 (20 June 1972).
6. A. Blumstein, Ed., "Mesomorphic order in polymers and polymerization in liquid crystalline media," *ACS Symp. Ser. 74* (1978).
7. C. Sadron, *Pure Appl. Chem.* **4**, 347 (1962).
8. Y. Bouligand, P. E. Cladis, L. Liebert, L. Strzelecki, *Mol. Cryst. Liq. Cryst.* **25**, 233 (1974).
9. L. Strzelecki and L. Liebert, *Bull. Soc. Chim. Fr.* **1973**, 597 (1973).
10. L. Liebert and L. Strzelecki, *C. R. Acad. Sci. Ser. C* **276**, 647 (1973).
11. F. Cser, K. Nyitrai, G. Hardy, in (*6*), p. 95.
12. H.-J. Lorkowski and F. Reuther, *Acta Chim. Acad. Sci. Hung.* **95**, 423 (1977).
13. G. Wegner and W. Sherman, *Colloid Polym. Sci.* **252**, 655 (1974).
14. F. Cser and G. Hardy, *Acta Chim. Acad. Sci. Hung.* **84**, 297 (1975).
15. R. H. Baughman and K. C. Yee, *J. Polym. Sci. Polym. Chem. Ed.* **12**, 2467 (1974).
16. E. Ruckenstein and J. C. Chi, *J. Chem. Soc. Faraday Trans. 2* **71**, 1690 (1975).
17. V. Luzzati, H. Mustacchi, A. Skoulios, F. Husson, *Acta Crystallogr.* **13**, 660 (1960).
18. F. Reiss-Husson and V. Luzzati, *J. Phys. Chem.* **71**, 957 (1967).
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Subicular Input from Temporal Cortex in the Rhesus Monkey

Abstract. *The subicular cortices of the primate hippocampal formation form a physical and connectional link between the cortex of the temporal lobe and the hippocampus. Their direct connections with all classes of cortex in the temporal lobe except primary sensory cortex underscore the pivotal role of these areas in the potential interplay between the hippocampal formation and the association cortices.*

Since their description nearly a century ago (*1*) the subicular cortices of the mammalian hippocampal formation (*2*) have had the vague anatomical distinction as simply the gray matter passageway interposed between the hippocampal allocortex medially and the occipitotemporal isocortex laterally. Little else has been known about these architectonically heterogeneous areas despite the fact that they reach their greatest relative size and elaboration in primates, including humans (*3*). Recently, however, anatomical results have made it increasingly clear that the subicular cortices in fact hold a pivotal position within the hippocampal formation for relaying the output of the hippo-

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campus to widespread regions of the brain (*4*). For example, it is now well documented anatomically and physiologically that the subicular cortices receive a major portion of the output from the hippocampus (*5*) and, in turn, project to several areas of the cerebral cortex, amygdala, anterior thalamus, and mammillary bodies (*4, 6*). In contrast, and contrary to the teaching for the past 100 years, the Ammonic pyramids (CA1 to CA3), which collectively form the hippocampus, have few projections that leave the structure, and those that do terminate predominantly in only the septum (*4, 7*). Instead of having long extrinsic projections, the axons of these Ammonic pyramids form the ipsilateral intrinsic and commissural circuitry within the hippocampal formation. One of these intrinsic pathways, which arises from hippocampal subfield CA1, terminates heavily in the adjacent subicular cortices and thus forms a powerful source of allocortical input to these relay or output areas of the hippocampal formation (*5, 8*).

Our studies in 17 rhesus monkeys (*Macaca mulatta*) have shown that, in addition to this allocortical input, the subicular cortices also receive periallocortical input from the nearby entorhinal cortex and isocortical and proisocortical input from virtually all areas along the base of the temporal lobe. Thus, the subicular cortices of the hippocampal formation in the monkey are related uniquely to all four classes of cortex (allocortex, periallocortex, proisocortex, and isocortex) that form this portion of the cortical mantle. Since we have previously shown that the subicular cortices project to many of these same areas (*4*), it is now apparent that the hippocampal formation participates prominently in much of the cortical circuitry of the temporal lobe.

In each of the monkeys, injections of ^{3}H-labeled amino acids (*9*) were made into the temporal cortex with direct microscopic guidance. After a survival period of 2 to 7 days, monkeys were perfused with saline and 10 percent formalin, and the brains were removed and later embedded in paraffin. After sectioning, autoradiographic (*10*) and Nissl staining methods were used to define the injection site and to detect and localize the anterograde axonal transport of the ^{3}H. Isotope injections were made in all four temporal gyri (Fig. 1, A and B). In one monkey, an injection in the superior temporal gyrus labeled Bonin and Bailey's area TA. In six, injections in the middle and inferior temporal gyri labeled areas TE and 35. Two injections were made in the temporal polar cortex to label area TG. In four monkeys, injections in the caudal parahippocampal gyrus labeled areas TF and TH. Three additional monkeys had isotope injections medial to the rhinal sulcus that labeled the entorhinal cortex, or Brodmann's area 28. A final one had an injection in the ventral part of area OA. Each series of sections derived was examined for evidence of ^{3}H over the hippocampal formation with the use of bright-field and dark-field light microscopy.

