muscles); 5, complete loss of righting reflex; 6, coma; 7, death. Animals were observed for 6 to 10 minutes after the administration of ethanol.

19. Blood ethanol was measured in parallel experiments in trunk blood [P. K. Wilkinson, J. G. Wagner, A. J. Sedman, *Anal. Chem.* **47**, 1506 (1975)] and was: Ro15-4513 pretreated, 257 ± 31 mg/dl; vehicle, 280 ± 14 mg/dl (n = 12); not significantly different by Student's t test.
20. R. D. Schwartz, P. Skolnick, E. B. Hollingsworth, S. M. Paul, *Fed. Eur. Biochem. Soc. Lett.* **175**, 193 (1984); E. B. Hollingsworth *et al.*, *J. Neurosci.* **5**, 2240 (1985); R. D. Schwartz, J. A. Jackson, D. Weigert, P. Skolnick, S. M. Paul, *ibid.*, p. 1963. For preparation of synaptoneurosomes brain tissue (1 g) was rapidly dissected on ice and homogenized in 7 volumes (weight to volume) of ice-cold buffer containing 20 mM Hepes-tris, 118 mM NaCl, 4.7 mM KCl, 1.18 mM $MgSO_4$, and 2.5 mM $CaCl_2$ (pH 7.4) with a glass-glass homogenizer (five strokes). The homogenate was diluted with 30 ml of buffer and then filtered by gravity through three layers of nylon mesh (160 μm, TETKO Inc., Elmsford, NY) placed in a Millipore Swinex filter holder. The resulting filtrate was then gently pushed through a 10-μm Millipore filter (LCWP 047) with a 10-ml syringe. The filtered preparation was centrifuged at 1000g for 15 minutes and, after discarding the supernatant, the pellet was washed once with buffer and then centrifuged (1000g for 15 minutes). The resulting pellet was resuspended in buffer to a final protein concentration of 20 mg/ml.
21. We thank W. E. Haefely (F. Hoffmann–La Roche and Co., Basel, Switzerland) for the gift of Ro15-4513, E. Lane (NIAAA, NIH, Bethesda, MD) for determining blood ethanol concentrations, and T. Welsh and J. Infante for typing the manuscript.

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Age of the Earliest African Anthropoids

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The earliest fossil record of African anthropoid primates (monkeys and apes) comes from the Jebel Qatrani Formation in the Fayum depression of Egypt. Reevaluation of both geologic and faunal evidence indicates that this formation was deposited in the early part of the Oligocene Epoch, more than 31 million years ago, earlier than previous estimates. The great antiquity of the fossil higher primates from Egypt accords well with their primitive morphology compared with later Old World higher primates. Thus, the anthropoid primates and hystricomorph rodents from Fayum are also considerably older than the earliest higher primates and rodents from South America.

The earliest anthropoid primates of Africa come from extensive early Tertiary deposits in the Fayum depression of Egypt, approximately 100 km southwest of Cairo. From their initial discovery in the beginning of the century, the fossil primate species from this area have played a critical role in our understanding of anthropoid origins and the evolution of monkeys, apes, and humans (*1–3*). Moreover, the Fayum provides the best record of Paleogene mammals from all of Africa and is critical for understanding the evolution of many mammalian groups on that continent including marsupials, pangolins, elephant shrews, bats, insectivorans, creodonts, hyracoids, elephants, anthracotheres, embrithopods, and hystricomorph rodents. Knowledge of the age of the Fayum deposits is critical for calibrating early aspects of higher primate evolution and for understanding the biogeography and evolution of many other mammals (*4, 5*).

The preponderance of apparently endemic African elements in the Fayum mammalian fauna, however, precludes precise faunal correlation between the Fayum and other paleontological localities that could place this fauna in a worldwide chronological framework. Comparison of the Fayum mammals with Eocene and Oligocene mammals from Eurasia showed only three common genera (*Peratherium*, *Pterodon*, and *Apterodon*) and five common families. All faunal comparisons indicated that the Egyptian fossils were most comparable to late Eocene and early Oligocene taxa from Europe, but sufficiently distinct that a more precise correlation was impossible (*6*).

All the Fayum primates and most of the terrestrial mammals have come from the fluvial Jebel Qatrani Formation (Fig. 1), which conformably overlies the nearshore marine and fluvial Qasr el Sagha Formation. The Jebel Qatrani Formation is comprised of 340 m of variegated alluvial rocks and fine to coarse sandstones, conglomerates, sandy mudstones, carbonaceous mudstones, and limestones, all of which show evidence of profound mechanical and geochemical alteration due to ancient soil (paleosol) formation. Vertebrate fossils have been recovered from dozens of localities throughout the formation (Fig. 1).

