therefore that the rate of excretion of APAP in urine cannot be used to determine the rate of phenacetin metabolism.

There is evidence suggesting that the disposition in vivo of compounds other than phenacetin may be affected by cigarette smoking. The duration of the paralysis elicited by zoxazolamine in rats and hamsters that were exposed to cigarette smoke was less than that found in rats and hamsters with no such exposure (*12*). An increased rate of excretion of nicotine metabolites in urine (*13*) and a decreased effect of pentazocine have been reported in human cigarette smokers (*14*). The results obtained here suggest a need to determine whether cigarette smoking influences the action and toxicity of phenacetin and other commonly used drugs.

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An Eocene Hystricognathous Rodent from Texas: Its Significance in Interpretations of Continental Drift

Abstract. *The earliest known representative of the fundamentally South American and African hystricognathous rodents has recently been found in the middle or late Eocene of southwestern Texas; this discovery supports the postulate of a northern and independent origin for the two southern groups and increases the evidence against mid-Tertiary trans-Atlantic migration of these rodents at a time when the South Atlantic was narrower than it is at present. The fossil seems to be related to the North American Eocene family Sciuravidae.*

One of the major problems confronting those interested in the evolution of the mammalian order Rodentia has been the origins and interrelationships, if any, of those members of the order, obviously not primitive, in which the angular process of the lower jaw has shifted laterally and originates from the side of the mandible lateral to the alveolus of the lower incisor, instead of arising from the ventral side of the alveolus, as in most members of the order. This condition, termed "hystricognathy," is normally associated with a forward expansion of the masseter muscle through the infraorbital foramen onto the snout, a condition termed "hystricomorphous." However, a number of hystricomorphous rodents are not hystricognathous, although all hitherto known hystricognathous rodents have been at least partially hystricomorphous.

At the present time, the hystricognaths are very abundant in South America (the suborder Caviomorpha) where they have been endemic since the early Oligocene, being known from the Deseado of Patagonia (*1*) and from equivalent beds of Bolivia (*2*). Some members of the suborder reached North America in late Pliocene or early Pleistocene times, the only successful immigrant having been the Canadian porcupine, *Erethizon*, now found over the entire continent as far north as Alaska and Labrador. Less abundant at the present time are the hystricognathous African rodents of the suborder Phiomorpha. These likewise appear in the early Oligocene [of Egypt (*3*)] but become highly diverse in the Miocene (*4*), and have survived to the present in considerably reduced diversity. Although phiomorphs have been largely restricted to Africa, they have recently been reported from the Miocene of the Aegean island of Chios (*5*). The African Bathyergidae, or blesmols, have been of doubtful relationships, but current work strongly suggests a phiomorph ancestry (*4*). A final group of hystricognathous rodents, the Hystricidae or Old World porcupines, are of completely unknown ancestry. Relationship to the phiomorphs has recently been postulated (*2*) and denied (*6*), in each case with no firm evidence.

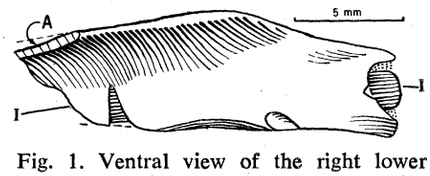

Fig. 1. Ventral view of the right lower jaw, lateral side to the top and anterior end to the right, Texas Memorial Museum No. 41372-179. *A*, angular process; *I–I*, projection of the vertical plane through the alveolus of the lower incisor.

It has been very clear from the fossil record that there has been no evidence of hystricognathous rodents in the richly fossiliferous deposits of Europe, Asia north of the Himalayas, or North America, until specialized members of the southern radiation appeared as obvious immigrants at varying but relatively recent times. Their simultaneous appearance in the early Oligocene of South America and Africa therefore raises important paleogeographic problems.

For many years, according to the standard explanation, the caviomorphs and phiomorphs were thought to have been derived from the European Eocene and Oligocene Theridomyidae, a group that was hystricomorphous but not hystricognathous. There are no great geographic problems (although there are morphologic ones) in deriving the African phiomorphs from such an ancestry, but there are obvious complications in getting the theridomyids to South America. The usual postulates vaguely proposed migration, either via Africa or direct from Europe, but the inability of all other terrestrial animals to use such a route militated against such a solution (*7*). It was therefore

suggested that the similarities between the Old and New World hystricognaths might be pure parallelism (*8*), a suggestion later formalized taxonomically (*1, 9*). Studies of the admittedly great similarities between the living Old and New World hystricognaths caused several students to question this separation (*10, 11*), doubting whether it would have been possible to achieve such similarities as a result of parallelism. Finally, the recent renewed interest in continental drift has convinced some workers that late Eocene or early Oligocene phiomorphs would have been able to cross the South Atlantic on natural rafts, since the ocean would then have been so much narrower than it is at present (*2*). However, deep-sea drilling has shown (*12*) that the late Cretaceous South Atlantic was at least 3000 km wide, and (since the ocean in the late Eocene could not, on the basis of current theory, have been narrower than it was in the late Cretaceous) it has therefore been argued (*6*) that such trans-Atlantic migration could not have occurred.

