injection of drugs in sufficient concentration to cause increased intake. At lower concentrations, and only with injections near the supraoptic nucleus, drinking began between 15 and 45 minutes after injection. At the highest concentrations, administered in all areas which produced eating, animals frequently made low grunting sounds and pounded their hind legs on the floor of the cage. There is a significant increase in food intake as the amount of carbachol injected is increased, as shown by the linear component of the trend of means ($P < .01$ $F = 32.09$, $df = 1,56$); there is significantly higher food intake at the optimum dosage than at the lower or higher dosages, as shown by the quadratic component of the trend of means ($P < .01$, $F = 22.85$, $df = 1,56$). Water intake at the lower doses is significantly greater than at the higher doses, as shown by the linear component of the trend of means ($P < .01$, $F = 19.95$, $df = 1,56$). The higher-order comparisons for water intake are not significant.

Our data were obtained from animals stimulated in the lateral hypothalamus, lateral preoptic area, and the area dorsal and anterior to the medial preoptic area. These areas were not differentiable by amount eaten. Animals with increased drinking at the low doses had the stimulating cannula relatively low between the medial and lateral preoptic areas near the supraoptic nucleus. Placements where stimulation yielded no significant changes in eating or drinking were in the lateral part of the anterior hypothalamus, fornical area, and the medial preoptic area. The close proximity of cannulas yielding effects and of those yielding no effects indicates a small amount of effective spread of the injected solutions. Animals that ate more with carbachol were tested with $1536 \times 10^{-4}M$ *l*-norepinephrine, but none ate or drank significantly more. Some animals were tested with injections of hypertonic saline, but no effects were observed.

In the rabbit, the optimum dose that effects eating is 4.3 μg. The optimum dose that causes drinking in the rat is 0.43 μg (*2*). These doses are approximately 1.0 μg per kilogram of body weight for both animals. The dose-response curve for eating after injections of carbachol in the rabbit shows an inverted U function (also shown for drinking in the rat), which indicates that there is an optimum dose; concentrations above and below this optimum are less effective. Rabbits and rats exhibit other behaviors at the highest concentrations of drugs which interfere with eating and drinking.

An increase in eating would normally be accompanied by an increase in drinking. At dosages producing the greatest amount of eating, there is also a decrease in drinking (Fig. 1). This effect was not limited to stimulation in any specific area. In view of the fact that these scores are for a period of 1 hour, this result is probably not due to a lack of time available to observe increased drinking. The rabbits were usually resting or grooming for the last 15 to 30 minutes of the observation period. This decrease in drinking may be similar to the reciprocal inhibition reported by Grossman (*1*), who observed that carbachol in rats inhibits eating and that *l*-norepinephrine inhibits drinking.

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Protein Metabolism in the Developing Brain: Influence of Birth and Gestational Age

Abstract. *Incorporation of carbon-14–labeled phenylalanine into brain protein of newborn pigs falls sharply within 24 hours after birth. This decrease is related to the time of birth rather than the gestational age of the piglets, although the latter is also associated with a gradual decrease in brain protein synthesis.*

A number of studies have indicated that brain protein synthesis, as determined by incorporation of isotopically labeled amino acids into protein fractions, decreases with age in young animals (*1*). The major decrease in protein synthesis seems to occur in the first days of life (*2*). However, the information available has been unclear as to whether this decrease is due to maturational factors determined by the gestational age of the animal, or to changes associated with birth itself. This report describes experiments suggesting that factors associated with birth result in a sharp decrease in amino acid incorporation into brain protein.

Miniature pigs were utilized in all experiments (*3*). The gestational period of the pig is 114 days, with relatively little variation. The piglets were procured by hysterectomy (*4*) at different gestational ages or allowed to farrow at term. The newborn piglets were immediately placed in a Gordon-Armstrong incubator maintained at 33°C throughout the experimental period. They were allowed to feed ad libitum on an artificial sow's milk replacement formula (SPF-lac, Borden) with varying degrees of success. Several farrowed litters nursed their dam in an ordinary stall.

Tracer doses of uniformly labeled L-phenylalanine-^{14}C (specific activity 300 mc/mmole) were administered intraperitoneally to the piglets at a uniform dose of 20 mc/kg. One hour after injection, the animals were exsanguinated and the brain removed within 2 minutes. The cortical mantle was removed for preparation of trichloroacetic acid soluble (free amino acid) and insoluble (protein) fractions (*5*). Radioactivity in the fractions was determined by conventional liquid scintillation techniques (*6*).

Phenylalanine incorporation into brain protein falls off sharply after birth (Fig. 1). This occurs irrespective of gestational age, as demonstrated by the even more abrupt fall occurring when the newborn animals were delivered by hysterectomy at varying gestational ages. The decreased rate of incorporation persisted even though the naturally delivered piglets quickly established nursing habits and established weight gains by 24 to 48 hours of age. The more immature (100 to 103 days) of the hysterectomy-delivered piglets were feeble and often fed little during the postnatal period. However, many of the piglets delivered at 110 days of gestational age fed vigorously and sustained little or no weight loss during the first

24 hours. The amount of weight loss or gain did not influence the decrease of phenylalanine incorporation into brain protein occurring after birth.