Monkeys 1 to 5 (Fig. 1B) exhibited no ^{3}H over the subicular cortices. The areas encompassed by these injections included area TA, the part of area TE that forms the middle temporal gyrus, and area OA. In contrast, monkeys 6 to 17 all had ^{3}H across one or more subdivision of the subicular cortices. For example, animals 6 and 7, which labeled area TG, each had a pronounced column of ^{3}H throughout the entire rostro-caudal extent of the parasubiculum, the most lateral subdivision of the subicular cortices. Animals 8 to 10, which labeled the inferior temporal gyrus, or areas TE and 35, had ^{3}H in the molecular layer of the subiculum proper and the prosubiculum, the most medial areas of the subicular cortices. For all of these monkeys, additional label was observed in the superficial pyramidal cells of these cortices. Animals 11 to 14, which labeled areas TF and TH, had two distinct projection patterns in the subicular cortices. The first was similar to that observed in animals 8 to 10, with ^{3}H localized over the molecular layer of the subiculum and prosubiculum. These projections were most prominent in the caudal half of the hippocampal formation, with ^{3}H occurring throughout the middle part of their respective molecular layers (Fig. 2, A and B). A second pattern of ^{3}H spread over the presubiculum subdivision of the subicular cortices. These projections were organized in a columnar fashion, with ^{3}H from ascending axons spread laterally and medially through layers 1 and 2 of the middle levels of the presubiculum.

In summary, labeling in animals 6 to 14 involved cortical areas rostral (TG), lateral (TE and 35), and caudal (TF and TH) to the rhinal sulcus. These are all

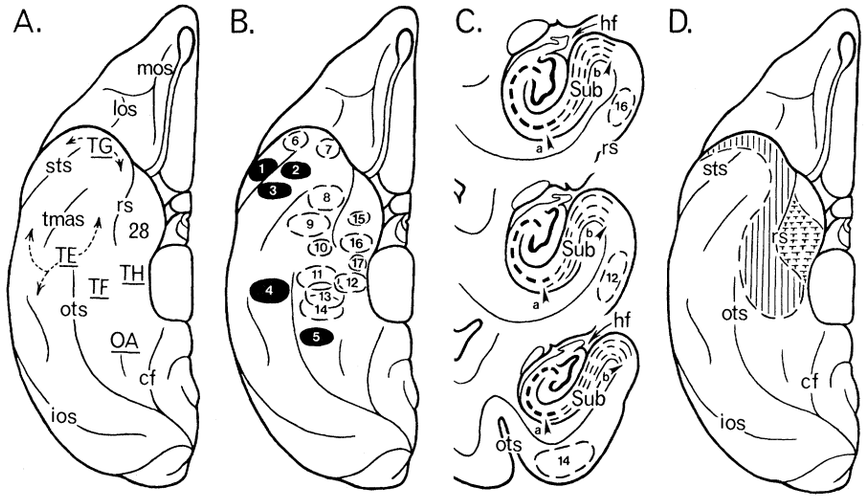

Fig. 1. (A) Ventral view of the cerebral hemisphere of the rhesus monkey brain depicting the major sulci and locations of cytoarchitectonically defined cortical areas. (B) Location of the 17 isotope injections. Animals 1 to 5 exhibited no ^{3}H in the subicular cortices. Animals 6 to 17 had ^{3}H in one or more subdivision of the subicular cortices. (C) Three cross sections through the hippocampal formation and ventromedial temporal lobe of the rhesus monkey. The upper cross section, the most rostral, bisects the injection site of animal 16. The lower cross section, the most caudal, bisects the injection site of animal 14. The components of hippocampal formation are defined with various lines: For example, the granule cells of the dentate gyrus are depicted by the solid heavy line; the Ammonic pyramids (CA1 to CA3) are depicted by the interrupted heavy line: the subicular cortices are depicted by multiple fine lines and further offset by the arrows at points *a* and *b*. The parasubiculum subdivision of the subicular cortices is laterally located near arrow *b*. The prosubiculum subdivision is medially located near arrow *a*. The subiculum proper borders the prosubiculum medially, and the presubiculum borders the parasubiculum laterally. (D) Areas of the ventromedial temporal lobe that project to the subicular cortices. Those left of rhinal sulcus (*rs*), corresponding to cortical areas TG, TE, TF, and TH, project predominantly to the subicular cortices. The area right of the rhinal sulcus corresponding to area 28—the entorhinal cortex—projects to all components of the hippocampal formation. Abbreviations: *mos*, medial orbital sulcus; *los*, lateral orbital sulcus; *sts*, superior temporal sulcus; *tmas*, temporalis medialis anterior sulcus; *ots*, occipitotemporal sulcus; *cf*, calcarine fissure; *ios*, inferior occipital sulcus; *hf*, hippocampal fissure; and *Sub*, subicular cortices.