For these reasons, the discovery of a fully hystricognathous fossil rodent in the middle (or late) Eocene of Texas is of the greatest importance. This specimen (Texas Memorial Museum No. 41372-179) from about 35 km north of the Big Bend National Park, in southwestern Texas, is a well-preserved lower jaw containing the alveolus of the premolar, all three molars, and the incisor. The angular process (Fig. 1) spreads laterally from the side of the mandible and descends well lateral of the alveolus of the incisor, in a fully hystricognathous condition. It is still too early to be sure of the special affinities of this specimen, but the structure of the cheek teeth is closer to that in some members of the predominantly North American Eocene family Sciuravidae than to that in any other rodent with which it has as yet been compared. It is impossible to determine whether or not this animal was hystricomorphous (although such is fundamentally the case in all other hystricognaths), since only a portion of the lower jaw is available.

This fossil is the first specimen of a fully hystricognathous Eocene rodent on record from anywhere in the world. The middle Eocene North American paramyid rodent *Reithroparamys* and some of its relatives show very incipient stages in hystricognathy (*10, 13*), but the gap between such incipiently hystricognathous forms and the fully hystricognathous Caviomorpha and Phiomorpha is such as to have permitted legitimate doubt about the actuality of any relationship. An Eocene hystricognath in Texas, however, suggests that the postulate of a pantropical subhystricognathous population, proposed recently (*6*), may well have been correct. This specimen also strengthens the evidence for the idea, proposed by Wood (*14*), that there was a very distinct late Eocene Middle American rodent fauna, the northern limits of which barely reached across the international boundary into what is now the southern United States, in southern California, in the Tierra Vieja area of west Texas, and now in the region of the Big Bend.

I anticipate that future investigators will discover rodents of the same general type, in the later Eocene of southwest Asia, properly placed to have been ancestral to the African phiomorphs.

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Nerve Growth Factor: Stimulation of Regenerative Growth of Central Noradrenergic Neurons

Abstract. *The growth of new axonal sprouts was studied from transected, ascending noradrenergic axons into transplants of iris tissue in the caudal hypothalamus of the rat. A single intraventricular injection of nerve growth factor, given at the time of axonal damage, resulted in an increased formation and growth of new noradrenaline sprouts 7 days later. The effect seemed to be proportional to the administered dose of nerve growth factor.*

Nerve growth factor (NGF) is a potent stimulator of growth of peripheral, sympathetic and sensory neurons [for review, see (*1, 2*)]. It is most effective on developing or growing neurons. When administered in vivo NGF causes hypertrophy and hyperplasia of the ganglia as well as increased innervation of the viscera. Only sympathetic and embryonic sensory neurons are known to respond to NGF, which indicates that it has a high specificity with respect to the target cell. No effect of NGF on the central nervous system has thus far been detected (*1*).

A remarkable capacity for regenerative sprouting and growth has been demonstrated for transected axons of central monoamine neurons in the adult rat (*3–5*). Abundant sprouting developed from either mechanically or electrolytically severed preterminal axons, and this appeared primarily during the second and third week after the trauma. The sprouting fibers grew into the brain tissue surrounding the lesion, into the necrotic tissue within the lesion, into and along the walls of intracranial blood vessels, and into adjacent cranial nerves. The growth of the central catecholamine neurons was attracted and directed by transplants of peripheral tissue normally innervated by sympathetic noradrenergic nerves (*4*). Because of the similarities between central and peripheral noradrenergic neurons we have now tested the ability of NGF to stimulate this growth. The growth of regenerating central sprouts into transplants of peripheral tissue was found most suitable for this study since it allows the selective observation of newly formed nerve fibers. At 7 days after transplantation the sprouting catecholamine fibers are beginning to grow into the transplant, which made it possible to reliably detect and quantitate a stimulatory effect of NGF on the regenerative growth of central noradrenergic neurons.

Twenty-one adult female Sprague-Dawley rats (180 to 200 g) were used.