In addition to the sharp postnatal fall in brain phenylalanine incorporation, a more gradual decrease was found during the first few hours of life related to the gestational age (Fig. 1). This is in agreement with previously reported data demonstrating decreases of incorporation of labeled amino acids into brain protein (*7*).

In contrast to the changes found in the protein fraction, the radioactivity in the free amino acid fraction of the brain showed an upward trend in the postnatal animals (Table 1). This ruled out the possible explanation that the postnatal reduction of labeled phenylalanine incorporation into brain protein was due to a diminished entry of the phenylalanine into the brain.

An apparent decrease of incorporation might result from dilution of the isotope if the precursor amino acid pool rapidly increased after birth. This seemed unlikely, as plasma phenylalanine levels did not rise after birth (Table 2). Furthermore, studies on free amino acid pools in rat brain have shown that free phenylalanine concentrations steadily fall after birth (*8*).

We conclude that a marked alteration in the pattern of brain protein synthesis occurs immediately after birth. Premature delivery is associated with a similar alteration, which indicates that the event of birth, rather than the gestational age of the animal, is the relevant factor. The reason for this alteration has not been identified in these experiments. It does not appear to be primarily a function of dietary factors, since naturally farrowed piglets who suckle immediately and gain weight rapidly manifest this change as clearly as hysterectomy-delivered fasting animals.

These experiments suggest that some factor present in the uterine environment promotes incorporation of amino acids into brain protein. A number of explanations might be offered to account for this effect. Protein synthesis in tissues might be maintained at a higher rate by placental delivery of amino acid and energy-supplying substrates. The newborn animal may be unable to duplicate entirely this placental function. Maternal hormones could conceivably play a role in stimulating protein synthesis that is lost subsequent to birth. Nucleic acid levels might not be maintained at prenatal levels after birth, thereby affecting tissue protein metabolism. Identification of these or other factors related to this phenomenon is a problem for further study.

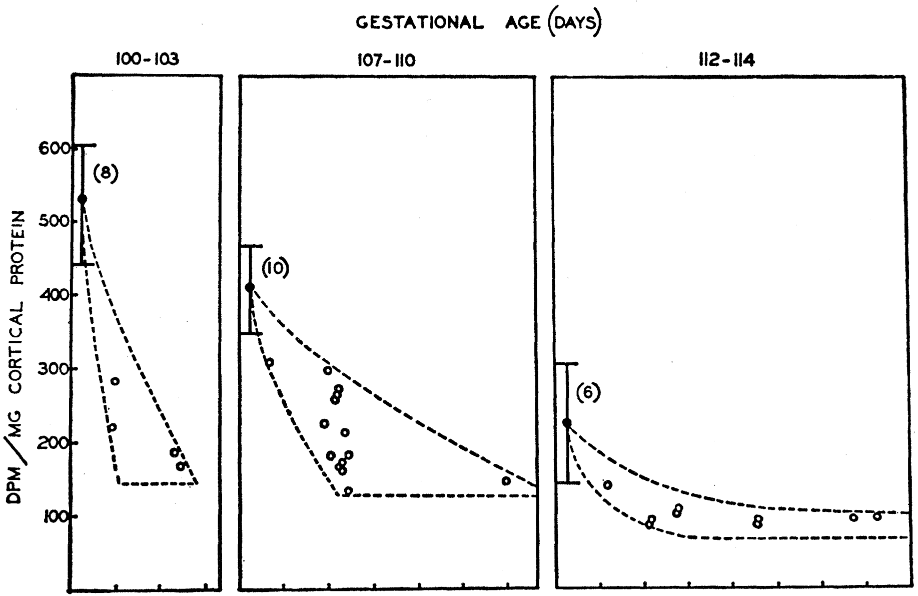

Fig. 1. Incorporation of ^{14}C-labeled phenylalanine into cortical protein fraction at different gestational and postnatal ages. The solid symbols indicate means of values from experiments performed within 6 hours after birth. Vertical lines through solid circles refer to one standard deviation. Figures in parentheses refer to the number of experiments. The open symbols indicate individual values of animals sacrificed at different postnatal ages (7 to 87 hours).

Table 1. Radioactivity in free amino acid fraction (means ± standard errors). Figures in parentheses are numbers of values. DPM, disintegrations per minute.

Postnatal age (hours)	DPM/g of tissue (wet wt.)
0 to 4	4400 ± 510 (15)
24 to 29	5340 ± 890 (16)
48 to 72	6240 ± 840 (6)

Table 2. Plasma phenylalanine values (means ± standard errors), determined according to the fluorimetric method of McCaman and Robins (*9*). Figures in parentheses are numbers of values.