The Jebel Qatrani Formation is a complex alluvial unit characterized by distinct large- and small-scale lateral and vertical facies changes (*7*). In general, deposition was by meandering streams. Local, small-scale changes in lithology reflect shifting from one local channel environment to another and transitions from channel to floodplain deposits. The Jebel Qatrani lithotope was low and had little relief. The occasional occurrence of sirenians and brackish water mollusks, sharks, and rays suggests that storms, tidal incursions, or both, increased the salinity of the streams for several kilometers inland. The flood basins of the Jebel Qatrani streams were apparently heavily vegetated in many areas, as evidenced by numerous fossil root casts and areas with abundant fossil trees. There were areally large, but shallow and probably ephemeral, nonsaline ponds; soils were generally damp with probably seasonal rainfall.

The fossil megafloras show affinities with present-day tropical Indomalaysian floras. They suggest a "tropical forest existing in a wet, perhaps monsoonal climate" (*5*). Like the paleoflora, the soils indicate seasonal wetness with good drainage in some areas and swampy conditions in others.

Inasmuch as neither the sedimentary rocks nor the mammalian fauna of the Jebel Qatrani Formation provide precise evidence regarding the age of the formation, the best evidence for the age of this formation and the primates found there comes from the respective ages of the immediately overlying and underlying rocks—the Widan el Faras Basalt above and the partly marine and partly fluvial Qasr el Sagha Formation below.

In the Fayum depression, the upper Qatrani escarpment is capped by 2 to 25 m of the Widan el Faras Basalt, a dark, densely aphanitic, iron-rich extrusive basalt that is exposed for over 50 km. In outcrops where the basalt is thinnest, it appears to be a single flow; however, weathered and scorched contacts within the basalt as well as lenses of gravelly sand containing basaltic clasts attest to the presence of at least two and probably three separate flows over much of the area of exposure. The flows overlie the Jebel Qatrani Formation with a pronounced erosional unconformity, evidenced locally by broad scours of up to 25 m in depth. The thickness, and even the presence of individual flows, is controlled by the topographic irregularities at the top of the Jebel Qatrani Formation. In places where the basalt flows are absent, the Jebel Qatrani Formation is

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overlain unconformably by the alluvial Kashab Formation of lower Miocene age.

Earlier, Simons (*8*) reported K-Ar ages of 24.7 ± .4 and 27.0 ± 3.0 million years for two samples of the Widan el Faras Basalt collected in the area between Widan el Faras and Tel Beadnell (where the flow is relatively thick). It is uncertain exactly where within the basalt these samples were obtained; however, they are almost certainly from basalts higher in the local paleotopography than a new sample collected in 1981 from 70 cm above the base of the lowest flow west-northwest of Widan el Faras. This sample was dated by one of us (J.D.O.) and yielded an age of 31.0 ± 1.0 million years (*6*). The two younger ages either were on rocks obtained from different flows higher in the basalt or were determined on partially altered samples.

The age of 31 million years for the lowest part of the Widan el Faras Basalt provides a minimum age for the underlying Jebel Qatrani Formation corresponding to late early Oligocene (*9*). Everywhere in the Fayum depression, the contact of the Jebel Qatrani Formation with the overlying basalt is a pronounced erosional unconformity. At present there is no way to estimate the time interval represented by this unconformity. The maximum possible age for the Jebel Qatrani Formation is provided by relatively inexact invertebrate faunal correlation of the conformably underlying Qasr el Sagha Formation. The uppermost part of this formation and its lateral facies equivalent, the Maadi Formation, contain an abundant echinoderm and oyster fauna of taxa that have traditionally marked the uppermost Eocene (*10*). Thus the minimum age of the Jebel Qatrani Formation and the primates found therein is substantially greater than previous radiometric dates had suggested.

Since they were first described in the beginning of this century, the Fayum anthropoids have been recognized as the earliest undoubted higher primates (*11*) and have generally been regarded as broadly ancestral to the younger fossil apes from the Miocene of Europe, East Africa, and Asia. However, there has been considerable debate concerning the phyletic relationships of the various Fayum primates with regard to the evolutionary divergence of later lineages leading to Old World monkeys, lesser apes, and hominids. When the Fayum "apes" *Propliopithecus* and *Aegyptopithecus* were known almost totally from fragmentary dental remains, individual species of Oligocene "apes" seemed to mark the evolutionary divergence of lineages leading to gibbons, great apes, and possibly even hominids. At the same time, the lineage leading to the living Old World monkeys seemed to be present in the sympatric and synchronous parapithecids (*2*).

