have their first fossil occurrence in the higher latitudes.

Table 2 shows the present distribution on the Atlantic continental margin and the fossil localities of species originating in the Pliocene. Sixteen of the 30 species are restricted to south of Cape Hatteras. Their first fossil records are from mid- and lower latitudes. Today seven of the species occur only north of Cape Hatteras, and their first occurrences were in mid- and higher latitudes. Seven species today occur from Florida to Newfoundland. Five of these have their first occurrence in mid- to lower latitudes. In both the Pliocene and the Pleistocene, the first recordings are from all over the world.

These data do not support the concept of a center of origin in either the higher or the lower latitudes. Our data indicate that benthic foraminifera are continuously evolving, albeit at different rates (*6*), at all latitudes all over the world. Dispersal of species is extremely rapid and worldwide within certain latitudinal limits. Their rapid dispersal makes any vicariance events insignificant (*8*).

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Technical Comments

Measurement of Brain Deoxyglucose Metabolism by NMR

Deuel *et al.* (*1*) have shown by phosphorus-31 nuclear magnetic resonance (^{31}P NMR) spectroscopy that deoxyglucose-6-phosphate (DG6P) accumulates in rat brain for at least 40 minutes after administration of an intravenous dose of deoxyglucose at 500 mg/kg and then at some time between 40 and 60 minutes begins to decline, with an apparent half-life of 120 minutes. Similar results were obtained by gas chromatography–mass spectroscopy analysis of derivatized DG6P extracted from brains of similarly treated rats. This is a rate of loss of DG6P that is greater than is commonly believed (*2*). The time course obtained by Deuel *et al.* (*1*) is, however, remarkably similar to the time course of calculated cerebral glucose utilization (LCGU) reported by Sokoloff (*3*) in 1982. The LCGU values of Sokoloff and the data of Deuel *et al.* (*1*) have been replotted in Fig. 1 after normalization to maximum values.

The agreement between the NMR curve and the data of Sokoloff is remarkably close between 40 and 120 minutes after administration of DG6P. The curves of Deuel *et al.* represent concentrations of phosphorylated deoxyglucose compounds in brain, whereas LCGU is largely determined by the ratio of the deoxyglucose metabolites to the integrated precursor-specific activity in the brain. The LCGU values are constant as long as deoxyglucose metabolites remain trapped; the fall in LCGU value after 45 minutes reflects almost entirely loss of products of deoxyglucose phosphorylation. The results of Deuel *et al.* (*1*) confirm this observation of Sokoloff and provide further evidence that glucose 6-phosphatase (G6Pase) has little if any effect in the first 45 minutes after administration of ^{14}C-labeled 2-deoxyglucose, the experimental period prescribed by the deoxyglucose method (*4*).

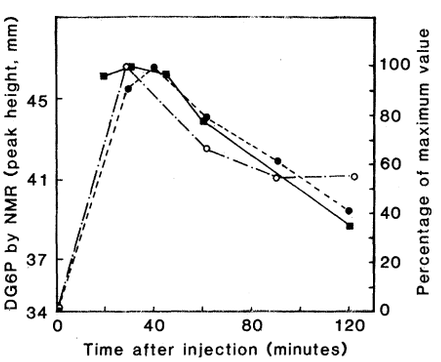

Fig. 1. Time courses of DG6P concentration (*1*) and LCGU (*2*) in rat brain after intravenous administration of deoxyglucose. Left ordinate, DG6P (NMR peak height). Right ordinate, percentage of maximum value of LCGU (■) and DG6P [gas chromatography–mass spectrometry (GC-MS)] (○) (*2*). Abscissa, portion of time course in (*1*) corresponding to same time period examined in (*2*). NMR data in (*1*), (●).

After this time the effects of G6Pase activity become apparent and develop progressively more influence on the results (*3*).