Postnatal age (hours)	Plasma phenylalanine (mg/100 ml)
0 to 4	2.8 ± 0.2 (26)
24 to 28	2.8 ± .2 (26)
48 to 72	2.2 ± .4 (10)

The fall in brain protein synthesis subsequent to birth may have clinical significance in relation to premature birth in humans. Prematurely born infants are high risks for the development of a variety of syndromes associated with brain dysfunction, such as mental retardation, cerebral palsy, and organically determined learning problems. Causes for these neurological disorders appearing during the subsequent development of premature infants are rarely established. A premature decrease in brain protein synthesis during a critical period of growth of the central nervous system may be responsible for cerebral syndromes manifesting themselves at a later time.

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Visual and Auditory Information Processing in Children and Adults

Abstract. *Children of three ages were compared with adults in a recognition experiment requiring continuous processing of information. The growth in precision for visually presented words is steeper than for auditorially presented words, largely because the former are harder for the first graders and, to a lesser extent, for the third graders. In adults, visual processing of information is at least as good as auditory. The use of receiver operating characteristic curves in describing the data permit greater precision in estimating the capacity of the individual subjects and are particularly useful since the errors of failure to recognize were different from ordinary errors of false recognition, and they occurred in large numbers.*

Many facets of the educational process depend upon accurate recognition of visually and auditorially presented linguistic information. As part of an extended study of the influence of linguistic redundancy upon the learning of verbal materials, we had sought a method which could be used with adults or young children which allowed stimuli to be shown either by eye or ear. We required a method which showed the word-frequency effect (*1*) in adults and bore some resemblance to the task of reading. The usual methods of measuring verbal learning used in our pilot studies (pair associates, serial lists) were too difficult for children or did not show the frequency effect (short-term retention) (*2*). The task finally used was adapted from an experiment with numbers by Shepard and Teghtsoonian (*3*). It requires the continuous processing of sequentially presented information for recognition after filled time intervals of variable length. In this respect the task closely resembles the reading or listening process. It also requires a very simple reponse of the subject—he merely says "old" or "new" at each presentation, so all the problems of response learning and of complex decision processes are avoided.

Ninety three-letter, three-phoneme words—30 very high, 30 very low, and 30 of zero (but still possible) frequency of occurrence in English (and therefore pronounceable)—appeared twice, first as new items, then as old items. There was always a delay of 2, 4, 8, 16, or 32 intervening items of the same set. Our lists were prepared by random selection from a pool to control for idiosyncracy, and they were presented either visually (Selectroslide projector) or auditorially (stereomagnetic tape). Sixty-four subjects were used at each of the four levels: first, third, and fifth reading level, and adult, making a total of 256 subjects. All were tested individually, half (32) of each age group with visually, half (32) with auditorially presented lists.

The major findings have been reported in detail (*4*). Modality was a significant factor in language processing, suggesting that the two are not equally effective avenues for presentation of verbal information at all ages. Moreover, children make more errors than adults both in failure to recognize and in false recognition, even on words of extremely high language frequency. This observation implies that, when some aspect of memory coding for verbal materials is involved, children will be inferior to adults. Following the numerous applications of signal detection theory to human psychophysics (*5, 6*) and recognition memory (*7*), as well as other fields (*8*), we combined the two sorts of errors in a receiver operating characteristic (ROC) curve. While many of the uses and interpretations of ROC curves depend on various theoretical models (*6*), geometrical considerations of ROC plots which are based on very few assumptions (*9*) are very descriptive. A simple total error score can be misleading because two subjects, although having equal scores, may reach the score in different ways. One may make very few errors by failure to recognize (that is, call old patterns "new") and the other may make many such errors. A better picture of the subject's performance is given by the detectability index, d', which relates both the detection rate, p ("new"/new), and the "new" error rate, p ("new/old). There are two very important properties of this index. One is that if the difficulty of a task is fixed during a series of trials, it is not possible for a subject to increase his number of correct detections without also making more errors by failure to recognize. The other is that the detectability index has been shown to be relatively independent of the subject's motivation, the costs of errors, the reward for hits, the experimental conditions, instructions, and the like (*5*).

In view of the descriptive precision of ROC curves, we plotted them for the eight groups of subjects (Fig. 1), to compare the progress of visual and auditory processing of information over the age range. In the graph of Fig. 1 for grade 3, auditory, the child represented by the point lying furthest to the right has a detection rate of .78 and an error rate of .55. There are, however, nine other children represented by points to his left (lower error rates) and lying on or above the horizontal line, p ("new"/new) = .78 (that is, those having an equal or better detection rate). There is a similar (and larger) area lying below and to the right of this point which defines an inferior performance. Norman (*9*) has derived a simple graphical procedure which allows comparisions to be made among experimental conditions, with limited assumptions about the underlying processes. He shows that the unit square (the ROC domain) may be partitioned into four regions in such a way that any arbitrary performance level represented by a single point may be related to that of any other point in the region. Thus in Fig. 1, grade 1, auditory, let us take that point given by the mean value of p ("new"/new) and p ("new"/old) (solid circle) to represent the mean performance level. The pair of straight lines drawn through the point from the two corner points define four regions. The performance levels of subjects whose points lie in the re-