More complete fossil material has brought increasing evidence that the early "apes" from the Fayum are extremely primitive with respect to living catarrhines (*3*). Although they share with living catarrhines a reduced dental formula with two premolars, *Aegyptopithecus* and *Propliopithecus* retain more primitive, platyrrhine-like features in many aspects of cranial and postcranial anatomy and certainly precede the monkey-ape divergence.

Compared with the Fayum anthropoids, the higher primates from the early Miocene of Kenya are more advanced morphologically and more similar to living catarrhines. Although there is debate regarding the precise relationship of the *Proconsul* group to living apes, they have all the features that characterize living catarrhines and a few distinctly ape-like characters (*12*). Similarly, the early Miocene monkeys from Napak and Buluk clearly document the presence of cercopithecoids in East Africa between 15 and 20 million years ago (*13*).

Thus, there appears to be a considerable morphological gap between the early anthropoids of the Fayum and the monkeys and apes of the early Miocene of East Africa. The former show only a few features that distinguish them from a generalized higher primate condition, whereas the latter document the divergence of lineages leading to living cercopithecoids and hominoids. In light of the revised minimum age of the Jebel Qatrani Formation we realize that this morphological gap corresponds to a substantial temporal gap of more than 10 million years between the two groups of fossil anthropoids. At present, we have virtually no evidence of anthropoid evolution between 30 and 20 million years ago, the time of a major adaptive radiation of catarrhines and probably the phyletic divergence of monkeys and apes.

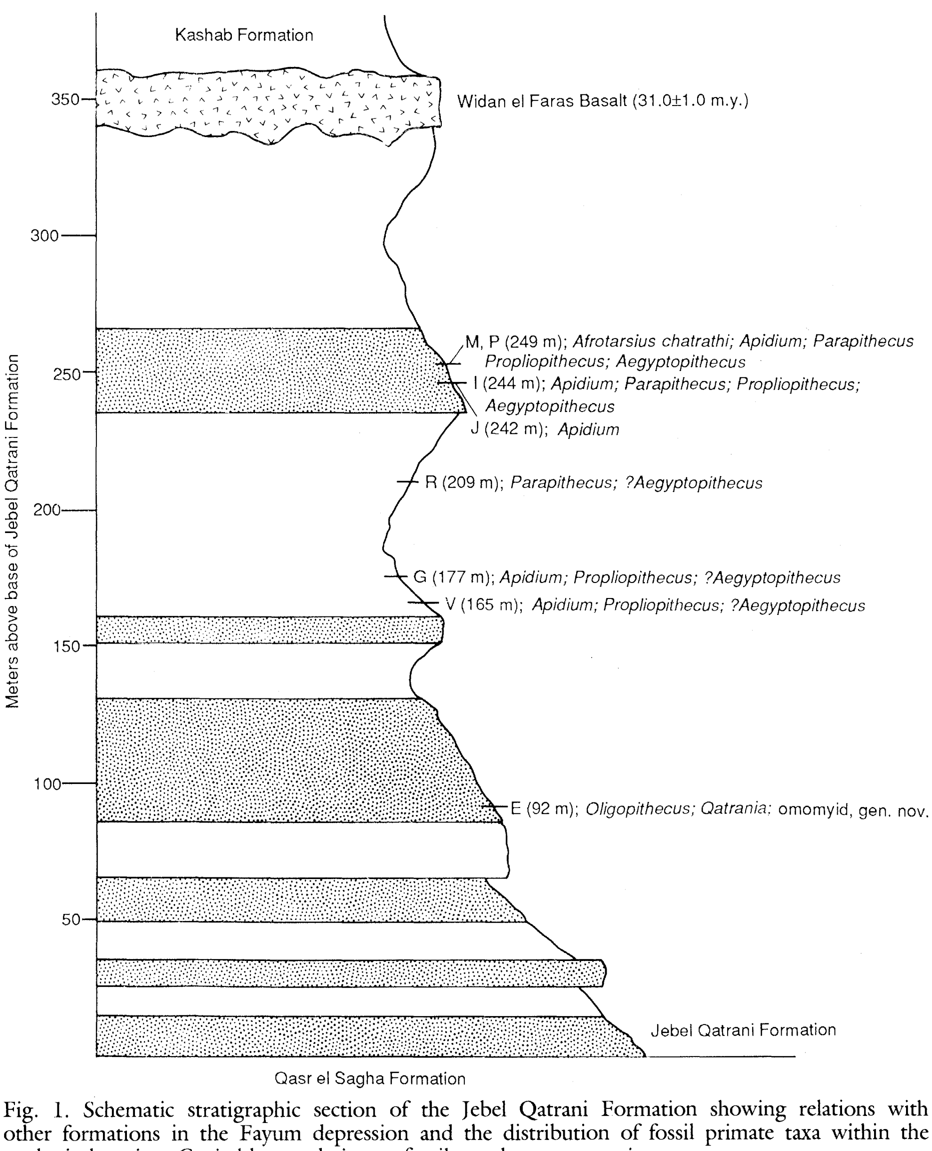

Fig. 1. Schematic stratigraphic section of the Jebel Qatrani Formation showing relations with other formations in the Fayum depression and the distribution of fossil primate taxa within the geological section. Capital letters designate fossil vertebrate quarry sites.