The data of Sokoloff (*3*) demonstrating that the influence of phosphatase activity is initially absent can be understood in light of the slow transport of G6P into the compartment containing the enzyme. Fishman and Karnovsky (*5*) have shown that the lag in appearance of G6Pase activity in the normal brain is due to the absence of a carrier for G6P, which delays substrate entry into the microsomal compartment where G6Pase is located.

The results of Sokoloff (*3*) demonstrate that there is no significant phosphatase activity up to 45 minutes after administration of tracer doses of deoxyglucose. The results of Deuel *et al.* (*1*) obtained with pharmacological doses of deoxyglucose are consistent with the conclusions of Sokoloff (*3*), and the demonstration of significant late G6Pase activity does not affect the validity of the deoxyglucose method for experiments concluded within 45 minutes after the administration of the tracer (*6*).

THOMAS NELSON
GIOVANNI LUCIGNANI
LOUIS SOKOLOFF
Laboratory of Cerebral Metabolism, National Institute of Mental Health, Bethesda, MD 20205

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2. Lower estimates of the half-life of DG6P in rat brain

reported by Sokoloff *et al.* (*4*) were made some 17 to 24 hours after administration of a dose of deoxyglucose at a time when the plasma level of deoxyglucose and resynthesis of DG6P should have been negligible. It was thought at that time that the only metabolite of deoxyglucose was DG6P. It is now known that some deoxyglucose is incorporated into glycogen, glycoproteins, and other compounds that are slowly turning over [T. Nelson *et al.*, *J. Neurochem.* **43**, 949 (1984)]. The half-lives observed after 17 to 24 hours probably therefore reflected the turnover of these compounds rather than DG6P.

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To augment the comments by Nelson, Lucignani, and Sokoloff, I note that ^{31}P NMR spectroscopy has allowed two radical departures from older methods of study of cerebral metabolism. First, it has allowed direct measurement of the compound itself, without inference from a label, and repetitive measurements in the same individual so that the status of cerebral 2-deoxyglucose-6-phosphate (2-dGlc-6-P) concentration could be tracked over a 4-hour time course. Second, it has allowed these observations in intact, healthy, working brains, rather than postmortem tissue. That glucose utilization as calculated from ^{14}C tracer in autoradiograms follows a time course similar to that of a 2-dGlc-6-P concentration observed by NMR thus strongly reinforces what Sokoloff and his colleagues have stated all along about the validity of the prescribed timing of the ^{14}C 2-dGlc autoradiographic method.

These observations raise further major questions about energy metabolism in the brain. The ^{31}P NMR and autoradiographic data taken together indicate dephosphorylation of 2-dGlc-6-P (it becomes ^{31}P NMR invisible over the described time course) and removal from the brain (^{14}C is negligible in autoradiograms). While hexose phosphatases are most likely involved in this removal, exactly how and under what contingencies 2-dGlc-6-P (and, more important, glucose—the brain's preferred energy-producing substrate) is dephosphorylated and shed from the cell now need to be elucidated. Perhaps there are physiological conditions (such as sleep) that enhance or retard this process, as suggested by Karnovsky (*1*). What controls glucose shedding from the brain? Because ion transport (the basis of the characteristic brain work of transmission of electrical impulses) involves cytosolic processes, at least in neurons, one thinks of a cytosolic control mechanism; yet the phosphatase described by Fishman and Karnovsky (*2*) is apparently microsomal and a poor candidate to help in any rapid cytosolic change. In summary, the recent attempts to understand the metabolism of 2-dGlc-6-P have brought questions concerning basic energy capacities of the brain into sharper focus. NMR spectroscopy, with its capacity to make direct measurements of metabolite concentrations from the brains of fully intact subjects, will undoubtedly help provide further understanding of these basic questions.

RUTHMARY K. DEUEL
Departments of Pediatrics and *Neurology* and *McDonnell Center for Study of Higher Brain Function, Washington University School of Medicine, St. Louis, MO 63178*

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