six-layered cortices with distinguishable cytoarchitecture. Injections in each resulted in evidence of axonal termination in one or more parts of the subicular cortices.

Animals 15 to 17 had injections medial to the rhinal sulcus that labeled the entorhinal periallocortex, or Brodmann's area 28. This well-defined cortex is characterized by large multipolar star-shaped cells in layer 2 and a conspicuous acellular lamina dissecans where layer 4 would occur in homotypical isocortex. In these cases, ^{3}H was distributed across a broad expanse of the molecular layer of the subicular cortices, encompassing to some extent all subdivisions. These projections, however, were most intense over the subiculum, and formed part of a large projection that terminated on the distal parts of the apical dendrites of the Ammonic pyramids (CA1 to CA3) and the outer two-thirds of the molecular layer of the dentate gyrus. They were present throughout the extent of the hippocampal formation, although they were notably more dense at its anterior end. All considered, this distribution of ^{3}H corresponded well to the known distribution of the perforant pathway (*11*).

The results demonstrate that the subicular cortices in the monkey (Fig. 1C) receive a host of cortical inputs arising from a large expanse of temporal cortex both medial and lateral to the rhinal sulcus (Fig. 1D). The former area constitutes the entorhinal cortex (area 28), while the latter constitute areas TE, TF, TG, TH, and 35. Combined with previous results demonstrating allocortical projections from the CA1 subfield of the hippocampus and the cortical amygdaloid area (*12*) to the subicular cortices (*4, 5, 8*), our results underscore the fact that these parts of the hippocampal formation receive input from all classes of cortex (allocortex, periallocortex, proisocortex, and isocortex) in the temporal lobe. Since the output of the hippocampal formation is vested largely in the subicular cortices, and not in the adjacent hippocampus or entorhinal cortex, these cortices seem to be directly related to much of the anatomical circuitry of the entire temporal lobe.

Consequently, in primates it is no longer tenable to view the hippocampal formation as an area of the cortical mantle largely removed and isolated from the complex functions subserved by the cerebral cortex. Its primary output division, the subicular cortices, receive input from temporal cortical areas in turn projected onto by innumerable cortical association areas located in all four lobes (*13*). Subicular output reciprocates many of these projections (*4*). We believe that these widespread connectional relationships with so-called higher cortical centers of the cerebral hemisphere are correlated with progressive expansion of the subicular cortices in higher primates (*3*) and the structural elaboration of these areas in humans (*14*). In this regard, a growing body of clinicopathological data implicates the subicular cortices, and areas with which they have direct connections, in temporal lobe epilepsy, Alzheimer's disease, Pick's disease, and the alcoholic Korsakoff syndrome—clinical disorders characterized by complex changes in personality, attention, and memory (*15*).

Thus, from an anatomical viewpoint, the subicular cortices, as often reiterated by Cajal (*1*), are indeed a gray matter passageway between the hippocampus and cerebral cortex. In addition, however, they are also a connectional passageway whose integrity may be essential for many complex mental processes.