Some authorities have suggested that, because of their many primitive anthropoid characteristics, one group of Fayum primates, the parapithecids, may be related to the New World platyrrhines (*14*). A major line of evidence against an African origin for platyrrhines has been the apparent differences in the relative age of the earliest African and South American anthropoids. Earlier correlations placed the earliest platyrrhines at 35 million years ago, nearly 10 million years older than the supposed age of the Fayum primates. However, more recent studies of the geology of the Salla basin in Bolivia (*15*) have shown that the earliest platyrrhines are probably from about 25 million years ago, substantially younger than the Fayum anthropoids. Thus, the new minimum age estimate of the Jebel Qatrani Formation indicates that the Fayum primates are substantially older than the first appearances of all modern anthropoid radiations, a chronology that accords well with morphological analyses that place some species at the base of the higher primate radiation.

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A Critical Period for Macromolecular Synthesis in Long-Term Heterosynaptic Facilitation in *Aplysia*

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Both long-term and short-term sensitization of the gill and siphon withdrawal reflex in *Aplysia* involve facilitation of the monosynaptic connections between the sensory and motor neurons. To analyze the relationship between these two forms of synaptic facilitation at the cellular and molecular level, this monosynaptic sensorimotor component of the gill-withdrawal reflex of *Aplysia* can be reconstituted in dissociated cell culture. Whereas one brief application of 1 μ*M* serotonin produced short-term facilitation in the sensorimotor connection that lasted minutes, five applications over 1.5 hours resulted in long-term facilitation that lasted more than 24 hours. Inhibitors of protein synthesis or RNA synthesis selectively blocked long-term facilitation, but not short-term facilitation, indicating that long-term facilitation requires the expression of gene products not essential for short-term facilitation. Moreover, the inhibitors only blocked long-term facilitation when given during the serotonin applications; the inhibitors did not block the facilitation when given either before or after serotonin application. These results parallel those for behavioral performance in vertebrates and indicate that the critical time window characteristic of the requirement for macromolecular synthesis in long-term heterosynaptic facilitation is not a property of complex circuitry, but an intrinsic characteristic of specific nerve cells and synaptic connections involved in the long-term storage of information.

MEMORY, THE RETENTION OF learned information over time, is thought to have at least two components—short-term memory lasting minutes to hours, and long-term memory lasting for days to weeks or even years (*1*). Behavioral studies in vertebrates suggest that long-term memory requires the synthesis of new protein, whereas short-term memory does not (*2*). Moreover, long-term memory is most sensitive to disruption by inhibitors of protein synthesis when the inhibitors are applied during and immediately after training (*3*). There is no deficit in the retention of the learned behavior when the inhibitors are applied even 1 to 2 hours after training. This time window is remarkably characteristic and has been demonstrated for memory produced by associative as well as nonassociative forms of learning and for various vertebrate species (*3*). Although comparable data are lacking in humans, analogous clinical studies of convulsions and head trauma indicate that human long-term memory is particularly susceptible to disruption during and soon after acquisition (*4*).

The interpretation of earlier experiments, based on the systemic application of protein synthesis inhibitors, was limited, however, in two ways. First, the protein synthesis inhibitors often led to serious side effects such as seizure and sickness (*3*). Second, the studies were based on the examination of behavioral performance rather than on the analysis of the cellular correlates responsible for the neuronal plasticity underlying the altered behavior. Inhibitors of protein synthesis can affect behavioral performance not only through their action on memory processes, but also through their action on other systems that influence performance, such as attention or motivation. As a result, it has not been possible to determine whether new protein synthesis is important for memory and whether the characteristic time window for long-term memory reflects a specific requirement for macromolecular synthesis by particular neurons involved in the storage of long-term information.

To overcome these limitations, we analyzed memory processes at the cellular and molecular level, using the gill-withdrawal reflex of *Aplysia*. The neural circuitry of this reflex behavior has been delineated (*5*), and one important cellular locus has been identified in mediating short-term and long-term

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