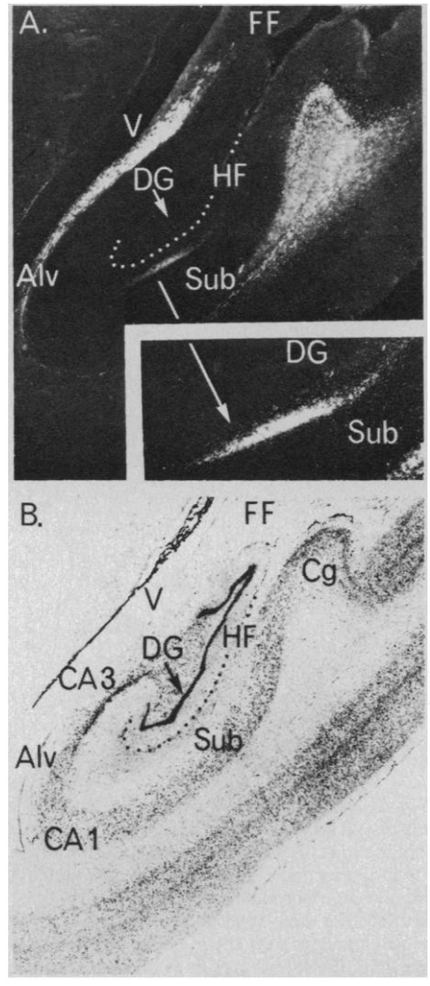

Fig. 2. (A) Dark-field photomicrograph of a cross section through the hippocampal formation of monkey 14. Note the location of ^{3}H (inset) on the molecular layer of the subicular cortices. (B) Bright-field photomicrograph of the same section depicting the Nissl architecture (thionine stain) of the section. Abbreviations: *FF*, fimbria-fornix; *V*, lateral ventricle; *Alv*, alveus; *DG*, dentate gyrus; and *Cg*, cingulum (see also legend to Fig. 1).

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References and Notes

1. S. Ramón y Cajal, *Studies on the Cerebral Cortex*, L. M. Kraft, Transl. (Yearbook, Chicago, 1955), pp. 28–32; R. B. Chronister, R. W. Sikes, L. E. White, Jr., in *The Septal Nuclei*, J. DeFrance, Ed. (Plenum, New York, 1976), p. 115.
2. As used here, hippocampal formation includes the dentate gyrus and associated hilum polymorphs (CA4), the hippocampus (CA1 to CA3), and the subicular cortices (prosubiculum, subiculum proper, presubiculum, and parasubiculum).
3. H. Stephan and O. J. Andy, in *The Primate Brain*, C. R. Noback and W. Montagna, Eds. (Appleton-Century-Crofts, New York, 1970), p. 109.
4. D. L. Rosene and G. W. Van Hoesen, *Science* **198**, 315 (1977).
5. A. Hjorth-Simonsen, *J. Comp. Neurol.* **147**, 145 (1973); P. Andersen, B. H. Bland, J. D. Dudar, *Exp. Brain Res.* **17**, 152 (1973).
6. L. W. Swanson and W. M. Cowan, *Science* **189**, 303 (1975); R. C. Meibach and A. Siegel, *Brain Res.* **88**, 518 (1975); *ibid.* **124**, 197 (1977); R. W. Sikes, R. B. Chronister, L. E. White, Jr., *Exp. Neurol.* **57**, 379 (1977).
7. L. W. Swanson and W. M. Cowan, *J. Comp. Neurol.* **172**, 49 (1977).
8. L. W. Swanson, J. M. Wyss, W. M. Cowan, *ibid.* **181**, 681 (1978).
9. Injections contained equal parts of [^{3}H]leucine and [^{3}H]proline with 10 to 50 μCi of ^{3}H in 0.2 to 1.0 μl of saline.
10. W. M. Cowan, D. I. Gottlieb, A. E. Hendrickson, J. L. Price, T. A. Woolsey, *Brain Res.* **37**, 21 (1972).
11. A. Hjorth-Simonsen, *J. Comp. Neurol.* **146**, 219 (1972); ——— and B. Jeune, *ibid.* **144**, 215 (1972); O. Steward, *ibid.* **167**, 285 (1976); G. W. Van Hoesen and D. N. Pandya, *Brain Res.* **95**, 39 (1975).
12. J. E. Krettek and J. L. Price, *J. Comp. Neurol.* **172**, 723 (1977).
13. D. N. Pandya and H. G. J. M. Kuypers, *Brain Res.* **13**, 13 (1969); E. G. Jones and T. P. S. Powell, *Brain* **93**, 793 (1970); G. W. Van Hoesen, D. N. Pandya, N. Butters, *Science* **175**, 1471 (1972).
14. H. Braak, *Z. Zellforsch.* **131**, 235 (1972); *Cell Tissue Res.* **190**, 509 (1978).
15. M. E. Scheibel, P. H. Crandell, A. B. Scheibel, *Epilepsia* **15**, 55 (1974); J. H. Margerison and J. A. N. Corsellis, *Brain* **89**, 499 (1966); M. W. Hooper and F. S. Vogel, *Am. J. Pathol.* **85**, 1 (1976); A. Hirano and H. M. Zimmerman, *Arch. Neurol.* **7**, 227 (1962); M. J. Ball, *Acta Neuropathol.* **42**, 73 (1978); J. A. N. Corsellis, in *Greenfield's Neuropathology*, W. Blackwood and J. A. N. Corsellis, Eds. (Arnold, London, 1976), p. 796; J. Barbizet, *J. Neurol. Neurosurg. Psychiatry* **26**, 127 (1963); T. L. Kemper, in *Senile Dementia: A Biomedical Approach*, K. Nandy, Ed. (Elsevier, Amsterdam, 1978), p. 105.

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